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un nuovo paradigma in oncologia

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Congress Proceedings

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Selected Oral Communications

B01

THE PSYCHOLOGICAL IMPACT OF COVID 19 EMERGENCY ON HEALTH PERSONNEL INVOLVED IN THE CARE OF ONCOLOGIC PATIENTS (PTS) IN A SINGLE NORTHERN ITALY - ASST: PRELIMINARY RESULTS OF AN ANONYMOUS QUESTIONNAIRE

M. Buglione di Monale e Bastia[1]*, C. Cristini[2]*, U. Gelatti[3], L. Pegurri[1], L. Triggiani[1], F. Barbera[4], P. Vitali[1], F. Terraneo[1], B. Caraffini[1], G. Facheris[1], S. Lamattina[1], N. Singh[1], A. Donofrio[1], A. Taddeo[1], E. Ranghetti[1], A. Guerini[1], L. Maruca[1], V. Santoro[5], M.A. Abrami[6]^, S.M.M. Magrini[1]^
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Aims: The COVID19 emergency involved all the person employed in oncologic departments both from personal and professional point of view. At ASST-Spedali Civili (SC), a questionnaire was submitted to all the persons involved in oncologic care to understand the psychological effect of this emergency.

Materials and methods: From April 24th through May 21st, 2020, a multiple choices questionnaire was distributed to all the health care employees (emp) serving in the SC oncological departments (Haematology, Medical and Radiation Oncology, Radiology, Nuclear Medicine, Medical Physics). The questionnaire was ideated in collaboration with Psychologists of SC and of the Brescia University. Answers were scored (p) between 1 (rarely; not at all) and 7 (frequently; surely); a scale measuring "anxiety" (SAS) was also submitted (p between 20 and 80).

Results: 370/493 (75%) emp answered (tab). 43.5% had >20y work experience; 33.3% lived with old people; 8.1% had covid19 disease with symptoms (sym), 3.5% were positive but without sym. Median points (mp) of answers regarding the COVID19 disease "fear" gradually increased from the arrival of first two cases in Italy to arrival in the hospital (mp 3.37 vs 6.26, p=0.000). The fear (6/7 p) of transmitting the infection to pts vs family was 49.4% vs 73.5%. 43% of responders think this experience can be a personal growth occasion (6/7p). 53.3% of the series did not consider heavy continuing care in oncologic pts (1/2p) and agree with the observation that these pts have to be considered different (6/7p in 57%). The empathy with human necessities of "Covidpts" was higher than "noCOVIDpts" (mp 5.64 vs 5.45, p=0.000). The collaboration with the colleagues(clg) increased more than that with superiors (mp 4.78 vs 4.06, p=0.000). 13.8% of emp had the sensation to be strongly supported in his/her work (6/7p). The future positive effect of emergency on relationships between clg mp's was higher

than with the superiors (mp 4.11 vs 3.62, p=0.000). Positive relations are considered more durable after the emergency than negative ones (mp 4.3 *vs* 3.95, p=0.002). SAS'mp was 35 (range 20-74 p, standard deviation 9.18)

Conclusion: The questionnaire has been a simple, cheap and easily administrable method of analysis to understand opinion and feelings of emp. These very preliminary results show that fear is present, but it did not influence the duty sense of most of the emp. The relationships between clg were stronger than those with superiors.

Table 1.

	n° ans/n°tot	% of the series (n°359)
medical doctors	105/128	28.4
nurses	106/139	28.6
radiation technologists	92/108	24.9
Auxiliary personel	36/82	9.7
Administrative secretary	11/16	3
Medical physicists	9/9	2.4
other	11/11	3

B02

CANCER AND COVID-19: THE IMPACT ON RADIOTHERAPY AT PIACENZA STATE HOSPITAL

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Aims: Since the end of February 2020, Italy has experienced the rapid spread of the new coronavirus (COVID-19), responsible for SARS-Cov-2, with a daily increase in the number of cases and consequent deaths. Our aim is to investigate the impact of Covid-19 on radio-treated patients in our operations unit.

Methods: We identified 119 patients who died in the period from 20 February to 31 May 2020 with active disease or previously malignancy treated with radiotherapy. Through ISTAT data we detected the number of patients who died in hospital with diagnosis of SARS-Cov-2. We also evaluated, in the same period, patients in treatment or who had made the first consultation, not deceased, suspended due to eventual infection with COVID-19.

Results: Out of 119 patients, 37 (31%) died from SARS-Cov-2. The average age was 79 years, 27 (72%) patients were 75 years old, 26 (70%) were male. 13% of patients were receiving treatment at the time of death. Most of the deceased patients (75%) were free from cancer at the time of death. The deceased patient characteristics are shown in Table 1. At the time of the analysis (31 May 2020) 11 patients postponed or suspended treatment and are still alive; only for one patient hospitalization has been necessary, the others have been assisted from home. The average age is 69 years, 7 pt out of 11 are male. The most represented cancers were prostate cancer (8 Pt) and head/neck cancer (6 Pt). Table 2.

Conclusions: The data presented are preliminary and collected on a small sample extremely heterogeneous, therefore so far insufficient to highlight an association between cancer and COVID-19. Probably in addition to cancer, advanced age and associated comorbidities played an important role in the development of often lethal complications related to COVID-19. Several clinical studies will be needed in the future to understand the real impact of COVID-19 on cancer patients.

Table 1. Characteristics of patients who died from covid-19.

N PZ DIED OF COVID-19 Reporting period 15-02-20/ 31-05-20	37
AGE (MEAN, years)	79 (41-96)
MALE	26
FEMALE	11
PREVIOUS RT	32 (since 2003-2019)
ONGOING RT	5

Table 2. Patients divided by pathology treated

	PREVIOUS RT, 32 Pt (died)	ONGOING RT, 5 Pt (died)	SUSPENDED RT, 11 Pt (alive)
BREAST	4		1
LUNG	3		
PROSTATE	7		1
H&N	5		2
NERVOUS SYSTEM			2
GASTROENTERIC	1	1	
GYNECOLOGICAL	3		3
HAEMATOLOGICAL	1	1	
SKIN (NO MELANOMA)	4		1
METASTASIS (BONE)	4	3	1

B03

ABSTRACT WITHDRAWN

B04

MOOD DISORDER IN CANCER PATIENTS UNDERGOING RADIOTHERAPY DURING THE COVID-19 OUTBREAK

A. Angrisani[1], V. Nardone[2], A. Sallustio[1], A. Reginelli[1], M. Gaetano[2], F.M. Giugliano[2], L. Di Rienzo[2], I. D'Onofrio[2], C. Ferrone[2], M. Capasso[2], A. Conte[2], M. Moniello[2], A. Cristiano[2], G. Del Gado[2], F. Lepone[2], S. Langella[2], A. Liparulo[2], C. Guida[2]

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Aims: Since the WHO declaring of novel coronavirus (COVID-19) outbreak a pandemic on 11th March, the virus has reached more than five million cases and 300.000 deaths all over the world in the mid-May. At the same time, COVID-19 is having a devastating psychological impact on patients, especially patients with cancer. This work aims to evaluate mood disorders of cancer patients undergoing radiation therapy.

Methods: We included all the patients undergoing radiation therapy at our Department in two-time points (each a week for a month in May 2019) and during the COVID-19 outbreak (in April 2020). All the patients were asked to fulfill a validated questionnaire (STAI-Y, State trait anxiety inventory scale), the Symptom Distress thermometer (SDT) (from 0 to 10 score), and the Beck Depression Inventory v.2 (BDI-2). We took into account the COVID-19 outbreak and also sex, age, week of radiation treatment, and disease. We calculated the differences in anxiety scales for the clinical variables (sex, age, disease, week of treatment, and COVID-19) with the Chi-square test (for STAI-Y and BDI-2) and with the Anova test (for SDT). Multivariate linear regression was used to test all the clinical variables.

Results: We included 458 patients (220 males and 238 females), with a median age of 64 years (mean 63,9 years, range 29-88 years), tested before COVID-19 (380 patients, 83%) and during COVID-19 outbreak (78 patients, 17%). STAI-Y median score was 40 (mean 41,3, range 19-79), 227 patients (49,6%) showed a STAI-Y <40, whereas the median score of SDT was 5 (mean 4,6, range 0-10) and BDI-2 median score was 11 (mean 13,8, range 4-53). STAI-Y, SDT and BDI-2 were significantly correlated with COVID-19 outbreak ($p<0,001$ for all the tests), sex (p: 0,016 for STAI-Y, $p<0,001$ for SDT, p:0,013 for BDI-2), week of treatment (p: 0,012 for STAU-Y and p: 0,031 for SDT) and disease (p:0,015 for STAI-Y, $p<0,001$ for SDT and p:0,020 for BDI-2).

Conclusions: The prevalence of mood disorders in patients undergoing radiation therapy is higher than expected and even higher during the COVID-19 outbreak. These measurements could be useful as a baseline to start medical humanities programs to decrease these scores.

B05

EXTREME HYPOFRACTIONATED ADJUVANT WHOLE BREAST RADIOTHERAPY DURING THE COVID-19 EMERGENCY

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Purpose: During the COVID-19 emergency international guidelines suggested the wider use of hypofractionated schedules. In the meantime, the FAST-forward trial reported the non-inferiority of a five-fraction schedule of adjuvant whole breast radiotherapy (WBRT) to the standard hypofractionated RT (15-16 fractions) for early breast cancer patients. Since March 2020 we have adopted the FAST-forward trial schemes to minimize the number of hospital visits. We report our preliminary results.

Methods and Materials: 5-fraction schedule was proposed to patients aged at least 18 years with early breast cancer or ductal carcinoma in situ (DCIS), who had received breast conserving surgery. Patients candidate to RT to the draining nodes were excluded. Sequential or concomitant boost to the tumor bed was delivered according to clinical and pathological risk factors. Acute toxicity was evaluated using the Common Terminology Criteria for Adverse Events version 5.0 and by photographs.

Results: 27 patients were treated from March 2020 to June 2020. Median age was 62 years (range 30-85). 2 patients had a DCIS and 25 an infiltrating T1 tumor. 20 patients were N0 and 5 N1. The tumor grade was G1, G2 and G3 in 8, 14 and 5 patients, respectively. Estrogen receptor (ER) and progesterone receptor (PgR) were positive in 22 patients. HER-2 receptor status was positive in only 2 patients. 6 patients were treated with adjuvant chemotherapy. The 22 receptor positive patients received endocrine therapy and the 2 HER2+ patients Trastuzumab. The RT administered total dose was 27 Gy and 26 Gy in 5 fractions to 8 and 19 patients, respectively. Of these, 5 underwent to boost on tumor bed with a total dose of 7.6 Gy in 2 fractions. The organs at risk dose constrains reported by the FAST forward trial were respected for all patients. Acute $\leq$G2 toxicity was recorded in 8 patients (erythema, oedema and epidermolysis), 2 of whom had received chemotherapy.

Conclusions: Our preliminary experience showed that the FAST-forward schedules are safe. The clinical outcomes would encourage to adopt 5-fractions in clinical practice as a valid alternative to standard hypofractionated RT in early stage breast cancer patients. On the basis of the FAST-forward results, 26 Gy are now administered in our Centre. This schedule must be taken into consideration, also for the uncertainties related to other pandemic waves.

B06

SBRT IN 3 FRACTIONS FOR T1 GLOTTIC CANCER: ACUTE TOXICITY AND EARLY FUNCTIONAL RESULTS

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Aims: To assess the feasibility and early functional activity of an ultrahypofractionated schedule for T1 glottic cancer on an initial group of patients.

Methods: This a prospective phase I-II study at a single Institution enrolling patients with T1 glottic cancer. Before treatment, all patients underwent MLS under general anesthesia to perform a NBI-guided biopsy and a simultaneous endoscopy with 0° and 70° rigid telescopes. The true vocal cords (TVC) were divided in thirds and the third(s) containing biopsy proven SCC prescribed 36 Gy in 3 fractions. The portions of the TVCs next (ant and post) to the involved portions were planned to receive 30 Gy in 3 fxs. The remaining parts of the TVCs was tentatively spared. Hard dose volume constraints (Dmax 30 Gy to 0.1 cc) were placed on the thyroid, cricoid and ipsilateral arytenoid cartilages. CTV to PTV included an anisotropic expansion of 3 (AP, LL) to 5 (CC) mm. SBRT was delivered by a LINAC-based approach using multiple (2-3) arcs (VMAT) as appropriate. Toxicity was scored by CTCAE v4.0. Acute toxicity was defined as the onset of any GR2+ acute reaction within 3 months after SBRT. Voice quality was investigated by both VHI and GRBAS at regular intervals. A generalized linear model was used to analyze longitudinal functional data. All included patients have a 6-month minimum follow up.

Results: Seventeen patients have been included in the analysis. Mean (SD) age was 66.2 (7.6) yrs. All patients but 3 were current (N=8) or past (N=6) heavy smokers. T stage was as follows: T1a: 11 pts (64.7%); T1b: 6 pts (35.3%). The mean number of involved thirds per pt was 2 (0.9). Mean PTV30 and PTV36 D95 at planning were 28.8 (1.7) Gy and 31.7 (3.3) Gy, respectively. All but 3 pts developed acute toxicity after a mean time of 8.5 (5.0) days after SBRT. The prevalence of acute toxicity at 30 days after SBRT is 70.6%. All patients recovered from acute toxicity after a mean time of 34.9 (13.6) days after SBRT. Compared to baseline (mean: 5.2/SD: 4.0), median GBRAS score worsened at 1 month after SBRT (6.8/4.2, p=0.036), returned to baseline scores at 2 months (5.5/3.6, p=0.724) and improved at 6 months (2.8/1.9, p=0.014). VHI scored showed a similar behavior with a baseline mean score of 26.5 (20.5) that improved significantly at 6 months after treatment end (15.6/13.8, p=0.001).

Conclusions: A 3-fraction SBRT schedule for T1 glottic cancer is feasible and both acute toxicity rates and early functional results are promising.

B07

ROLE OF 18F-FET/PET IN THE RELAPSE OF HIGH OR LOW GRADE GLIOMA

D. Badii[1], N. Mazzuca[2], O. Santonocito[3], S. Cassani[1], V. Mazzotti[1] R. Pratali[2], M. Della Porta[2], C. Gambacciani[3], G. Allegrini[4], A. Farnesi[4], I. Stasi[4], G. Musettini[4], L. Forte[1], M. Nocita[1], R. Odantini[1], L. Lastrucci[1]

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Aim: PET imaging with radiolabeled aminoacids allows a precise tumor extent and an evaluation of the response to treatment in high (HGG) and low grade gliomas (LGG), as well as recognaize the pseudo-progression from a real progression of disease.

Methods: We analyzed 19 patients with a median age of 61 years (range 75-37). One was studied only in pre-surgical setting, while18 patients underwent EBRT (DT 60 Gy, standard fractionation, IMRT-IGRT technique) in association with TMZ according to STUPP protocol. Of 18 patients who underwent EBRT, in 15 patients post-treatment MRI images showed a suspected recurrence of glioblastoma; 3 patients had a suspected anaplastic turning of a previous LGG. PET was performed with 18F-FET, a radiotracers with an absorption kinetics in gliomas variable according to the degree of malignancy. Two 3D tomographic acquisitions of the brain were performed early and late (40 min from injection) which allowed the generation of activity/time curves on 2 volumetric ROI (Region Of Interest), one on the dubious area of injury and one on a disease-free contralateral zone. Tomographic acquisitions were corrected with CT data. The study of the activity/time curves, expression of the different absorption kinetics of 18F-FET, allowed to classify, in relation to the peak of uptake of the radiotracers, 3 groups of patients and consequently to differentiate the degree of disease (high, medium and low). Each group is typical by characteristic curves: an early uptake peak is indicative of high-grade recurrence while a late peak is typical of a LGG.

Results: The study had determinate the real recurrence of glioma (according to WHO classification), confirmed in all cases also by the histological examination on the surgical specimen, excluding radionecrosis. Of 12 HHG patients, 5 have MGMT+, 7 MGMT-. Of the latter, 2 patients reported progressive degree compared to the first surgery (Grade III to IV) while the remaining 5 did not change their degree. 3 patients switched to II line chemotherapy.

Conclusions: 18F-FET/PET combined with conventional neuroimaging techniques (CT/MRI) in the management of patients with recurrent brain gliomas, is not only improving the diagnosis but also differentiating suspected recurrences in patients already operated or treated with RT-CT. Although the lack of definitive data, this method could have an important role in the therapeutic process of these patients, directing towards increasingly personalized treatments.

B08

A PROSPECTIVE STUDY COMPARING THE DETECTION RATE OF MULTIPARAMETRIC MR AND 3 PET/CT RADIOTRACERS FOR A PRESUMED LOCAL FAILURE AFTER PROSTATECTOMY

A. Faiella[1], M. Bottero[1,2], A. Farneti[1], L. Bertini[1], R. Sciuto[1], D. Giannarelli[1], S. Rea[1], V. Landoni[1], M. Masi[1], G. Sanguineti[1]

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Aim: To assess the detection rate of positron emission tomography/computed tomography (PC) with various tracers in patients referred for salvage radiotherapy (sRT) with a presumed local recurrence (LR) at multiparametric magnetic resonance (mpMR) after radical prostatectomy (RP).

Methods: The present prospective study was conducted at a single Institution between August 2017 and June 2020. Eligibility criteria were: undetectable PSA after RP; subsequent biochemical recurrence (2 consecutive PSA rises 0.2 ng or greater); a presumed local failure at mpMR; no distant metastases at choline-PC (ChPC); no previous history of androgen deprivation therapy. Accrued patients were offered 64Cu-PC (CuPC) and 64Cu-PSMA-PC (PPC) before sRT. No attempt was made to correct for the anatomic location of the presumed nodule at the various imaging studies. Data were analyzed in terms of detection rates (DR) and compared with the McNemar test for correlated proportions. Confidence intervals (CI) were computed with the Wilson score method without continuity correction while inter-study agreement with Cohen's kappa. Statistical significance was claimed for p values <0.05.

Results: 62 patients with 72 nodules at mpMR were accrued. The number of available diagnostics tests were 72, 71, 72 and 67 for mpMR, ChPC, CuPC and PPC, respectively. Compared to mpMR (DR=100%, 95%CI: 94.9-100%), prostatic fossa failures were detected in 27 (DR: 38.0%, 95%CI: 27.6-49.7%, p<0.001), 65 (DR: 90.3%, 95%CI: 81.3-95.2%, p=0.016) and 55 (DR: 82.1%, 95%CI: 71.3-89.4%, p<0.001) cases for ChPC, CuPC and PPC, respectively. Compared to mpMR, PC detected 7 more presumed local nodules in 7 patients, 4 at PPC and 5 at CuPC. Overall, the inter-study agreements between mpMR and ChPC, CuPC and PPC were 0.10 (95% CI: -0.08/+0.28), 0.17 (95% CI: -0.27/+0.60) and 0.17 (95%CI: -0.20/+0.53), respectively. Compared to ChPC, the distribution of detected nodules was highly different for CuPC and PPC (p<0.001 for both). Finally, between CuPC and PPC, the inter-study agreement was 0.41 (95% CI: +0.10/+0.72) and the distribution of cases was not statistically different (p=0.146).

Conclusions: Both CuPC and PPC are highly superior to ChPC though they both miss a significant number of presumed local failures compared to mpMR.

B09

REPEATED COURSES OF RADIOTHERAPY IN BREAST CANCER PATIENTS AS SALVAGE THERAPY FOR RECURRENT BRAIN METASTASES

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Aim: Brain metastases (BM) may affect up to 30% of patients with advanced breast cancer. The incidence is rising with more effective systemic agents and brain recurrence may develop despite stable extracranial disease. The aim of this study was to evaluate the impact of radiotherapy (RT) retreatments in patients with isolated brain recurrence.

Methods: A cohort of consecutive patients with breast BM treated with stereotactic fractionated RT (SFR) were retrospectively identified from institutional databases. Patients with isolated recurrent BM after a first course of RT (either WBRT or SFR) were identified. Brain progression-free survival (BPFS) and Overall Survival (OS) rates from the diagnosis of BM were calculated from the date of first radiotherapy treatment using the Kaplan-Meier method.

Results: 68 patients with 122 BM treated with SFR were included in this analysis. Median age was 62 years (35-80). Thirty patients (44.1%) received more than one radiotherapy course. 26.7% of this population was estrogen receptor positive, 50.0% was HER2 positive, and 10% was triple negative. Eighteen patients (26.5%) had received previous whole-brain radiotherapy (WBRT). Twelve patients (17.6%) received more than one SFR course (8 patients 2 courses, 5 patients 3 courses and 1 patient 4 courses) for a total of 25 new BM treated. 4/12 patients who underwent additional courses of stereotactic radiotherapy course had already received WBRT. Median BPFS after first course of RT was 7.9 months (IC 95% 10-41 months) and 7.6 months (IC 95% 1-15 months) after 2 courses. For the entire cohort of patients 1-2 year OS from the diagnosis of BM was 82.6% and 73.8 respectively. For patients who received more than one course of RT the 1-2 year OS was 85.7% and 76.2% (p=NS).

Conclusions: Patients affected by breast cancer BM may experience long survival rates even if presenting with diffuse brain disease at diagnosis. Additional courses of radiotherapy are likely to be needed and represent a reasonable treatment option.

B10

EFFICACY AND SAFETY OF MAINTENANCE IT AFTER RADICAL CHEMORADIOTHERAPY FOR UNRESECTABLE NON-SMALL CELL LUNG CANCER: AN ITALIAN MULTICENTRIC "REAL LIFE" RETROSPECTIVE STUDY ON 234 PATIENTS

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Background Pacific: Study showed an impressive clinical benefit of adding immunotherapy (IT) to radical chemo-radiotherapy (CRT) in terms of progression-free survival (PFS) and overall survival (OS) among patients with unresectable locally advanced non-small-cell lung cancer (LA-NSCLC), which was the basis for EMA-AIFA approval (sequential/concurrent CRT, PD-L1>1%).

Materials and Methods: From April 2018 to February 2020, 234 patients from 10 Italian Institutions were retrospectively evaluated. All patients had unresectable LA-NSCLC (stage IIIA-IIIC) and were treated with CRT being eligible to consolidative IT. Chemotherapy and RT regimens and type of IT were explored as well as the reasons why IT was not administered even if potentially indicated. Aim of our study was to examine diffusion,efficacy and side effects related to IT in a "real world" scenario.

Results: At a median FUP of 9 months,135 pts received concomitant CRT, while 99 pts were treated with a sequential regimen. RT dose in 165 pts was 60Gy, in 29pts 66Gy and in 39 pts (17%) lower total doses (mainly hypofractionated) were applied. After CRT,158 pts were given consolidative IT,90% of whom were treated with Durvalumab. Only 22% of patients started IT within 40 days from the end of CRT, 67% within 90 days and 11% after 90 days. 75 pts did not start IT: 24% for negative PDL-1 expression,16% for persistent CRT-related toxicities, 30% for disease progression and 30% for other causes (5pts had severe pulmonary dysfunction related to SARS-COV 2) and thus were not considered suitable for starting IT.One-year OS and PFS were 83.5%±ES3.2% and 53.2%±ES4,2%, respectively. Comparing maintenance IT versus follow up alone, IT resulted statistically significant for both PFS and OS ($p<0,0001$ and $p<0,0001$) at univariate analysis. During FUP, 63pts developed metastases, with main affected sites being bone (n=12), lung (n=18), brain (n=24) and liver. Thirty-nine pts progressed locoregionally.

Conclusions: Our real-life analysis confirmed that CRT followed by IT is an active and safe treatment with survival results comparable to prospective phase 3 registrative study (PACIFIC). However, some issues of the treatment paradigm outside the study environment, also emerged such as the interval between CRT and IT initiation, the toxicity management of concomitant treatments, appropriate use of molecular assays and the unexpectedly high number of patients progressing after CRT. Further prospective controlled trials are needed to clarify these issues.

B11

QUALITY OF LIFE IN SYMPTOMATIC BONE METASTASIS PATIENTS AFTER PALLIATIVE RADIOTHERAPY

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Background: Metastatic patients have a significant impairment of quality of life (QoL) due to several concurrent symptoms. Palliative radiotherapy (PRT) are effective methods of controlling pain and improving QoL. Despite the high prevalence of these symptoms, its reports have been limited. We report the symptom

prevalence in patients attending palliative radiotherapy for symptomatic bone metastasis and the changes in QoL scores after PRT.

Methods: Patients were asked to rate symptom distress using EORTC 15PAL and BM22 questionnaires before and after PRT. Analgesic use and pain score were used to calculate international pain response category. Complete response (CR) was defined as pain score of 0 with no increase in analgesic intake whereas Partial response (PR) was defined as pain reduction ≥2 without analgesic increase or analgesic reduction in ≥25% without increase in pain at the treated site. Descriptive statistics were used to represent changes in symptom and functional scales over time and to determine their clinical significance.

Results: 41 pts (median age 65 yrs;24 male, 17 female) self-completed the questionnaires before and on days 30 post-PRT. Prevalent tumor primary site were breast (34%) and lung (29%). 16 pts (39%) had also visceral metastasis. Baseline mean KPS was 77%; mean NRS pre-RT was 5,7 (range 2-10) vs post RT 1,46 (range 0-8). RT scheduling used was 20 Gy/5fx days (63%). Prevalent symptoms distress (15-PAL score ≥50) at first consultation were pain (41%), insomnia (36%), poor appetite (26,8%) fatigue (26,8%), constipation (24%), nausea (19%) and dyspnea (9,7%).In the general population at baseline, Global QoL mean score was 53,3, Emotional functioning mean score was 64,2, improving after treatment to 70,4 and 74,8 respectively. Instead physical functioning mean score had only a minimal improvement (53,6 *vs* 57,7). An overall response to PRT (CR+ PR) succeeded in 26 pts (56%), 16 pts has a CR (39%). Pts responders had a clinically improvement in physical functioning, mean score 61(range 93-27) and emotional functioning mean score 82 (range 100-42). In this group prevalent reported symptoms remain insomnia (52%) and constipation (43%).

Conclusion: Careful evaluation of prognosis and symptom burden is recommended in order to personalize treatments. PRT confirms its role on pain reduction and QoL improvement. Post treatment QoL evaluation can enhance capacity to highlight symptoms changes and focus clinician management of residual symptoms

B12

ASSESSMENT OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC SARCOMA: SAFETY AND EFFECTIVENESS DESPITE INTRINSIC RADIORESISTANCE

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Aims: The purpose is to assess the effectiveness and safety of Stereotactic Body Radiotherapy (SBRT) in oligometastatic sarcoma despite the theoretical intrinsic radioresistance.

Methods: We retrospective evaluated data of sarcoma patients with oligometastatic disease treated in our institution between April 2001 to March 2020. SBRT sites, Biologically Effective Dose (BED), concurrent systemic treatments, toxicity, local control (LC) rates, Disease Free Survival (DFS) and biological and clinical characteristics of primary tumor were collected.

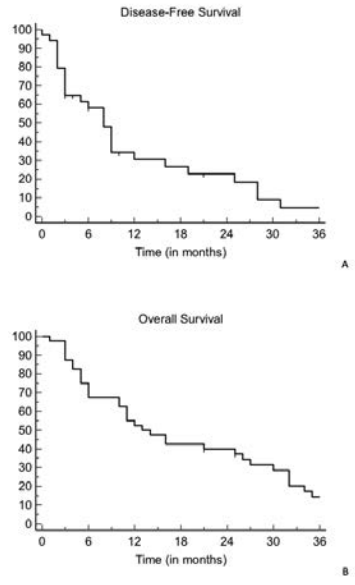

Figure 1. Kaplan-Meier plot for Disease-free survival (DFS) and Overall Survival (OS).

Results: 40 patients with oligometastatic sarcoma were treated with SBRT, accounting for 77 metastases, including 29% lung and 71% extrapulmonary metastases. In 21 (52.5%) patients, first metastatic relapse occurred within 24 months from primary tumor diagnosis; eight (23.5%) patients had metastatic disease at diagnosis. Median age was 50 years (range 18-83). Nine (26,5%) patients received concomitant chemotherapy for metastatic disease during SBRT. Median follow-up from first SBRT was 11 months (range 9-20). Median number of metastases treated per radiation course was 2 (range 1-3). Median prescribed dose was 30Gy (range 30-54) in 5 (range 3-12) fractions, and median BED was 60 Gy10 (range 48 - 105). Local control (LC) rate at 1 and 2 years was 74,0%, and 67.1%, respectively. At univariate statistical analysis extrapulmonary metastases (p=0.02), BED < 100Gy10 (p=0.001), diameter of the lesion > 3 cm (p=0.04) and age < 51 years (p=0.03) identified patients with poorer LC, although only BED < 100Gy10 (HR 3.9 CI 95 1.6-9.7 p=0.028) was confirmed at multivariate analysis. Disease-free survival (DFS) rate at 1 and 2 years was 30.4%, and 23.2%, respectively. Overall survival at 1 and 2 years was 52.1% and 40.4%, respectively. An interval between primary tumor diagnosis and first metastatic relapse >24 months was correlated to both improved DFS (HR 0.41, CI 95 0.19-0.92, p=0.032) and OS (HR 0.42 CI 95

0.23-0.97, p=0.042). No acute or chronic grade ≥3 toxicities were observed.

Conclusions: LC of SBRT was satisfying with minimal toxicity in patients with oligometastatic sarcoma. Particularly in the subgroup of patients with slowly progressive tumors, SBRT alone may lead to an extended disease-free interval and a delay of new line of chemotherapy.

B13

TMLI-BASED LOW-TOXIC CONDITIONING REGIMEN IN HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACUTE LEUKEMIA

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Aim: Hematopoietic stem cell transplantation (HSCT) is an elective post-remission treatment for patients (pts) with acute myeloid and lymphoid leukemia (AML/ALL). The best donor is the matched sibling, available for 25% of cases. The haploidentical donor is a valid alternative as it is immediately available in the family for 95% pts. In haploidentical HSCT TBI is an essential component of the conditioning regimen but, in elderly or young unfit pts, it is associated with high toxicity and non-relapse mortality rates. To reduce the HSCT-related toxicity we designed a conditioning regimen with total marrow/lymphoid irradiation (TMLI) and low chemotherapy doses. To induce a Graft versus Leukemia (GvL) effect with a low incidence of Graft versus Host Disease (GvHD) the graft contained, as adoptive immunotherapy, a ratio of conventional T cells (Tcons) and T regulatory cells (Tregs).

Methods: The conditioning regimen consisted in TMLI followed by Thiotepa (2.5 or 3.75 mg/kg per day for 2 days), Fludarabine (30 mg/m^2 per day for 5 days), Cyclophosphamide (15 mg/kg per day for 2 days).TMLI target volumes were skeletal bones, major lymph node chains and spleen. TMLI was delivered by helical Tomotherapy in 4 and half days in 2 daily fractions (total doses 13.5Gy TMI and 11.5Gy TLI). Haploidentical grafts consisted of 2 x10^6/kg Tregs, 1x10^6/kg Tcons and a "megadose" (~10x10^6/kg) of purified CD34+cells. No post-transplant immunosuppression was given.

Results: From August 2015 to March 2020, 52 pts (44 AML, 5 ALL, 3 myelodysplastic syndromes; 31 male and 21 female; median age 59 years) were enrolled. 46 received a haploidentical and 6 a matched HSCT. Table 1 shows dosimetric results. 50 pts engrafted at a median of 13 days (range 10-23) after transplantation. Acute toxicity was G1-G2 in 32 patients, G3 in 17 and G4 in 2, G5 in 1. 21 pts (40%) developed Grade II-IV acute GvHD and none moderate or severe chronic GvHD. Relapse occurred in 5 pts (3 ALL and 2 AML), 4 of which died. 14 pts died of transplant-related causes. At a median follow-up of 23.5 months (range 2-59 months) 34 pts (65%) are alive.

Conclusion: Our strategy was successful in transplantation for elderly and young unfit AML pts.TMI provides strong myeloablation and TLI provides efficient immunosuppression with low toxicity and mortality. The appropriate Tcon/Treg ratio exerted a powerful T-cell dependent GvL effect with no moderate or severe chronic GvHD. In ALL patients TBI remains the standard treatment.

Table 1. Dosimetric results.

Organ	D10 (Range)	D50 (Range)	D80 (Range)	Average (Range)
PTV bone				13.15 (10.31 – 13.83)
PTV lymph node chains and spleen				11.66 (11.25 – 13.37)
Large bowel	11.04 (1.28 – 17.27)	7.58 (5.52 – 11.22)	5.97 (4.04 – 9.38)	7.93 (6.34 – 11.73)
Lens (right)	3.85 (2.17 – 6.07)	3.31 (1.73 – 5.29)	2.9 (1.67 – 5.71)	3.3 (1.92 – 4.91)
Lens (left)	3.66 (2.09 – 6.1)	3.1 (1.78 – 5.2)	2.82 (1.67 – 5.16)	3.2 (1.85 – 5.19)
Heart	9.81 (7.52 -13.63)	5.66 (4.77 – 8.13)	4.6 (3.49 – 6.54)	6.35 (5.30 – 9.04)
Brain	12.46 (10.17 – 13.72)	8.79 (7.3 – 13.58)	6 (4.18 – 13.47)	8.87 (7.74 – 13.57)
Liver	11.62 (7.93 – 16.26)	6.84 (5.06 – 8.84)	5.5 (3.77 – 7.88)	7.72 (5.7– 10.21)
Small bowel	9.75 (8.51 – 15.36)	5.8 (4.59 – 9.75)	4.65 (3.65 – 7.92)	6.43 (5.61 – 10.59)
Lung (right)	12.3 (12.3 – 16.58)	8.69 (6.48 – 10.47)	5.64 (3.65 – 12.75)	8.7 (6.31 – 10.65)
Lung (left)	12.62 (3.08 – 16.76)	9.5 (6.94 – 11.03)	5.98 (4.32 – 7.82)	8.97 (6.35 – 10.98)
Rectum	10.91 (7.44 – 18.03)	6.97 (4.49 – 11.64)	6.03 (3.42 – 11.18)	7.75 (5.55 – 11.66)
Bladder	12.4 (9.81 – 18.68)	8.58 (5.45 – 12.93)	6.91 (3.8 – 12.03)	8.98 (6.44 – 13.37)
Kidney (right)	8.87 (6.39 – 12.66)	5.19 (3.4 – 7.91)	4.17 (3.03 – 7.17)	5.69 (4.42 – 8.85)
Kidney (left)	9.75 (7.73 – 13.34)	5.68 (3.8 – 8.22)	4.16 (3.22 – 7.33)	6.27 (5.08 – 9.3)
Stomach	10.74 (6.62 – 17.86)	8.09 (5.33 – 12.59)	6.86 (4.43 – 10.95)	8.39 (5.5 – 12.81)
Esophagus	13.37 (11.03 – 18.42)	11.67 (9.42 – 13.11)	10.02 (7.1 – 11.86)	11.4 (8.47 – 13.9)
Oral cavity	11.55 (6.93 – 13.7)	8.66 (5.12 – 12.77)	7.15 (4.17 – 11.21)	8.83 (5.59 – 12.45)
Anus	7.97 (3.53 – 17.25)	7.2 (3.06 – 16.09)	6.64 (2.92 – 12.1)	7.2 (3.14 – 14.81)
Thyroid	12.08 (10.8 – 18.57)	11.21 (9.28 – 13.52)	10.2 (7.82 – 12.74)	10.95 (7.31 – 13.94)

B14

BRACHYTHERAPY OR EXTERNAL BEAM RADIOTHERAPY AS A BOOST IN LOCALLY ADVANCED CERVICAL CANCER: A POSITION PAPER FROM THE GYNAECOLOGY STUDY GROUP IN THE ITALIAN ASSOCIATION OF RADIATION AND CLINICAL ONCOLOGY (AIRO)

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Aim: The present review critically analyzed the experience and trends in external beam radiotherapy (EBRT) use to deliver the boost in locally advanced cervical cancer (LACC), identifying whether radiation therapy modalities impacted upon outcomes, with the ultimate aim of evaluating alternatives to brachytherapy.

Methods: Three independent radiation oncologists working in different Italian Radiation Oncology Centres each conducted a literature search on boost modalities in LACC. Of the 31 selected studies, 8 dosimetric studies, evaluating target coverage and dose to organs at risk, and 10 clinical investigations, reporting clinical outcomes, were analysed in the present position paper. They have been classified according to the external beam boost technique: 3D conformal RT, CyberKnife, helical tomotherapy, volumetric arc therapy, intensity modulated RT, intensity modulated proton therapy.

Results: The present position paper showed that dosimetric studies comparing EBRT with brachytherapy achieved contradictory results, while clinical studies were limited by their retrospective nature, heterogeneous doses, fractionations, volumes and techniques, diverse follow-up times and small cohorts of patients other than a selection bias, since patients were generally not candidates for brachytherapy.

Conclusions: Evidence emerged that high-tech EBRT seemed no better than image-guided brachytherapy (IGBT) for delivering a boost in LACC. Prospective clinical studies comparing high-tech EBRT and IGBT would be attractive.

B15

IMPACT OF BIOLOGICAL FEATURES IN RADIOSURGERY FOR BRAIN METASTASES FROM NON SMALL CELL LUNG CANCER

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Purpose: Stereotactic radiosurgery (SRS) and tyrosine kinase inhibitors (TKIs) are the standard options for patients with brain metastases (BM) from non-small cell lung cancer (NSCLC) who arbor targetable mutations (EGFR and ALK). For the other patients, immunotherapy (IO) is an emerging treatment. This analysis aimed to determine the influence of mutations on oncological outcomes in patients with BMs from NSCLC, treated with SRS and TKIs or IO.

Materials and Methods: A total of 195 patients with synchronous and metachronous BMs from NSCLC treated with CyberKnife radiosurgery (CKSRS) and concomitant pre- or post-systemic therapy were analyzed. The primary endpoint was distant brain failure (DBF). Time to DBF was calculated from the start of SRS to DBF. Overall Survival (OS) was the secondary endpoint. We stratified our cohort of patients with GPA prognostic index in three prognostic categories and subsequently the impact of mutation on OS was tested for each category.

Results: Median time free from DBF for our patients cohort was 15.3 months (95% CI 11.6-20.4). No statistically significant differences were found between the mutated and not mutated patients (p-value 0.414). For the cohort of patients with the PDL-1 expression (N= 41), no statistically significant differences were found in DBF (p-value 0.371). Considering free from DBF at 12 months (Figure 1a), we observed a better trend for patients with expression of PDL-1>1%, 50.6% (95% CI 30.1-68.0), compared to patients without PDL-1 expression (<1%), 31.2% (95% CI 8.1-58.2). Median OS was 19.9 (95% CI 15.1-27.4) months; no statistical significant differences in OS were noted in patients with targetable mutations (p-value 0.110), even if there was a trend in favor of mutated patients. For patients included in prognostic GPA<2 category we obtained a statistical significative difference in OS (p-value 0.026) in favor of patients with targe-

table mutations (Figure 1b).

Conclusion: This analysis demonstrates that targetable mutations do not influence the locoregional control of the patients treated with SRS. Otherwise, potential benefits in oncological outcomes could be represented by association of SRS with immune-modulatory therapies. For patients with a worse expected prognosis (GPA<2), the presence of targetable mutations seems to improve OS. Our findings represent an encouraging hypothesis generating findings to select patients who benefit for personalized treatments.

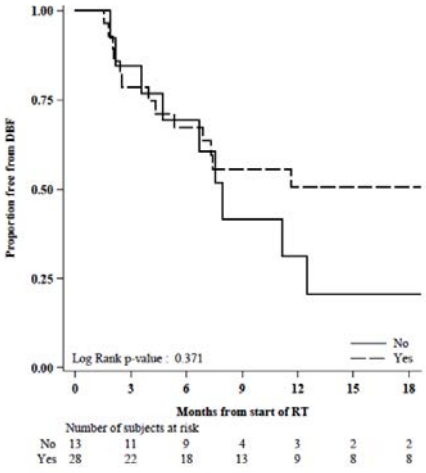

Figure 1a. Proportion free from DBF divided by PDL-1 (N=41).

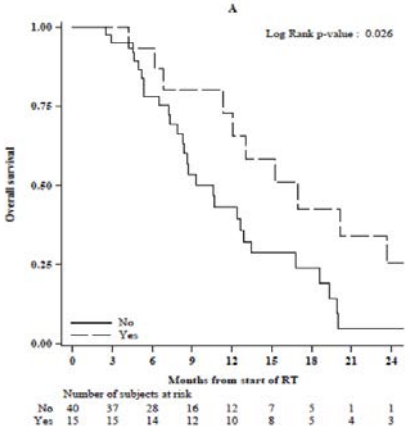

Figure 1b. Overall survival by EGFR and ALK mutations among patients with GPA≤2

B16

CLINICAL AND MOLECULAR CHARACTERISTICS OF 46 PATIENTS WITH METASTATIC THYROID CANCERS: A RETROSPECTIVE EVALUATION OF A SINGLE INSTITUTION

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Aims: Differentiated thyroid carcinoma (DTC) has usually an excellent prognosis, as only a minority of cases exhibit a poor clinical outcome. A deep knowledge of clinical, pathological and molecular features of aggressive DTC is essential to improve the diagnostic framework and lead to tailored therapy and follow-up protocols. Distant metastases (DM) occur in less than 10% of patients with DTC, but represent the most frequent cause of thyroid cancer-related death. We retrospectively studied clinical and molecular characteristics of 46 DTC patients with DM.

Methods: We analyzed 46 patients from 2007 to 2016. The selection criteria were: 1) metastatic DTC; 2) the presence of adequate frozen tissues after first surgery. Clinical outcomes and molecular aspects were analyzed. A BRAF, RAS, TP53, PTEN and PIK3CA genes and TERT promoter analysis has been assessed in all patients.

Results: Of the 46 patients, 30 presented with DM at diagnosis and 15 developed DM during follow-up. All patients underwent surgery and a first radioactive iodine (RAI) treatment with a median dose of 200 mCi. Clinical characteristics at diagnoses: median age was 61 years; clinical Stage I in none of the patients, II in 15 patients (32.6%), III in 1 (2.2%), IV in 30 (65.2%); histotype: papillary thyroid cancer in 35 (76%) and widely invasive follicular thyroid cancer in 11 (24%). Molecular characteristics: BRAFV600E mutation was found in 12 patients (26.1%); RAS in 3 (6.5%), TERT in 15 (32.6%), TP53 or PTEN in none, PIK3CA in 2 (4.3%). A second treatment was needed in 78% of patients: RAI re-treatments in the majority (25 patients), but also external beam radiation, surgery, bisphosphonate in cases with bone lesions and tirosin-kinase drugs in progressive radio refractory disease. State of disease after a median follow-up of 55 months (12-237 months) was: remission in 10 patients (22%), biochemical disease in 4 (8.7%) and structural disease in 22 (47.9%). The DTC-related deaths were 10 (21.7%). By multivariate analysis lymph node involvement, older age and, among molecular markers, TERT promoter mutations, resulted as independent factors of a worse outcome.

Conclusion: The survival of a DTC patient even with DM can be very long compared to patients with other metastatic solid tumors, thus a better knowledge of factors that can have an impact on outcome is essential. Our data show how lymph node involvement, older age and TERT promoter mutations resulted independent factors of a worse outcome.

B17

1.5T MR-GUIDED DAILY ADAPTIVE RADIOTHERAPY: PRELIMINARY CLINICAL REPORT OF THE FIRST 100 PATIENTS TREATED AT ADVANCED RADIATION ONCOLOGY DEPARTMENT (ARO) IN NEGRAR (VR, ITALY)

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Aims: 1.5T MR-linac improves target and adjacent organs-at-risk (OARs) visualization, ensuring high precision in treatment delivery. Daily MR-imaging allows on-table adapted planning and real-time intra-fraction imaging without additional exposure to radiation. This represents an extraordinary resource and a step-forward in the field of precision radiation medicine. We present the report of the first 100 patients treated at our department, implementing the first 1.5T MR-linac in the southern Europe. We aim to describe the clinical workflow, feasibility and patient-reported tolerability of daily adapted MR-guided radiotherapy.

Methods: Since 15th October 2019, Elekta Unity MR-linac is clinically available in our department. The hybrid system consists of 1.5T MR scanner with 160-leaf multi-leaf collimator (MLC) equipped 7MV FFF beam linear accelerator. Two different workflow were used depending on the OARs daily anatomical situation: Adapt To Position (ATP) workflow where the reference plan position is adjusted rigidly to match the position of the targets and OARs, and Adapt To Shape (ATS) workflow where a new plan is created to better match the anatomy of the day. Both workflows include an initial 3D MRI scan for plan adaptation, another one for verification after planning and before beam on, a real-time intra-fraction MR imaging, and a last 3D MRI scan to check intra-fraction movements and OARs deformations. Disease sites and primary histology, radiation dose prescribed and fractionation scheme as well as treatment duration, safety and tolerability were analyzed.

Results: Between October 2019 and May 2020, 100 patients with 120 target sites were treated with MR-guided radiotherapy in 676 total fractions. Median patient age was 70 years (range, 49–86). The most frequently treated regions were lower abdominal and pelvic (n=21, 17.5% and n=90, 75%, respectively). The most common diagnosis was prostate cancer (n=98). On–table plan adaptation was used at every treatment session: ATP in 52 fractions (7.7%) and ATS in 624 fractions (92.3%). Median dose was 35Gy (range, 20–67.5 Gy) in 5 fractions (range, 5–30). Mean total treatment time was 46 min (range, 20–56), whereas the median was 39 min. Treatments were well tolerated and no acute G>2 toxicities were reported.

Conclusions: MR-guided radiation treatment using 1.5T MR-linac has been successfully implemented into routine clinical use at our department. Despite being preliminary, the data here reported support an optimal profile of tolerability and feasibility of daily adaptive radiotherapy in acceptable time schedules.

B18

CLINICAL OUTCOMES AND PROGNOSTIC FACTORS IN PATIENTS AFFECTED BY LOCALIZED PROSTATE CANCER TREATED HDR BRACHYTHERAPY

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Aim: To evaluate clinical outcomes and prognostic factors in patients (pts) affected by localized prostate cancer (LPC) treated with 3D Conformal high dose rate (HDR) brachytherapy (BT) as monotherapy.

Materials and Methods: Between March 2004 and October 2017, 277 pts with (LPC) (T1c-T2cN0M0) were treated in our institute with HDR BT. The mean age was 67 years (range=47-81). Of them, 166 pts were low risk, 145 intermediate risk, and 15 high risk. Overall, 154 pts received 38 Gy in 4 fractions (2 ff/day in 2 days), 36 pts received 27 Gy in 2 fractions (1 ff/day) and 87 pts received 19 Gy in 1 fraction. The treatment plan was elaborated using CT based software to perform 3D conformal dose planning using these dosimetric constraints: Rectum D2cc <75% of prescription dose (PD); D2cc of bladder <80%PD. For the urethra: (D1%) <115%PD and D10%<110%PD. The prescription for the target was D90%>95%PD.

Results: Overall survival and cancer specific survival rates were 90% and 97% respectively. The median follow-up was 6 years (range=6-160 months) and biochemical-free disease (BFD) rate was 78%. Patients with low and intermediate risk disease had one advantage in terms of BFD compared to pts with high risk disease (p=0.04, HR=2.453). Also, in pts patients with (iPSA)<9.5 ng/ml there was one advantage in terms of BFD compared to pts with iPSA≥9.5 (p=0.022, HR=2.042, 95% CI=1.123-4.081). Moreover, pts who reached a nadir of PSA <0.2 ng/ml and had a PSA value<0.5 ng/ml 3 months after BT treatment had a benefit in terms BFD (p=0.003 and p=0.001, respectively). In the same way, pts who reached the nadir

within 12 months after BT treatment reported a statistically significant advantage in terms of biochemical recurrence (p=0.01). Patients treated with 38 Gy in 4 ff or 27 Gy in 2 ff showed a benefit in terms of BFD compared to pts treated with a total dose of 19 Gy in one fraction (p=0.0001, HR=6.813). Finally, pts with low-intermediate risk disease had an advantage in terms of OS compared to pts with high risk (p=0.034). There were not statistically significant differences regarding the analyzed risk factors and overall survival.

Conclusion: High risk disease, iPSA<9.5 ng/ml, nadir of PSA<0.2 ng/ml, PSA<0.5 ng/ml three months after BT, NADIR reached within 12 months after BT, and total prescribed doses were prognostic factors regarding bochemical recurrences. High risk disease was the only prognostic factor for overall survival.

B19

IMPACT OF METASTASES DIRECTED RADIATION THERAPY ON CDK4/6 INHIBITORS DOSE REDUCTION AND TREATMENT DISCONTINUATION FOR METASTATIC HR+/HER2- BREAST CANCER

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Aims: The aim of this study was to evaluate the impact of metastases directed radiation therapy (RT), both for palliative and radical purposes, on cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) dose reduction or discontinuation in hormonal receptors positive/human epidermal growth factor receptor 2 negative metastatic breast cancer (MBC) patients (pts).

Methods: We analyzed 85 consecutive pts treated in I (n=47) and II line (n=38) for MBC with CDK4/6i from April 2017 to September 2019 (63 Palbociclib, 22 Ribociclib) in our Radiation Oncology Unit. Overall, 25 (29.4%) patients received metastases directed RT during CDK4/6i treatment, including 14 concomitant (16.5%) and 11 sequential (12.9%). The estimated half-life for CDK4/6i is 26 and 30 hours for Palbociclib and Ribociclib, respectively. Five half-lives are required to reduce drug concentration by 95-97%; thus, we also analyzed CDK4/6i treatment as non-concomitant to RT. Main endpoints of our analysis were impact of RT on dose reduction and discontinuation of the systemic therapy, neutropenia grade ≥2 and overall adverse events rate (any grade and grade ≥2) according to CTCAE scale version 5.0.

Results: At a median follow up of 12 months (IQR 3-29), we detected a CDK4/6i dose reduction in 35 patients (41.2%) and 5 patients (5.9%) discontinued treatment due to adverse events; 82 patients (96.5%) experienced toxicity of any grade. Among these a grade ≥2 toxicity occurred in 72 patients (84.7%) and a grade ≥2 neutropenia in 70 patients (82.4%). We observed no significant differences in terms of CDK4/6i dose reduction or discontinuation, neutropenia grade ≥2, any grade or grade ≥2 toxicity, in the comparison between patients receiving RT versus no RT and between patients receiving concomitant RT versus sequential RT versus no-RT (Table 1).

Conclusions Our results showed that metastases directed RT during treatment with a CDK4/6i as I-II line for MBC did not significantly impact on dose reduction or discontinuation caused by an increase in adverse event rate. Despite these promising results, caution should be recommended.

Table 1. Comparison between patients receiving RT versus no RT and between patients receiving concomitant RT versus sequential RT versus no-RT.

Endpoint	**RT** (n=25) ***vs*** **No-RT** (n=60) P-value	**Concomitant RT** (n=14) ***vs*** **Sequential RT** (n=11) ***vs*** **No-RT** (n=60) P-value
CDK4/6i dose reduction	1.0	0.88
CDK4/6i discontinuation	1.0	0.56
Adverse events, any grade	1.0	0.47
Adverse events, grade ≥2	0.096	0.14
Neutropenia, grade ≥2	0.057	0.087

B20

A MULTICENTER LARGE RETROSPECTIVE DATABASE ON THE PERSONALIZATION OF STEREOTACTIC ABLATIVE RADIOTHERAPY FOR LUNG METASTASES FROM COLON-RECTAL CANCER: EARLY RESULTS FROM THE LAIT-SABR STUDY

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Introduction: Stereotactic ablative radiotherapy (SABR) has been shown to increase survival rates in oligometastatic disease (OMD), but local control of colorectal metastases still remains poor. We aimed to identify potential predictive factors of SBRT response through a multicenter large retrospective database and to investigate how lung SBRT can delay the progression to the polymetastatic disease (PMD).

Material and methods: The study involved 17 Italian centers, and was approved by the Ethical Committee (Prot. Negrar 2019-ZT). The early results from the first 463 lung metastases treated with SBRT in 276 patients are hereafter reported. EGFR, KRAS, NRAS and BRAF were evaluated as potential predictive biomarker for SBRT response. Lesion diameter GTV, PTV volume, site of primary tumor were also evaluated. Secondary end-point was the time to the polymetastatic conversion (ttPMC).

Results: The median follow-up was 26 months (range 3-80 months). The median lesion diameter was 13 mm (range 5-58 mm). The 2- and 3-year local progression-free survival (LPFS) were 71.8% and 70.2%, respectively. At the univariate (UV) analysis KRAS was significantly correlated with better LPFS (3-year LPFS: 85% versus 56% for mutated and wild-type KRAS; p=0.002). Moreover at the ROC curve analysis a lesion diameter threshold <20 mm significantly correlated with LPFS (p=0.00). The median ttPMC was 17 months (range 14-22 months) and the 1- and 2-year ttPMC was 59.5% and 40.4%, respectively. At the median follow-up, 66 patients were free from disease and the other progressed as sequential oligometastatic disease (SOMD) (189), and polymetastatic (21).

Conclusion: The present interim results support a local ablative treatment of lung metastases using SBRT in oligometastatic colorectal cancer patients as it might delay the transition to PMD. Mutated KRAS seems to be associated with improved control of treated metastases and can be considered as a potential predictive factor.

B21

BREAST RECONSTRUCTION AND RADIATION THERAPY: A LITERATURE REVIEW FROM THE BREAST CANCER GROUP OF THE ITALIAN ASSOCIATION FOR RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO). BASIS FOR A MULTIDISCIPLINARY EXPERT PANEL CONSENSUS

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Aims: The conservative or implant/expander reconstruction as oncoplastic approaches reserved for breast cancer patients and the optimal surgical timing before adjuvant radiation therapy (RT) is still controversial. We performed a literature review to determine the impact of breast irradiation on cosmetics results, surgical failure, and patients' quality of life. Key topics and key statements on this challenging issue were generated to perform a national expert panel consensus.

Methods: The review was conducted using MEDLINE and EMBASE database, from 2015 to 2020. The search strategy included terms related to breast reconstruction and RT. Election criteria for inclusion were: retrospective and prospective studies, full-text articles, toxicity, and/or safety reported as cosmetics outcome and English language.

Results: The oncoplastic breast-conserving reconstruction is a correction of the ipsilateral defect using volume displacement and RT could condition the cosmetics outcomes and patients' quality of life. Moreover, tissue rearrangement can alter the original position of the tumor bed making it difficult for the delimitation of the boost. The immediate breast reconstruction can be performed as "one or two-stage", or else delayed procedure after several months; both can be performed with or without nipple-skin sparing mastectomy. Overall, the risk of reintervention was 14.4%: 6.20% for poor aesthetics results and 8.2% was for breast asymmetry. Moreover, the risk of oncoplastic surgical failure in 8.5% of the case adjuvant RT related. The most frequent acute toxicities observed are infections on complicated radiodermatitis with the necessity of subsequent surgical revision in 6.7% which can provoke skin necrosis in delayed autologous flap reconstruction (2.8%). The late toxicities were implant/expander contracture in 9%, and dehiscence with implant exposition in 2.39%. The rupture expander occurred in 1.7%. 40.8% of the patients answered the Breast-Q during the surgical course and follow-up: 18.4% were satisfied, 17.7% had a positive psychologi-

cal impact, and only 4.7% had a positive impact on sexual life.

Conclusions: A low level of evidence exists and poor-quality studies preclude full consensus. A multidisciplinary approach is crucial. The adoption of breast reconstruction is rapidly increasing; tailored approaches considering both surgical techniques and RT planning and high-quality evidence studies are required. Key evidence from this challenging issue will be the basis for a national expert panel consensus.

B22

IMPACT OF DELAY OF POST-OPERATIVE RADIOTHERAPY VS TREATMENT PACKAGE TIME IN THE ADJUVANT TREATMENT OF HEAD AND NECK CANCER: ANALYSIS OF 92 CONSECUTIVE CASE

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Aims: The impact of treatment timing on clinical outcome in the context of post-operative (p-op) radiotherapy (RT) for advanced head and neck cancer (HNC) is still debated. Based on initial data it was estimated that p-op RT should ideally start within 6-8 weeks after surgery. As also unplanned breaks during p-op RT have been shown to be detrimental in terms of local control and overall survival (OS), the concept of 'treatment package time' (TPT) was later introduced, defined as the overall time elapsed from surgery to the end of p-op RT. According to most guidelines TPT should not exceed 100 days. The aim of this retrospective review is to evaluate if clinical experience at our center is consistent with literature findings.

Methods: Our analysis includes 92 consecutive patients diagnosed with HNC and treated from 2009 to 2018 with surgery and p-op RT at our center. Time from surgery to start of p-op ranged between 43 and 162 days (median 76 days) and TPT ranged between 94 and 204 days (median 120). RT technique employed was 3D planning in all cases and delivery with intensity modulation in most cases, median dose was 60 Gy (range 44 to 70 Gy). For the aims of this analysis the study population was divided in two equivalent groups according to the median value of both delay of RT start (76 days) and of TPT (120 days). OS and time to any failure (TTF) was estimated (Kaplan-Meier) and compared between the "short" (< median) and "long" (≥ median) groups. The median follow-up of all surviving pts was 46 months.

Results: At 3 years OS was 78% and TTF 71% in the whole population (N=92). Considering time from surgery to start of RT, TTF was 75% (short group) vs 68% (long group), while considering TPT, TTF was 78% vs 64% and OS 88% vs 67%. If the population was splitted into 3 groups according to TPT (<113, 114-129 and >129 days), the 2 groups with shorter interval showed similar OS rates (85-90%) vs 60% in the longer interval group. This result is maintained at 5 years with OS rates of 81-85% in the "short" groups vs 44% in the group with TPT > 129 days.

Conclusions: Our data confirm that TPT is a better prognosticator of outcome than time elapsed from surgery to start of p-op RT. However, a cutoff of 129 days is apparently adequate to predict prognosis in our population.

BA1

RADIOSENSITIZING EFFECTS OF INHIBITING HDACS BY PXD-101 (BELINOSTAT) IN IN VITRO AND *IN VIVO* MODELS OF HUMAN RHABDOMYOSARCOMA CELL LINES

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This study describes the in vitro and *in vivo* activity of PXD-101 (Belinostat), a novel hydroxamic acid-type pan-HDACs inhibitor characterized by a larger safety and efficacy, on myogenic-derived PAX3/FOXO1 fusion protein positive (RH30) or negative (RD) expressing rhabdomyosarcoma (RMS) cell lines. PXD-101 at low doses efficiently inhibited HDACs activity and counteracted the transformed phenotype of RMS by inducing growth arrest and apoptosis, affecting cancer stem cells population and inducing differentiation in RD. Notably, PXD-101 induced oxidative stress promoting DNA damages and affected the ability of RMS to assemble mitotic spindle. PXD-101 radiosensitized by inducing G2 cell cycle growth arrest, enhancing the radiation's ability to induce ROS accumulation and compromising both the ability of RMS to detoxify from ROS and to repair DNA damage. PXD-101 transcriptionally and post-transcriptionally affected c-Myc expression, key master regulator of rhabdomyosarcomagenesis and RMS radioresistance. All in vitro data were corroborated by *in vivo* experiments showing the cytostatic effects of PXD-101 when used alone and at low dose and its ability to promote the RT-induced killing of RMS. Taken together, our data confirm that altered HDACs activity plays a key role in RMS genesis and suggest PXD-101 as a valid therapeutic strategy particularly in combination with RT.

BA2

CLINICALLY RELEVANT RADIORESISTANT RHABDOMYOSARCOMA CELL LINES: FUNCTIONAL, MOLECULAR AND IMMUNE-RELATED CHARACTERIZATION

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The probability of local tumor control after radiotherapy (RT) remains still miserably poor in pediatric rhabdomyosarcoma (RMS). Thus, understanding the molecular mechanisms responsible of tumor relapse is essential to identify personalized RT-based strategies. Contrary to what has been done so far, a correct characterization of cellular radioresistance should be performed comparing radioresistant and sensitive cells with the isogenic background. Herein, we have developed clinically relevant radioresistant (RR) embryonal (RD) and alveolar (RH30) RMS cell lines by irradiating them with clinical-like hypo-fractionated schedule. RMS-RR cells were compared to parental isogenic counterpart (RMS-PR) and studied following the radiobiological concept of the "6Rs", which are repair, redistribution, repopulation, reoxygenation, intrinsic radioresistance and radio-immuno-biology. RMS-RR cell lines, characterized by a more aggressive and in vitro pro-metastatic phenotype, showed a higher ability to i) detoxify from reactive oxygen species; ii) repair DNA damage by differently activating non-homologous end joining and homologous recombination pathways; iii) counteract RT-induced G2/M cell cycle arrest; re-start to growth and repopulate after irradiation; iv) express cancer stem-like profile. Bioinformatic analyses, performed to assess the role of 41 cytokines after RT exposure and their network interactions, suggested TGF-β, MIF, CCL2, CXCL5, CXCL8 and CXCL12 as master regulators of cancer immune escape in RMS tumors. These results suggest RMS could sustain intrinsic and acquire radioresistance by different mechanisms and indicate potential targets for future combined radiosensitizing strategies.

BA3

MODULATING THE DOSE-RATE DIFFERENTLY AFFECTS THE RESPONSIVENESS OF HUMAN EPITHELIAL PROSTATE- AND MESENCHYMAL RHABDOMYOSARCOMA-CANCER CELL LINE TO RADIATION

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Purpose: Radiation therapy (RT), by using ionizing radiation (IR), destroys cancer cells inducing DNA damage. Despite several studies are continuously performed to identify the best curative dose of IR, the role of dose-rate, IR delivered per unit of time, on tumor control is still largely unknown.

Materials and Methods: Rhabdomyosarcoma (RMS) and prostate cancer (PCa) cell lines were irradiated with 2 or 10 Gy delivered at dose-rates of 1.5, 2.5, 5.5 and 10.1 Gy/min. Cell-survival rate and cell cycle distribution were evaluated by clonogenic assays and flow cytometry, respectively. The production of reactive oxygen species (ROS) was detected by cytometry. Quantitative polymerase chain reaction assessed the expression of anti-oxidant-related factors including NRF2, SODs, CAT and GPx4 and miRNAs (miR-22, -126, -210, -375, -146a, -34a). Annexin V and caspase-8, -9 and -3 activity were assessed to characterize cell death. Senescence was determined by assessing β-galactosidase (SA-β-gal) activity. Immunoblotting was performed to assess the expression/activation of: i) phosphorylated H2AX (γ-H2AX), markers of DNA double strand breaks (DSBs); ii) p19Kip1/Cip1, p21Waf1/Cip1 and p27Kip1/Cip1, senescence-related-markers; iii) p62, LC3-I and LC3-II, regulators of autophagy; iv) ATM, RAD51, DNA-PKcs, Ku70 and Ku80, mediators of DSBs repair.

Results: Low dose-rate (LDR) more efficiently induced apoptosis and senescence in RMS while high dose-rate (HDR) necrosis in PCa. This paralleled with a lower ability of LDR-RMS and HDR-PCa irradiated cells to activate DSBs repair. Modulating the dose rate did not differently affect the anti-oxidant ability of cancer cells.

Conclusion: The present results indicate that a stronger cytotoxic effect was induced by modulating the dose-rate in a cancer cell-dependent manner, this suggesting that choose the dose-rate based on the individual patient's tumor characteristics could be strategic for effective RT exposures.

BA4

ENHANCEMENT OF RADIOSENSITIVITY OF SOFT TISSUE SARCOMA (STS) CELLS BY TRABECTEDIN

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Aims: STS are aggressive tumors with a poor prognosis and limited effective therapeutic options. Trabectedin is indicated for the treatment of adult patients with advanced STS, after failure of anthracyclines and ifosfamide, or who are unsuited to receive these agents. The aim of the study is to evaluate if trabectedin could enhance the efficacy of radiotherapy by increasing cell radiosensitivity and modulating the tumor micro-environment.

Methods: Four human sarcoma cell lines: a fibrosarcoma cell line (HS 93.T), leiomyosarcoma (HS5.T), liposarcoma (SW872), and rhabdomyosarcoma cell line (RD) have been irradiated with a dose of 2,4 or 6 Gy with or without trabectedin. Clonogenic survival curves were analyzed and radiosensitization enhancement ratio at 50% survival (ER50) was calculated. Matrigel invasion assay has been performed in 4 groups of treatment: irradiation (4 Gy); 4 Gy + trabectedin; trabectedin; control. After incubation, non-invasive cells on the upper surface of matrigel were wiped off. Remaining cells were stained and the number of cell was counted. Subsequently, invasive cells were extracted and read at 595 nm.

Results: Liposarcoma and leiomyosarcoma showed a significantly reduction of surviving fraction in the combined treatment compared to radiation alone with an ER50 of 1,45 and 2,35, respectively. We observed a synergistic effect in leiomyosarcoma and liposarcoma cells ($p<0.05$ vs expected combination), whereas rhabdomyosarcoma and fibrosarcoma cell lines showed an additive effect with a reduction of clonogenic survival but without reaching statistical significance. Both leiomyosarcoma and liposarcoma showed a significant reduction of invasive cells when treated with trabectedin alone or combined treatment compared to control without treatment. Further, in those cell lines we observed a statistically significant reduction in combined treatment compared to radiation alone. Interestingly, liposarcoma showed a significant increment of invasive cells in radiation alone and combined treatment compared to trabectedin alone.

Conclusions: The addition of trabectedin to radiation induced a significant reduction of surviving fraction with a synergistic effect in leiomyosarcoma and liposarcoma. Invasive cells were significantly reduced when treated with trabectedin alone or combined with radiation compared to control. Furthermore, the combined treatment showed a significant reduction compared to radiation alone.

BA5

THE ROLE OF SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN HIGH-GRADE GLIOMAS (HGG) TREATED WITH CONCOMITANT RADIOCHEMOTHERAPY (RTCT)

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Aim: XRCC3 is a member of the RecA/Rad51-related protein family that participates in homologous recombination DNA repair (HRR), maintaining chromosome stability and participating in DNA repair. Through these activities, XRCC3 proteins play a role in resistance to RTCT in several solid tumors. With these basis, the aim of the present study was to evaluate the impact of XRCC3 -SNPs on HGG patients treated with up front RTCT

Methods: This analysis is an mono-institutional, prospective pharmacogenetic study approved by the CEAVNO, Pisa, Italy. From October 2010 to August 2019, 75 pts with proven diagnosis of HGG (7 anaplastic astrocytoma and 68 glioblastoma), IDH 1/2 wild type, ECOG PS 0-2, age>18 years were recruited. All patients were treated with post-operative RTCT and sequential chemotherapy with TMZ. All genetic evaluations were performed simultaneously by histological examination. Polymerase chain reaction amplification was performed using AmpliTaq Gold DNA polymersare. Kaplan Meier curves were performed for statistical association with genotypes

Results: In May 2020, at the data analysis, median progression-free survival (PFS) and overall survival (OS) were 11 and 18 months, respectively. A statistically significant association with PFS in univariate and multivariate COX regression analysis was found with XRCC3 rs1799794 polymorphism (p = 0.013 and p = 0.037 on univariate and multivariate analyses, respectively). The median time of PFS of XRCC3 rs1799794 AG versus AA + GG genotypes was 20 months (CI95%: 13-27 months) and 9 months (CI95%: 6-12 months), respectively. A statistically significant association with OS in univariate and a trend in multivariate COX regression analyses was found with the same polymorphism (p = 0.012 and p = 0.068 on univariate and multivariate analyses, respectively). The median time of OS of XRCC3 rs1799794 AG versus AA + GG genotypes was 27 months (CI95%: 21-33 months) and 16 months (CI95%: 12-20 months), respectively

Conclusions: The present pharmacogenetic study describes for the first time a significant association between XRCC3 rs1799794 and PFS and OS in HGG patients treated with upfront RT-CT with TMZ. We demonstrated that the XRCC3 rs1799794 AG genotype was a predictive marker for longer PFS and better OS in patients with HGG treated with RTCT. The present, pilot study may represent the stimulus to prospectively investigate the role of XRCC3 rs1799794 polymorphisms as a target for new drug therapies for GBM patients

BA6

MOLECULAR INVESTIGATION ON A TRIPLE NEGATIVE BREAST CANCER XENOGRAFT MODEL EXPOSED TO PROTON BEAMS

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Aim: The triple-negative breast cancer (TNBC) subtype is a clinical challenge for oncologists, for its aggressivity and the absence of effective therapies. Proton Therapy (PT) is a good therapeutic option both for tumors located in inaccessible area or more radioresistant forms of cancers, thus representing a promising therapeutic choice for TNBC. Our study aimed to analyze the PT *in vivo* molecular response and efficacy in a MDA-MB-231 triple-negative Breast Cancer xenograft model.

Method: TNBC xenograft models were subjected to 2, 6 and 9 Gy as single shot of PT, and the biological response analyzed 72h and 10 days post-PT. Gene expression profile (GEP) analysis was conducted by whole-genome cDNA microarray and immunohistochemical assay (ICC) were performed to highlight specific pathways and key molecules involved in cell response to the radiation.

Results: The ICC and GEP analysis showed a certain tumor radioresistance signals at the lower doses sustained by the positive modulation of cell cycle and stem cell process. Only the dose of 9 Gy showed evident effects of moving balance toward tumor cell death. In addition, a great immune response is activated by the MDA-MB-231 tumor cells in response to irradiation, confirming the role of inflammation in driving tumor resistance. Moreover, an important role is also recognized for innate immunity and macrophage cells, which were attracted within the tumor, to remove tumor dead cells and debris, a process more evident at higher doses, even in our cell models of nude mice.

Conclusions: The major efficacy offered by higher doses suggest the use of PT for the treatment of more resistant tumor forms, as a dose escalation can be easily performed using proton beams, which permit to target tumors with higher total doses and dose per fraction, while saving closed healthy tissues and organs at risks. *This study was supported by National Institute for Nuclear Physics (INFN)-LNS-funded ETHICS project and by GeSeTON project (funded by Italian MISE grant n. 489 of 21/02/2018).

BA7

BIOLOGICALLY EFFECTIVE DOSE AND STEREOTACTIC RADIOTHERAPY FOR TREATING LUNG TUMORS: PRELIMINARY RESULTS

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Aims: To observe whether biologically effective dose (BED), including the duration of radiotherapy (overall treatment time, OTT) could have an effect on overall survival (OS) and on tumor response in patients treated for lung tumors with stereotactic body radiation therapy.

Methods: Clinical data of 21 consecutive patients (with 27 lung lesions) treated using stereotactic radiation therapy in the period November 2017-January 2020 were reviewed and collected, regarding age, histology of primitive tumor (adenocarcinoma vs squamous), chemotherapy (yes/no), performance status (0, 1, 2 -ECOG), BED (BED = $n \cdot d \cdot [1 + d / (\alpha/\beta)] - [(0.639/\alpha) \cdot (T/Tpot)]$. Doses and fractions were as follows: 25 Gy in five fractions (repeated after one month), 50 Gy in five fractions, 70 Gy in ten fractions. BED values were computed taking into account the dates of start and end of radiotherapy, in terms of days of treatment, including any treatments interruptions and weekends. The Kaplan-Meier method (validated with long-rank test) was used to calculate OS rates. The Cox proportional hazard regression analysis was used to search for prognostic variables for OS, choosing the best model on the basis of the Gonen and Heller concordance probability estimate (CPE). The final model was converted graphically in a nomogram in order to predict the risk of death. The radiological response after radiation treatment was evaluated and classified as complete response (CR), partial response (PR), stable disease (SD) or progression (P).

Results: Median age of patients (3 females, 18 males) was 72 years (range 58-83). Median BED value was 47 Gy (range 22-94). Median follow up was 8 months (range 6-31). Eight-months overall survival was 50%. After restaging, 13 lesions were classified as CR, 3 lesions as PR, 3 lesions as SD and 8 lesions as P. In Cox proportional hazard regression analysis the best model included age, chemotherapy, performance status, BED. Non of these variables resulted statistically significant. The Gonen and Heller concordance probability estimate was 0.698.

Conclusions: The preliminary results of this study are encouraging, although not statistically significant in Cox regression analysis. More studies are needed to evaluate whether a "programmed" treatment interruption or other timings of fractionations could produce some benefit for patients in terms of PR or even CR.

BA8

BIOLOGICALLY EFFECTIVE DOSE AND EXTERNAL RADIOTHERAPY FOR TREATING SKIN TUMORS OF THE FACE: PRELIMINARY RESULTS

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Aims: To evaluate whether biologically effective dose (BED), including the duration of radiotherapy (overall treatment time, OTT) could have an effect on overall survival (OS) and on tumor response in patients (pts) treated for skin tumors of the face.

Methods: Clinical data of 44 consecutive pts treated using external beam radiation therapy (photons or electrons) in the period November 2014-January 2020 were reviewed and collected, regarding age, histology of primitive tumor (basocellular vs squamous), surgery (yes/no), performance status (PS) (0, 1, 2 - ECOG), site (nose vs cheek vs other sites), comorbidity (diabetes vs dementia vs other), BED (BED = $n \cdot d \cdot [1 + d / (\alpha/\beta)] - [(0.639/\alpha) \cdot (T/Tpot)]$. Doses and fractions were as follows: 44 Gy in 10 fractions, 35 Gy in 5 fractions. BED values were computed taking into account the dates of start and end of radiotherapy, in terms of days of treatment, including any treatments interruptions and weekends. The Kaplan-Meier method (validated with long-rank test) was used to calculate OS rates. A competing risk analysis (CRA) was made in order to evaluate if death was provoked by tumor or by other causes. The Cox proportional hazard regression analysis was used to search for prognostic variables for OS, choosing the best model on the basis of the Gonen and Heller concordance probability estimate (CPE). The final model was converted graphically in a nomogram in order to predict the risk of death. The clinical response after radiation treatment was evaluated and classified as complete response (CR), partial response (PR), stable disease (SD) or progression (P), analyzed by ordinal logistic regression (OLR).

Results: Median age of pts (10 females, 34 males) was 85,5 years old (range 66-98). Median BED value was 64 Gy (range 16-82). PS was 2 for 25 pts, 1 for 9 pts and 0 for 10 pts. Median follow up was 6 months (range 2-28). Median overall survival was 11 months. CRA did not result statistically significant. After clinical restaging, 36 lesions were classified as CR, 7 lesions as PR and 1 lesion as P. In Cox regression analysis the best model included age, PS and BED. None of these variables resulted statistically significant. The CPE was 0.680. OLR was not statistically significant.

Conclusions: The preliminary results of this study (in terms of CR) are encouraging, although not statistically significant. The strategy based on these doses and fractionations seems valid for aged and often unfit pts.

Oral Communications

CO001

DAILY DOSIMETRIC VARIATION BETWEEN IMAGE-GUIDED VOLUMETRIC MODULATED ARC RADIOTHERAPY AND MR-GUIDED DAILY ADAPTIVE RADIOTHERAPY FOR PROSTATE CANCER STEREOTACTIC BODY RADIOTHERAPY

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Aim: to evaluate differences between MR-guided daily-adaptive RT (MGRT) and IGRT with or without fiducial markers in prostate cancer (PCa) stereotactic body radiotherapy (SBRT) in terms of dose distribution on critical structures.

Material and methods: 200 treatment sessions in 40 patients affected by low and intermediate PCa were evaluated. The prescribed dose was 35 Gy in 5 fractions delivered on alternate days. MGRT patients (10) were daily recontoured, re-planned, and treated with IMRT technique. IGRT patients without (20) and with (10) fiducials were matched on soft tissues or fiducials and treated with VMAT technique. Respective CBCTs were retrospectively delineated and the prescribed plan was overlaid for dosimetric analysis. The daily dose for rectum, bladder, and prostate was registered.

Results: MGRT resulted in a significantly lower rate of constraints violation, especially for rectum V28Gy, rectum V32Gy, rectum V35Gy, rectum Dmax, and bladder Dmax. IGRT with fiducials reported high accuracy levels, comparable to MGRT. MGRT and IGRT with fiducials reported no significant prostate CTV underdosage, while IGRT without fiducials was associated with occasional cases of prostate CTV under dosage.

Conclusion: MR-guided daily-adaptive SBRT seems a feasible and accurate strategy for treating prostate cancer with ablative doses. IGRT with the use of fiducials provides a comparable level of accuracy and acceptable real-dose distribution over treatment fractions. Future study will provide additional data regarding the tolerability and the clinical outcome of this new technological approach.

CO002

1.5T MR-GUIDED AND DAILY ADAPTED SBRT FOR PROSTATE CANCER: PRELIMINARY REPORT ON FEASIBILITY, CLINICAL TOLERABILITY, QUALITY OF LIFE AND PATIENT-REPORTED OUTCOMES DURING TREATMENT

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Aims: 1.5T MR-Linac allows improved target and Organs-at-risk (OARs) visualization as well as daily adapted treatments. Since October 2019 Unity Elekta has become clinically available at our department and a prospective observational study is currently ongoing. We present our preliminary report on the feasibility, quality of life (QoL), and patient-reported outcomes measures (PROMs) for localized prostate cancer (PC) treated with stereotactic body radiotherapy (SBRT).

Methods: The study was approved by the ethical committee in April 2019 (Protocol MRI-Linac 23748). Inclusion criteria were WHO PS≤2, histologically proven adenocarcinoma, low-intermediate risk, no previous surgery, prostate volume <80cc, and a pre-SBRT International Prostatic Symptoms Score (IPSS) <15. The SBRT protocol consisted of a 35Gy schedule delivered in 5 fractions. SBRT was delivered with 1.5T MR-linac with a 7MV FFF accelerator using "Adapt to Shape" workflow as adaptive daily strategy. Toxicity and QoL were assessed at baseline and after treatment using the CTCAE v5.0, IPSS, ICIQ-SF, IIEF-5, and EORTC-QLQ-C30 and PR-25 questionnaires. SpaceOAR™ gel was implanted in selected cases to increase the anatomical space between the prostate and the rectal wall.

Results: At the time of the analysis, 55 patients with localized PC were recruited. The median age was 70 years (range,49-86); 28 were low risk, whereas 27 were favorable intermediate risk (IR). Median iPSA was 6.8ng/ml (range,1-19), and nine of these patients (36%) received concurrent androgen deprivation therapy. Median prostate volume was 36cc (range,20-61); median baseline IPSS was 5 (range,0-10). Median time for fraction was 42min (range,27-86). The plans of care were adapted at every session based on daily critical structure and target anatomy. No grade ≥3 acute adverse event was observed, 7 patients (13%) reported grade 2 acute genitourinary toxicity (urinary frequency, urinary tract pain and urinary retention), while only one patient reported mild rectal pain. No relevant deteriorations were reported in PROMs. SpaceOAR™ was implanted in 19 patients. PSA reduction from the pre-treatment value of the marker was documented in all patients.

Conclusions: The here reported preliminary data support that MR-guided prostate SBRT is feasible and well-tolerated in acute setting, as also confirmed by PROMs questionnaires. Moreover, the data on technical feasibility and timing of online daily adapted planning and delivery are promising. Longer follow-up is needed to assess late toxicity profile and long-term clinical outcome.

CO003

MRI-ONLY RADIOTHERAPY WORKFLOW FOR A PROSTATE CANCER PATIENT WITH BILATERAL METAL HIP PROSTHESES: A CASE STUDY

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Aims: To report a possible solution to perform prostate cancer radiotherapy in patients with bilateral metal hip prostheses.

Methods: This case concerns a 73-year-old man with high-risk acinar adenocarcinoma in both prostate lobes, with a PSA of 10.1ng/mL and a GPS of 4+4=8 (right lobe) and 3+3=6 (left lobe). The presence of bilateral metal hip prostheses created relevant CT artifacts; for this reason, the conventional CT planning procedure was not feasible. To overcome this problem, MR images with assigned Electron Densities (ED), called synthetic CT (sCT), were used for planning purposes. The MRI-only planning workflow consisted of several steps: the acquisition was performed on a 1.5T Siemens Aera MRI scanner with the patient in supine position with full bladder over a flat table, with ankles and knees supports. A large FOV 3D T1 VIBE-Dixon sequence was used (slice thickness of 1mm), which lasts less than 3 minutes. The images were contoured by an auto-segmentation software (Admire®, Elekta), based on an internal database of 20 volunteers. The sCT was then generated by assigning averaged ED to each structure to allow calculation of dose distribution; the prostheses values were taken from their data sheets. Two VMAT plans with 10MV X-rays, a complete arc and a partial one, were calculated by Monaco®, trying to avoid as much as possible the prostheses regions. The prescribed dose in 30 fractions was 72Gy for PTV1 (Prostate) and 63Gy for PTV2 (Seminal Vesicles). Finally, the feasibility of matching the daily CBCT with MR reference images was tested, after previous verification that the CBCT did not present CT-like relevant artifacts.

Results: The complete arc was selected; indeed, for the same coverage of both PTVs and a similar OARs sparing, the mean and maximum doses to both prostheses were significantly lower (<15%). The D95 were 95.0% and 99.3% for PTV1 and PTV2, with a considerable sparing of rectum and bladder, whose volumes receiving 40Gy were 33.8% and 27.1% respectively. The prostheses received a mean dose equal to 9.8Gy (max 37.6Gy) and 9.1Gy (max 29.2Gy). Finally, the match between CBCT and MR images was performed manually by the physician, who considered it acceptable in several fractions.

Conclusions: The proposed method seems to be promising for those patients who otherwise could not be

planned for a radiotherapy treatment, showing a good agreement with the conventional CT-based workflow both in terms of dosimetry and of in-room verification.

CO004

HOW TO PREDICT HEART DOSE REDUCTION IN LEFT BREAST CANCER IRRADIATION: A DOSIMETRIC COMPARISON OF DEEP-INSPIRATION BREATH-HOLD AND FREE-BREATHING TECHNIQUES IN 116 PATIENTS

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Aims: To analyze organs at risk dose reduction between deep inspiration breath-hold (DIBH) and free-breathing (FB) techniques in left breast cancer (LBC) radiotherapy (RT) and to assess a rapid and intuitive method for predicting dose reduction to cardiac structures.

Methods: 116 LBC patients received adjuvant RT and were retrospectively analyzed. Treatment plans with conformal tangential fields were generated on both DIBH and FB computed tomography scans and patients were monitored by the Varian RPM respiratory gating system. Dose prescriptions were 50 Gy/25 fractions (conventional schedule) or 40.05 Gy/15 fractions (hypofractionated schedule), with or without sequential boost. For the comparison we considered: the mean dose to the heart and to the left anterior descending coronary artery (LADCA), the volume receiving 20 Gy and 30 Gy for the ipsilateral lung, the maximum dose for LADCA and heart. The maximum heart distance (MHD), defined as the maximum distance between the anterior cardiac contour and the posterior tangential field edges, was measured and correlated with cardiac mean dose difference between FB and DIBH techniques using a linear regression model.

Results: A statistically significant reduction of cardiac and pulmonary doses using DIBH technique was achieved compared to FB plans, maintaining an equal coverage of clinical target volume (CTV). Based on the previous results obtained, now confirmed by a larger sample size, we are able to provide new interesting correlations between the tangent fields distance (TFD), the CTV and the percentage of reduction of MHD in FB compared with DIBH. We found a positive correlation between CTV and TFD: increasing the CTV requires generally a greater TFD. In particular, starting from a breast volume of 650 cc we recorded a MHD reduction constantly > 25%, as well as starting from a TFD greater than 22.5 cm we found a MHD reduction systematically > 35%. This resulted in a decrease in the mean dose to heart and consequently to LADCA, as further confirmed by the positive linear correlation found between MHD in FB and the mean heart dose difference ($r^2 = 0.73$): 73% of mean heart dose difference is explained by MHD.

Conclusions: Our study confirms the DIBH technique advantage in reducing cardiac and pulmonary doses for LBC patients. Moreover, through easily detectable anatomical parameters, it is possible to assume a priori which patients benefit most from DIBH technique to achieve a significantly less cardiac toxicity.

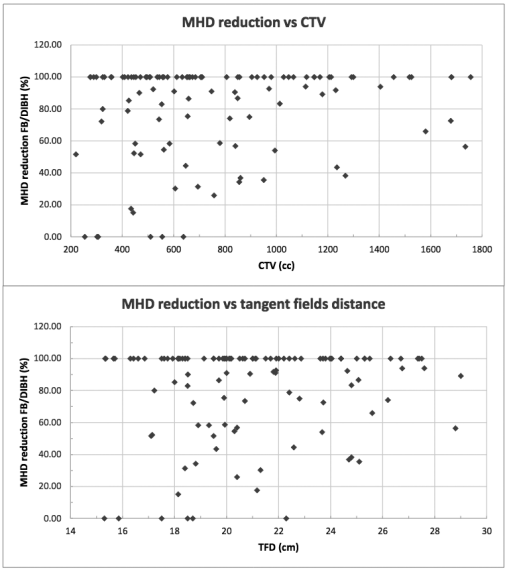

Figure 1. Tangent fields distance (TFD) and clinical tumor volume (CTV) are predictor parameters for maximum heart distance (MHD) reductionin free-breathing (FB) versus deep inspiration breath hold (DIBH).

CO005

PREDICTIVE MODELS BASED ON RADIOMICS AND MACHINE LEARNING DATA ANALYSIS IN PATIENTS WITH NSCLC TREATED WITH SBRT BY MEANS TOMOTHERAPY

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Aims: The use of biomedical images in the workflow of radiotherapy is a well-established practice. Modern diagnostic techniques offer much more than simple anatomical representations. From them, it is possible to extract a considerable amount of numerical data which escape the pure observation. Radiomics is the articulated process of extraction and analysis of quantitative imaging features, which thanks to the machine

learning and deep learning approaches can be used to build predictive models that integrate biological and clinical data, and can represent a tool to support medical decisions, improve diagnosis, prognosis, and predictive accuracy. We explored the predictive power of radiomic features extracted from radiotherapy pre-treatment image, to predicting tumor histology, tumor stage, and survival time of patients with non-small cell lung cancer (NSCLC) candidates to stereotactic body radiation therapy with Tomotherapy hi-ART.

Methods: For this task, we considered a subset of 130 subjects from the public NSCLC Lung1 Maastro database as a training-set and a set of 47 subjects (L-RT), treated with SBRT, that we used as a test-set, collected in collaboration with ARNAS Civico Palermo, University of Palermo and INFN. 3dSlicer and pyradiomics are used to extract 107 features for each patient. Matlab and python scripts were developed to test and validate the predictive model. The model's predictive performance was measured using the area method under the ROC curve (AUC).

Results: The best performances, expressed in terms of area under the ROC curve (AUC), in the histological classification of NSCLC were obtained considering the Random Forest classifier: AUC = 0.72 ± 0.11 limiting the analysis to stage I tumors and II. The results achieved in the overall stage classification are considerably above the random guess. In particular, the best performances are obtained by considering the SVM with linear kernel classifiers (AUC = 0.84 ± 0.03). Concerning the survival time prediction, fairly satisfactory performances, expressed in terms of the mean absolute error (MAE), were obtained only in the training phase with the Random Forest Regressor (MAE = 5.0 ± 0.3 months).

Conclusion: This result is difficult to generalize for invisible test data. Therefore, to allow for more accurate and reliable performance, a longer follow-up and expansion of training and test data samples are foreseen.

CO006

THE APPLICATION OF THE LEAN THINKING IN A RADIOTHERAPY DEPARTMENT: "WHO KNOWS WHO KNOS" PROJECT

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Aims: Lean Thinking (LT) is an operational strategy frequently applied in healthcare area in order to increase efficiency and eliminate waste. Between June and October 2019 at our Department a project ("Who knows who knows") relating of spatial arrangement of devices for simulation step was implemented.

Methods: In our Department positioning devices for simulation were placed randomly without criterion and mixed to discarded material in different locations, inside and outside TC room, in both 0 floor and -1 floor. Starting in June 2019 over a period of one month using "red tags" method we monitored frequency of use of different devices. We used "spaghetti chart" diagram to display operator's flow in searching for devices. Starting from CT room we calculated number of steps and time needed to reach devices stored in different locations (CT room itself, containers on -1 and 0 floors). We performed a root causes analysis, using the "5 why" method, examining critical issues in organization of devices and we proposed corrective actions for each of them.

Results: We found that many devices were no longer in use, so we eliminated them. All room of storage, except the TC room, were emptied and destined for something else. Routinely used devices, divided by type and identified by a color code for immediate visual retrieval, were placed in TC room. At last, the stock devices were placed inside the cabinet located on floor -1, at 20 steps from the TC room. Before implementing LT, starting from the CT room, we calculated the number of steps needed to reach the devices differently positioned, that were between 10-160/patient (corresponding to 15"-5'). Moreover the time wasted in searching devices ranged between 3-10'. At the end of our project we measured a reduction in the steps needed to find devices: no more than 20, corresponding to 30". Wasted time in searching devices was reduced on average to 3-5'.

Conclusion: For each patient there was a slot of 30 minutes to perform simulation. Before implementing our project the average wasted time to search for devices was 3-15', reducing the time remaining to perform simulation. After implementing it, the wasted time was reduced to 3-5', increasing the time dedicated to patient. In our opinion LT applied in a Radiotherapy Department can actually reduce wasted time by improving efficiency and potentially patient and operators' satisfaction.

CO007

CLINICAL KICK-OFF OF RAYPILOT• HYPOCATH• REAL TIME TRACKING: A NOVEL ELECTROMAGNETIC NON-DEVICE WITHOUT SURGICAL INTERVENTION TO EVALUATE THE INTRAFRACTION MOTION DURING EXTREME HYPOFRACTIONATION OF LOCALIZED PROSTATE CANCER SBRT

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Aims: Extreme hypofractionation requires tight

CTV to PTV margins, high dose gradients and strict adherence to planning criteria in terms of patient positioning and preparation regime. Precise target definition and intra-fraction motion awareness are mandatory. RayPilot® system with RayPilot® HypoCath® was implemented, which is an electromagnetic (EM) tracking device for prostate and urethra localization and monitoring during prostate cancer SBRT. The aim of this case study was to assess this strategy feasibility in the very first patient worldwide.

Methods: A patient with high-risk localized prostate cancer underwent hypofractionated SBRT treatment of 40 Gy in 5 fractions (BED1.5= 253 Gy). The EM tracking device consisted in an integrated Foley catheter with a transmitter in a dedicated lumen, which was placed before the CT simulation and removed after the last treatment fraction. Its positioning was guaranteed by a balloon inflated with sterile water anchored to the bladder wall. Preparation reproducibility was obtained by a rectal micro-enema and a 100 cc bladder filling. The VMAT treatment consisted in two 6FFF full arcs optimized to have the prescription to the mean dose of the PTV (2 mm isotropic expansion of the CTV). After the daily CBCT, the system monitored the transmitter position and the beam delivery was interrupted whenever the displacement exceeded 2 mm. In the case of a prolonged drift outside this tolerance, a new CBCT was acquired and matched to correct for prostate motion.

Results: CTV and PTV volumes were 70.4 and 95.6 cm3 respectively. All the predefined planning objectives were fulfilled. Total treatment time lasted on average 15 minutes, 12 minutes for setup and 3 minutes for beam delivery. On average, one CBCT was acquired prior each arc delivery. The transmitter shifts for every fraction are reported in the table 1: lateral shifts were always less than 1 mm, while longitudinal and vertical shifts were up to 4.1 and 2.8 mm respectively across all fractions.

Conclusions: The EM tracking system provided a real time non-ionizing organ localization, allowing to fulfill strict planning criteria and to keep the average target motion within 2 mm during the beam delivery. The procedure resulted well tolerated and less invasive than the surgically implanted RF transmitter. The final catheter removal allows an MRI artifact-free follow-up. Further fine-tuning of the workflow procedure on a larger scale may result in an improved accuracy.

CO008

INCIDENT REPORTING: AN EFFECTIVE METHOD TO REDUCE ERRORS IN RADIATION THERAPY

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Abstract Background and purpose: The potential for adverse errors in radiotherapy is real and should be studied because radiotherapy is a highly complex, multistep process which requires input from numerous individuals from a variety of different areas during both the planning stage and the delivery of treatment. The 'Incident' (I) is a consequences of which are not negligible from the point of view of protection or safety. A 'near miss' (NM) is defined as a potentially significant but did not occur. The purpose of this work is to show that through the reporting and analysis of adverse events (E) can be reduced.

Materials and methods: Staff were invited to highlight every type of E, and to provide a full description of it. A reporting worksheet was developed in 2001 to collect the errors discovered in our centre.

Results: By 2018, 110 worksheets had been collected, with an average of 6.1 E per year (with 780 patients treated per year, meaning an average incident rate of 0.78%). In 2001–2009, 37 E occurred (13 I and 24 NM) the majority E in the prescription phase (12/37), while in 2010–2013, 42 E (1 I and 41 NM) in both the dose-calculation and transfer phase (19/42). In 2014–2018, 31 E (1 I and 30 NM) the events were equally distributed across the phases of the radiotherapy process.

Conclusion: The complexity of the radiotherapy workflow is prone to errors, and this must be taken into account. Incident reporting is a very useful technique for reduced the errors through the modification of each single procedure, analysis of each errors and discussion after each event.

CO009

INTENSIVE NEOADJUVANT CHEMORADIATION PROTOCOL FOR LOCALLY ADVANCED ESOPHAGEAL CANCER: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Neoadjuvant chemoradiotherapy (NCRT) has been shown to increase survival in patients with locally advanced esophageal cancer (EC) compared to surgery alone. A single intensive protocol of NCRT (NP) was previously tested in phase I and II trials at our Center, resulting in encouraging results, thus becoming our standard in trimodality approach. The aim of this analysis was to retrospectively evaluate the efficacy and safety of this NP in the daily clinical practice and "real life" patients.

Materials/Methods: Data of EC patients treated at our Center from January 2008 to December 2017 were prospectively collected. The NP schedule consists of an induction phase of weekly administered docetaxel, cisplatin, and 5-fluorouracil (TCF) for 3 weeks, followed by a concomitant phase of weekly TCF for 5 weeks

concurrent with radiotherapy (50-50.4 Gy in 25-28 fractions). Primary endpoints were overall survival (OS), event-free survival (EFS) and pathological complete response (pCR or ypT0N0). Secondary endpoint was toxicity.

Results: 122 consecutive patients were included in the analysis, 55 (45.1%) squamous cell carcinoma (SCC) and 67 (54.9%) adenocarcinoma (AC). The estimated median follow-up time was 62.1 months (95% CI 50-67.6 months). The median OS and EFS were 78.5 months (95% CI 42.3-not reached) and 39.5 months (95% CI 27.8-82.6), respectively. The 3-/5-years OS rates were 64.2% (95% CI 54.7-72.2)/54.8% (95% CI 44.7-63.9), and the corresponding EFS rates were 51.1% (95% CI 41.8-59.6)/42.7% (95% CI 33.1-51.9), respectively. After NP, 107 (87.7%) patients underwent surgery, 105 of them (98.1%) achieved a radical resection (R0) and 55 (51.4%) a pCR, including 71.1% of SCC patients and 37.1% of AC patients (p=0.001). At multivariate analysis pCR was a strong predictor of OS (median: 117 vs 30.6 months, HR 0.30, 95% CI 0.16-0.56, p<0.0001) and EFS (median: 117 vs 24.2 months, HR 0.35, 95% CI 0.2-0.61, p<0.0001). A grade ≥ 3 hematological toxicity occurred in 32 (26.9%) patients and non-hematological toxicity in 23 (19.3%) patients. A potentially treatment-related death occurred in 4 (3.4%) patients.

Conclusions: This retrospective study suggests that this intensive NP was able to achieve a high pCR rate and considerable long-term survival also in "real life" patients. Further research is necessary to evaluate whether surgery on demand is feasible in selected patients, such as complete responders with SCC.

Table 1. Univariate and Multivariate Hazard Ratios and 95% CIs of factor associated with overall survival (OS) in resected patients (n = 107) after intensive protocol of NCRT. ns: non significant.

OS		Univariable Analysis		Multivariable Analysis	
Variable		HR (95% CI)	*p value*	HR (95% CI)	*p value*
Age	< 60	1			
	60-69	0.91 (0.50-1.65)	*0.7582*		
	≥ 70	0.73 (0.35-1.53)	*0.4066*		
Gender	Male	1		1	
	Female	0.44 (0.24-0.83)	***0.01***	0.33 (0.15-0.75)	***0.0076***
Histology	SCC	1			
	AC	1.72 (0.99-2.99)	*0.05*		
pCR	No	1		1	
	Yes	0.30 (0.16-0.56)	***<0.0001***	3.06 (1.62-5.80)	***<0.0001***
TRG	1	1			
	2-4	2.71 (1.29-5.67)	***0.008***		*ns*

CO010

ARISE: ADEQUACY OF PHARMACOLOGICAL TREATMENT OF PAIN IN RADIOTHERAPY DEPARTMENTS: PRELIMINARY RESULTS OF THE ARISE STUDY

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Aim: Inadequate treatment of pain is frequent in neoplastic patientsFurthermore, studies on adequacy of analgesic treatment during Radiotherapy (RT) are lackingThis is an ongoing multicentric observational prospective trial to evaluate the adequacy of analgesics prescriptions in RT Departments (Dept), using the Pain Management Index (PMI)In this preliminary analysis we evaluated the correlation of PMI with intensity of pain and potential predictive factors.

Methods: 2000 patients (pts) will be enrolled in RT Dept and data on gender, age, presence/absence of pain, intensity of pain (measured with Numeric Rating Scale-NRS and pain score), type of pain (cancer pain-CP, non-cancer pain-NCP, mixed pain-MP), prescribed analgesics (analgesic score), aim of RT treatment, ECOG Performance Status (PS) will be collected. Pain scores will be assigned as values between 0 (no pain; NRS: 0) and 3 (severe pain; NRS: 7-10). Analgesic score includes values between 0 and 3, no pain medication and "strong" opioids, respectively. PMI is calculated by subtracting the pain score from the analgesic score. A negative value of PMI indicates an inadequate analgesic prescription.

Results: Table 1 shows the characteristics of the first 1525 pts enrolled in 13 Italian RT Dept. Of these, 70.9% (1082 pts) had pain: in 49% cases it was CP, 33.8% was NCP, 17.2% was MP. PMI was < 0 in 47% and ≥ 0 in 53% of pts. MP is related to higher NRS than CP e NCP (p <0.001). NCP is related to lower analgesic

score values (48.2% of these pts had analgesic score = 0) than CP and MP (p <0.001). Pts with CP and MP had more adequate analgesics prescription than NCP pts (p <0.001). Higher NRS values were related to worse PS in all pts with CP (p <0.001). At univariate analysis, a worse adequacy of analgesic prescription (PMI <0) was more frequent in women (p <0.001), pts without metastatic disease (p <0.001), and pts receiving curative RT treatment (p <0.001). Higher pain intensity measured with NRS was more frequent in pts with metastatic disease (p <0.001), pts receiving palliative RT treatment (p <0.001), and pts with poor PS (p <0.001).

Conclusions: these results suggest that a negative PMI is not related to a higher pain score but rather to an inadequate management of pain by physician. Radiation Oncologists approach, when prescribing analgesics, should not be negatively influenced by the more favourable pts characteristics. However, it's remarkable that the pain management in critical pts is accurate.

Table 1. Patients characteristics.

		N (%)
Patients		1525 (100.0)
Gender	M	679 (44.5)
	F	846 (55.5)
Age	≤ 70	978 (64.1)
	71 – 80	414 (27.1)
	> 80	133 (8.7)
Aim of RT treatment	Curative	948 (62.2)
	Palliative	577 (37.8)
ECOG-PS	0	326 (21.4)
	1	754 (49.4)
	2	271 (17.8)
	3	146 (9.6)
	4	28 (1.8)
Tumor stage	Non metastatic	886 (58.1)
	Metastatic	639 (41.9)
NRS	0	493 (32.3)
	1 – 4	441 (29.0)
	5 – 6	382 (25.0)
	7 – 10	209 (13.7)
		N (%)
Patients with pain		1082 (100.0)
Type of pain	Cancer Pain-CP	530 (49.0)
	Non Cancer Pain-NCP	367 (33.8)
	Mixed Pain-MP	186 (17.2)
PMI	< 0	508 (47.0)
	≥ 0	574 (53.0)

CO011

RADIATION AS BRIDGE THERAPY BEFORE CAR-T CELL THERAPY IN RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL AND PRIMARY MEDIASTINAL B-CELL LYMPHOMAS. PRELIMINARY EXPERIENCE AT FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI (INT) IN MILAN

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Aims: Relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal B-cell lymphoma (PMBCL) have poor outcomesChimeric antigen receptor (CAR) T-cell therapy, a novel immunotherapy, has demonstrated efficacy in this setting of patients (pts) achieving durable remission and long term overall survivalCAR-T cell preparation requires a period of [3]0-[4]0 daysDuring this interval disease could progress and pts performance status declineSome preliminary experiences showed that radiotherapy (RT) plays a useful role as bridge therapy before CAR-T infusion to treat rapidly growing or symptomatic diseaseWe retrospectively evaluated the role of bridge RT in pts treated at INT Milano.

Methods: Since April 2019 and May 2020, 29 pts (17 DLBCL, 12 PMBCL) were treated with CAR-T cells [17 Axicabtagene Ciloleucel (axi-cel), 12 Tisagenlecleucel (tisa-cel)]; 11 (7 DLBCL, 4 PMBCL) received bridge RT.

Results: Clinical characteristics were: age 20-55 years (median 34); 100% refractory to previous lines (2-7, median 3) of therapy; 2/11 relapsed post ASCT. To avoid potential harm to T-lymphocyte collection, RT started after leukapheresis with a median interval of 15 days. At first a conventionally approach was used: 2 pts were treated with 36 Gy/ 20 fractions (fr); 2 were reirradiated with 20 Gy/10fr and 8 Gy/2fr according to the dose previously received. Afterwards, hypofractionation was used to further reduce overall treatment time: 2 received 24 Gy/12fr and 5 20 Gy/5fr. Intensity modulated arc-RT was used in 10/11 treatments. 2 pts received concomitant chemotherapy for a better disease control. RT toxicities were mild. Erythema and esophagitis were the most frequent side effects. No meaningful impairments of blood cells count were observed. All pts achieved CAR-T infusion and RT did not delay therapeutic plan. Median interval between end of RT and CAR-T infusion was 22 days (range 6-68). 6 pts received axi-cel, 5 tisa-cel. 9/11 pts experienced cytokine release syndrome(CRS): G1 3pts, G2 4pts, G3 2 pts. All pts recovered from CRS. No neurologic toxicities (ICANS) were observed. CRS and ICANS were superimposable to not irradiated pts. At a

median follow-up of 4 months, 6/11 (55%) achieved a response (CR+PR) with no evidence of disease in all irradiated sites and OS was 80%.

Conclusions: This preliminary experience showed that bridge RT might be a safe and effective therapeutic option to clinically stabilize pts waiting to receive CAR-T infusion.

CO012

ADDING RADIOTHERAPY TO A TREATMENT WITH IMMUNE-CHECKPOINT INHIBITORS CAN INCREASE OVERALL SURVIVAL? A META-ANALYSIS OF PUBLISHED STUDIES

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Background: Combination of radiotherapy with immune-checkpoint inhibitors (ICI-RT) seems very interesting biologically and can emerge as a new treatment in a variety of solid tumors. However, little is known about the magnitude of benefits and potential clinical predictors.

Objective: To assess the effects of this combination on the increase of overall survival.

Data Sources: Computerized bibliographic searches of MEDLINE and CANCERLIT (1970–2019) were supplemented with hand searches of reference lists.

Study selection: Studies were included if they were comparative studies between combination ICI-RT and immune-checkpoint inhibitors (ICI). Overall survival (OS) was analysed according to treatment strategy. In 6 studies, 522 and 3873 patients were treated with association of ICI-RT and ICI alone, respectively.

Data extraction: Data on population, intervention, and outcomes were extracted from each study, in accordance with the intention to treat method, by two independent observers, and combined using the DerSimonian method and Laird method.

Results: Association ICI-RT compared to ICI alone significantly increases the 1-year (OR 0.36; 95%CI 0.18-0.70, p=0.003) and 3-year overall survival (OR 0.70; 95%CI 0.56-0.88, p=0.003).

Conclusions: In patients with solid cancer, combination ICI-RT increases 1 and 3 year overall survival compared to ICI alone.

CO013

LOCALLY ADVANCED, UNRESECTABLE, PANCREATIC CANCER ADENOCARCINOMA TYPE. A "TOTAL" THERAPEUTIC NO-SURGICAL APPROACH

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Aims: To evaluate efficacy, toxicities, progression-free survival (PFS), and overall survival (OS) in locally advanced, unresectable, adenocarcinoma pancreatic cancer treated with a "total" therapeutic non-surgical approach. The novel course provided the induction systemic therapy before concomitant radiation therapy (RT) and chemotherapy (Phase 1), followed by stereotactic body radiotherapy boost (SBRT) – (Phase 2).

Methods: From May 2016 to June 2020 we retrospectively analyzed all patients with a diagnosis of clinical-stage III pancreatic cancer, treated with RT in our center. Among these, we evaluated the records of patients submitted to dose escalation radiation therapy with the SBRT boost.

Results: In the period of observation, twelve unresectable pancreatic cancer patients, with histological diagnosis of pancreatic adenocarcinoma, were submitted to external beam irradiation. At the time of primary diagnosis, all patients were staged cT4, cN0/1, cM0. During Phase 1, all patients received induction chemotherapy (7/12 GEM+ABRAXANE; 5/12 GEM) followed by external beam radiotherapy (V-MAT 4 patients; IMRT 8 patients). We delivered a median total dose of 50.6 Gy (range 48-51.25 Gy). Three patients had an early progressive disease with liver metastases. One patient interrupted the treatment for uncontrolled diabetes mellitus with cardiovascular complications at the dose 48Gy. One patient had surgery for down-staging tumor after radiotherapy. Therefore, seven patients have completed the treatment purposed, with the Phase 2 SBRT boost. We delivered a median total dose of 11Gy/1 fraction (range 10-12 Gy). The cumulative BED10 was 80-90Gy. Of these, the acute toxicities were: 3/7 patient had nausea and diarrhea G1. 2/7 patients had nausea and vomit G2. 1/7 Diarrhoea G2. None of the patients showed acute toxicities of grade 3-4. Better results were obtained with BED10 >85Gy. The median PFS was 20 months (range 10 – 27). The median OS was 24 months (range 11 – 34).

Conclusions: The "total" no-surgical approach was feasible and well tolerated with better results in terms of PSF and OS for BED10 >85Gy. These preliminary results seem to indicate that this kind of therapy could emerge as a novel therapeutic option in this clinical scenario.

CO014

THE ROLE OF MULTIDIMENSIONAL EVALUATION IN CURATIVE RADIOTHERAPY FOR ELDERLY PATIENTS (AGED ≥75)

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Aims: Despite the high cancer prevalence in elderly people, the optimal treatment for elderly patient remains challenging, due to the incidence of age–related pathologies that could affect patient's functional capabilities. The concept of frailty is a complex, multidimensional, cyclical state of vulnerability, recognized as one of the most important issues in health care that can affect treatment approach and outcomes. In this contest, the aim of the study was the identification of frail patients candidate for curative radiotherapy (RT), and to measure by a multidisciplinary and multidimensional approach the impact of frailty on toxicities and outcomes.

Methods: A prospective observational study was designed in our Center for all patients with ≥ 75years, candidate for curative RT. Frail patients were identified by radiation oncologist, before and at the end of RT, by Geriatric8 questionnaire (G8q). All frail patients (score ≤14) were then evaluated by a multidimensional geriatric assessment, investigating cognitive (MMSE, GDS), functional (ADL, IADL, Tinetti), nutritional (MNA short) domains, to define the frailty phenotype. The geriatric assessment was repeated at 3, 6, 12 months after RT.

Results: From December 2019 to March 2020 G8q was submitted to 53 patients. Due to the COVID-19 pandemic, the evaluation was suspended until June 2020. Nineteen patients (35%) were baseline identified as frail (G8 score range 3-14). Ten of 19 patients agreed to underwent a multidimensional geriatric assessment (Table 1). Vulnerable patients were monitored during RT according to geriatric prescriptions. All frail patients, except 1 that refused RT, completed treatment without acute toxicity > grade2 (RTOG). The G8q at the end of RT resulted worse in 5 patients. Two patients showed a benefit from RT, reporting a G8 score improvement. Overall, only 2 no-frail patients reported a worse G8 score at the end of RT.

Conclusions: Since the number of elderly oncologic patients is progressively increasing, it is important to ensure older-person-centered care plans. Although the study is still ongoing, preliminary results confirmed that G8q represents a simple tool to identify frail patients in daily practice and that most of elderly patients with indication to curative RT did not show a fragile phenotype. Moreover, the support of a multidisciplinary approach in vulnerable patients resulted useful in order to obtain their compliance to the treatment without increased toxicity.

Table 1. Patient evaluation tools and respective scores, assessed before and at the end of RT.

PRE-RT EVALUTATION N°	FIT 4	VULNERABLE 6	
	mean (SD)	mean (SD)	p
G8	13.75 (0.50)	12.00 (2.28)	0.176
(range)	13-14	9-14	
MMSE	27.75 (3.86)	26.00 (3.03)	0.444
ADL	5.75 (0.50)	5.50 (1.22)	0.713
IADL	6.00 (1.83)	6.17 (1.72)	0.887
MNA (short)	12.25 (2.36)	11.17 (2.56)	0.519
GDS	2.00 (0.82)	7.33 (3.88)	0.029
TINETTI	27.00 (1.41)	23.17 (6.68)	0.299
POST-RT EVALUTATION N°	**FIT 4**	**VULNERABLE 5**	
	mean (SD)	mean (SD)	p
G8	12.38 (1.89)	13.75 (0.96)	0.242
(range)	11-14	13-15	
Acute toxicity grade (%)			0.12
0	2 (50.0)	1 (20.0)	
1	0 (0.0)	2 (40.0)	
2	2 (50.0)	2 (40.0)	

G8 (Geriatric 8 questionnaire), MMSE (minimental state examination),
ADL (Activity of daily living),
IADL (Instrumental activity of daily living),
MNA – short (mini nutritional assessment),
GDS (geriatric depression scale), Tinetti assessment tool (gait and balance test).

CO015

SAFETY AND EFFICACY OF CONCURRENT STEREOTACTIC RADIOTHERAPY AND IMMUNOTHERAPY IN METASTATIC CANCER: THE EXPERIENCE OF TWO CENTERS IN EMILIA-ROMAGNA

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Aims: Concurrent immunotherapy with immune check-point inhibitors (ICI) and stereotactic radiotherapy (SRT) or radiosurgery (SRS) is a new approach to treat advanced and metastatic cancers. Although several retrospective trials show that concomitant immunotherapy and SRT/SRS increase local control (LC) in metastatic disease, there is limited prospective data to evaluate safety and efficacy, as well as the optimal timing of this association therapy. In this study, we investigate the efficacy and the profile

of toxicity in metastatic patients treated with ICI administration 30 days before or after stereotactic radiotherapy.

Methods: From January 2011 to December 2018, we recruited metastatic non-small cell lung cancer (NSCLC), renal cell cancer (RCC) and melanoma patients. They received a combination of ICI (nivolumab, pembrolizumab or ipilimumab) and SRT/SRS at 30 days from one another. In this retrospective trial, we included patients treated in two different centers: Parma and Reggio Emilia. Progression-free survival (PFS) and overall survival (OS) were estimated using Kaplan-Meier survival curves, while logistic regression was used to identify local toxicity and adverse events (AE).

Results: We identified 33 patients who were divided into two groups: first of all, those with brain metastases; secondly, those with body metastases. The first group, consisting of 14 patients with 19 treated brain lesions, showed 13 adverse events (AE): of these, two events were categorized as G4 (skin rash and anaphylactic shock) and only one as G3. The second group included 19 patients with 24 body metastases. For these, we observed 36 AEs: six of these were accounted for as G3, while no event was classified as G4. The one-year OS rates were 90% and 50% in body metastatic patients and brain metastatic patients, respectively. The one-year PFS rate was 18% in the first group, and 30% in the second, respectively.

Conclusions: These data suggest that delivering SRT/SRS may be associated with concurrent immunotherapy, because it is safe and increases survival outcomes.

Table 1. Adverse events of brain metastases patients.

Adverse events	G1	G2	G3	G4
Headache	2			
Dizziness	1			
Ataxia/weakness			1	
Skin rash				1
Anaphylactic shock				1
Thush		1		
Asthenia	2			
Hepatic impairment		2		
Hypothyroidism	1			
Dyspnea		1		

Table 2. Adverse events of body metastases patients.

Adverse events	G1	G2	G3	G4
Actinic pneumonia	1		1	
Pleural effusion		1		
Skin Rash	3	1	1	
Itch	2	3		
Dizziness		2		
Dysgeusia	1			
Nausea	1	1		
Diarrhea	1	2		
Hypothyroidism	1	1		
Hyperthyroidism	1			
Immunoinduced pneumonia			3	
Dyspnea	1			
Nephritis				
Asthenia	3	1	1	
Headache	2			
Hyperglycimia	1			

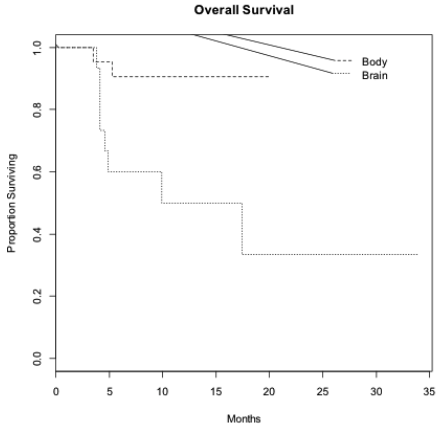

Figure 1. OS of brain and body metastatic patients.

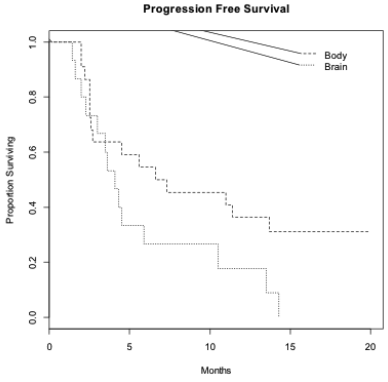

Figure 2. PFS of brain and body metastatic patients.

CO016

PRELIMINARY ANALYSIS FROM A PHASE II RANDOMIZED TRIAL EXPLORING ABLATIVE RADIATION THERAPY IN PATIENTS WITH OLIGOMETASTATIC CASTRATION RESISTANT PROSTATE CANCER UNDERGOING TREATMENT WITH ABIRATERONE ACETATE (ARTO TRIAL-NCT03449719)

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Aim: NCT03449719 is an ongoing multicenter, randomized trial, started in January, 2019. Nine italian centers are currently enrolling patients, and uptodate 30% of the overall target accrual has been reached. The present analysis is a preliminary report about clinical outcome and adverse events within the trial.

Methods: Patients with oligometastatic Castrate Resistant Prostate Cancer (CRPC), defined as < 3 non-visceral metastatic lesions, are randomized 1:1 to receive standard I line therapy with Abiraterone Acetate alone (control arm) or associated with stereotactic body radiation therapy (SBRT) on all sites of disease (treatment arm). Assessment comprehensive of clinical examination, PSA and quality of life evaluation by EORTC QLQ-C30 and BPI-SF was performed every three months. Toxicity was assessed by the Common Terminology Criteria for Adverse Events toxicity scale (CTCAE v.4.03). Descriptive statistic about available data from the current enrolled population are reported.

Results: Overall, complete data at 3 months after treatment start were available for 41 patients, 21 and 20 in the control and treatment arm of trial, respectively. One patient in the treatment arm refused SBRT and will be included in intention to treat analysis. Twenty-eight metastatic lesions were treated in the SBRT arm, LINAC based intensity modulated RT, Cyberknife(R) robotic technique and helical Tomotherapy(R) were used in 12, 5 and 3 patients, respectively. Median PSA drop after 3 months was 1.51 (-13.5 to 13.2) and 4.2 (-0.8 to 29.4) ng/ml in the control and treatment arm, respectively. All patients are alive, with 1 biochemical progression event occurred in the control arm. No adverse events occurred in both arms of treatment. SBRT had no significant impact on Global Health Status of patients included in treatment arm.

Conclusions: SBRT+Abiraterone acetate yielded promising biochemical response if compared to standard approach. No increase in terms of adverse event rate or quality of life impairment was detected in the treatment arm. These results suggest that concomitant association between SBRT and Abiraterone Acetate is an effective and feasible treatment strategy. Mature data are awaited to detect the magnitude of benefit provided by SBRT addition to standard Therapy in I line oligometastatic CRPC.

CO017

HIPPOCAMPAL SPARING WHOLE BRAIN RADIATION THERAPY: THE EUROPEAN INSTITUTE OF ONCOLOGY EXPERIENCE

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**At time of data collecting*

Aim: Whole brain radiation therapy (WBRT) still represents standard treatment for multiple brain metastases (BM). Hippocampal sparing WBRT (HS-WBRT) technique using intensity-modulated RT (IMRT) has significantly shown lower memory decline compared to WBRT. The aim of this study is to retrospectively evaluate peri-hippocampal recurrences on our HS-WBRT cohort.

Methods: A retrospective data collection of patients (pts) who underwent HS-WBRT at our Institute from January 2016 to July 2019. Inclusion criteria: 1) diagnosis of BM; 2) pts naïve for any BM treatment; 3) KPS>70; 4) life expectancy more than 6 months; 5) available brain magnetic resonance imaging (MRI) before RT; 6) written informed consent. Treatment performed using IMRT scheduled in 30 Gy in 10 or 12 fractions; dose constraints for Hippocampus by Gondi hippocampal-sparing RT guidelines (median dose of 7.8 Gy and maximum dose of 15.3 Gy). Oncological outcomes were clinically and radiologically assessed every 3 to 6 months after HS-WBRT. This study was part of the research notified to our Ethic Committee.

Results: One-hundred and six pts were treated with HS-WBRT. Of which, 37 were excluded due to poor life expectancy, KPS<70 and previous brain treatments. A total of 69 pts matched inclusion criteria. Most represented histologies were breast (52%) and NSCLC (41%). 71% of pts underwent concomitant systemic therapies: 27 chemotherapy, 8 target therapy, 7 hormonotherapy, 6 immunotherapy. 32 pts (46.4%) had KPS 90, 20 (30%) KPS 100, 11 (16%) KPS 80 and 6 (8.7%) KPS 70. Median dose to hippocampus was 7.6 Gy (range 5.4-9.8). Twenty-eight pts (40.5%) experienced a brain recurrence, of which 4 (14%) were peri-hippocampal. In total peri- and hippocampal relapse was 0.6%, in line with literature data. Median time to recurrence was 8.4 months (range 0.5-32.9). Three pts (4%) reported a G1 radionecrosis. After a median follow-up of 5.4 months (range 0-40), 27 pts (39%) were dead, 20 pts (29%) were lost in follow-up. The radiological evaluation at 6 and 12 months were available for 16 and 18 pts respectively.

Conclusions: Our preliminary data show low risk of peri-hippocampal relapse after HS-WBRT, less than 1%, according to literature. HS-WBRT has shown to be a reliable and safe treatment both with palliative and prophylactic aim. Further research is warranted to

define better the patient population that benefit most from this advanced WBRT technique.

CO018

TREATMENT RELATED ACUTE LYMPHOPENIA IS ASSOCIATED WITH POOR SURVIVAL OUTCOME IN GLIOBLASTOMA PATIENTS FOLLOWING POST-OPERATIVE CHEMO-RADIOTHERAPY

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Aim: In this study, we retrospectively investigated clinical and dosimetric predictors of treatment-related acute lymphopenia and its association with overall survival (OS) of a series of GBM patients treated with postoperative chemo-RT.

Methods: From December 2014 to August 2019, a total of 64 GBM patients, median age 62.5 (53.3-69.8), were treated at the same Institution with postoperative chemo-radiotherapy (CT-RT), and had available data including peripheral lymphocyte count (PLC) and RT dose-volume histogram parameters (DVH). Acute lymphopenia (AL) was calculated as a PLC lower than $1.0\times10^3/mm^3$ following RT. Acute relative lymphopenia (ARL) was defined as the ratio between lymphocyte count recorded 1 month after RT and pre-treatment lymphocyte count lower than 0.50. Lymphopenia was graded according to the CTCAE v4.0. Survival rates were estimated using the Kaplan-Meier curves and compared with log-rank tests. Univariate and Multivariate Cox regression analyses were used to determine the most relevant clinical and dosimetric factors associated with AL/ARL and OS.

Results: Median follow up was 15.9 months (range 11.9-27.3). The median PLC was significantly decreased following CT-RT ($2200/mm^3$ Vs $690/mm^3$) and did not recover during the adjuvant TMZ treatment. A significant correlation was found between age (p=0.007), macroscopical radical surgery (p=0.001), MGMT hypermethylated (p=0.006), adjuvant CT (p=0.001), ARL (p=0.009) and 18-month OS. While there were no significant differences in OS rates in patients who developed Grade 1 and 2 lymphopenia compared with those who did not at 1 month after RT, patients with ARL had significantly worse OS than those without (median: 13.0 vs 26.0 months, respectively, p= < 0.0001). At multivariate analysis macrospical surgery was confirmed the most significant prognostic factor (OR 2.67; p=0.013), and a trend in favour of ARL (OR 3.82; p=0.060) was showed.

Conclusions: Our data show that treatment-related lymphopenia might adversely affect GBM survival. These findings add to the body of evidence that immunosuppression induced by CT-RT is associated with inferior clinical outcomes. An improved understanding of the biology behind AL/ARL might help to prevent inadvertent lymphocyte depletion or to restore lymphocytes during or after CT-RT. These strategies may result in improved OS in selected patients with GBM. Prospective studies are needed to confirm these findings.

CO019

ARE WE READY TO REDUCE MARGINS IN TARGET VOLUME DELINEATION FOR NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS?

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Aims: Currently, standard treatment for glioblastoma (GBM) is surgical resection followed by radiotherapy (RT) with concomitant and adjuvant temozolomide chemotherapy. According to ESTRO-ACROP (EA) guideline the target volume correspond to surgical cavity (GTV-EA) plus 2-3 cm to generate Clinical Target Volume (CTV-EA); an isotropic expansion of 3-5 mm is suggested to obtain Planning Target Volume (PTV-EA). The employ of advanced imaging (magnetic resonance imaging – MRI) could allow of reducing margins with a lower risk of RT related toxicity maintaining the same local control. Aim of the present study was to evaluate outcome of newly diagnosed GBM patients treated using advanced imaging and smaller margins. A comparison between target volume delineation in according to ESTRO-ACROP guideline and internal guidelines were performed.

Methods: Two different clinical target volumes were delineated and compared. According to internal guidelines (IG), we defined the CTV-IG as surgical cavity, contrast enhancing lesion (pre-,post-surgery and simulation MRI) and FLAIR-MRI area (post-surgery and simulation images). The PTV-IG was generated adding 5 mm. Retrospectively, we defined target volumes according to ESTRO-ACROP. Clinical outcome was evaluated by clinical neurological examination and radiologically on brain MRI, 1 month after radiation therapy and then every 3 months. Response was recorded using the Response Assessment in Neuro-Oncology (RANO) criteria. The recurrence was defined as in-field (included in CTV) , marginal (partially out of CTV) and distant (not included in CTV).

Results: Target definition in sixty patients with HGG were compared. The overlap between CTV-IG and CTV-EA showed a low correlation between the two volumes with CTV-IG not always fully included into the CTV-EA, despite larger margins were added. Recurrences occurred in 33/60 (55%) patients at a median time of 12 months. In all cases recurrences were in-field in CTV-IG and in 16/33 (48%) partially outside CTV-EA (marginal). The 1- and 2-year DFS was 63%

and 43% and the 1- and 2-year OS was 87% and 83% respectively. Survival predictive factors were extent of resection, Karnofsky performance status (KPS) and O(6)-Methylguanine-DNA methyltransferase (MGMT) promoter status.

Conclusions: In conclusion, our study suggests that reduction of PTV margin in target delineation is feasible with a pattern of failure comparable to literature.

CO020

MULTIFRACTION RADIOSURGERY AND PERSONALIZED MEDICAL THERAPY FOR BRAIN METASTASIS: MONOINSTITUTIONAL EXPERIENCE

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Aim: Evaluate local control and toxicity in patients with brain metastases undergoing concomitant fractionated stereotactic radiotherapy (FSRT) and novel drugs.

Methods: Between January 2018 and March 2020, 52 patients were treated with FSRT for 82 brain metastases receiving concomitant immunotherapy or target therapy: 49 lesions (60%) were treated during anti-PDL1 (Nivolumab, Pembrolizumab, Durvalumab) or anti CTLA-4 treatment (Ipilimumab), 14 (17%) with anti HER2 drugs (Trastuzumab Emantesine, Pertuzumab, Trastuzumab, Lapatinib), 7 (8.5%) with anti EGFR (Osimertinib, Gefitinib, Erlotinib, Afatinib, Cetuximab), 7(8.5%) with antiangiogenetics (Bevacizumab, Sunitinib) and 5 (6%) with anti ALK (Crizotinib, Alectinib, Brigatinib). We offered concomitant FSRT in all cases where a tolerance to treatment had been demonstrated and with a safety interval, directly related to T ½, for drugs without evidence of safety (ex. Osimertinib, Trastuzumab Emantesine, Afatinib etc.). FSRT with volumetric modulated arc therapy (Rapid Arc) was adopted. The mean diameter of lesions was 11mm (range 5-32 mm). The mean volume of PTV was 7.44 cc (range 0.75-13.41 cc). The total dose to PTV ranged from 21 to 27 Gy in 3-5 consecutive fractions of 5-7-8-9 Gy each (Range: a/b 3 BED 70.0-108.0 Gy EQD2 42.0-64 Gy; a/b 10 BED 35.7-51.3 Gy EQD2 29.8-42.8 Gy) according to brain area and to concentration of drugs in the cerebrospinal fluid and plasma presumed in literature. V18 normal tissue was maintained < 25cc. All patients underwent a Magnetic Resonance Imaging (MRI) with a contrast enhanced within 4-6 weeks after the end of the treatment and subsequently every 3 months. Response to treatment was evaluated with RECIST criteria. Toxicity was reported according to CTCAE.

Results: After a median Follow up to 16 month (range 3-27) , 18/82 lesions showed a complete response to treatment , 42/82 a partial response and 12/82 had stable disease. MRI toxicity's evaluation showed developed of symptomatic radiation necrosis (from 10 and 12 months to treatment) in 3 lesions, radiologically and clinically regressed after medical therapy in 3-6 months.

Conclusions: Our data confirm efficacy and tolerance of FSRT for brain metastases concomitant with new therapies. Molecular target therapies could represent a criterion in the choice of FSRT for brain metastases.

CO021

MULTIPLE BRAIN METASTASES (BMS) RADIOSURGERY (SRS) WITH SINGLE ISOCENTER: AUTOMATIC LOWER DOSE OBJECTIVE (ALDO) OR INTRATUMOR LOWER DOSE APPROACH (ILA)?

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Aims: To compare 2 different optimization approaches in terms of isodose prescription, target coverage and organs at risk (OARs)dose sparing for multiple brain metastases (BMs) radiosurgery (SRS) with single isocenter.

Methods: From 08-10 2019, 69BMs(mean7, range4–21) have been treated by Single iscocenter SRS in 10patients. The prescribed dose (Dp) was27Gy in 3fractions. PTV was defined by 1mm isotropic margin from each lesion. None of PTVs was overlooking to chiasm or brainstem. Mono-isocenter VMAT plans with 5non-coplanar arcs(couch0°,±45°,±90°) were generated for all patients, 2different modalities of optimization – one based on mono-isocenter SRS dedicated optimization tool and the other on human experience – were compared: ALDO vs ILA. A dose normalization of 100%Dp at 98%PTV was adopted, while D2%(PTV) <150%Dp was accepted. OARs were defined as chiasm, brainstem and heathy brain minus PTVs. Plan-optimizations were compared by the isodose prescription, D100% and D2% for PTVs, maximum dose for chiasm and brainstem, V18Gy for the healthy brain, number of monitor units (MU) and OTT.

Results: PTVs sum PTVs, calculated for each patient as an index of intracranial disease, had mean dimension of 5.6cc (range 3.71–10.1cc). Isodose prescription for ALDO was included between 60-65%, while for ILA between 75-80%. For both optimizations, D100% ranged between 25,05-27,3 Gy, while the D2% was higher for ALDO than ILA: 38-39Gy for ALDO and 33-34 Gy for ILA. All plans had to respect the constraints and no difference was highlighted by comparing ALDO-ILA. The mean of the maximum dose to chiasm was 4.7Gy and 4.4Gy for ALDO and ILA, respectively. The mean of the maximum dose to brainstem was 9.8Gy and 9.4Gy for ALDO and ILA, respectively. For all cases, V18Gy<30cc, as prognostic factor for radionecrosis, was respected (range5.4-15cc for ALDO and 6.2-20cc for ILA). Mean MU and OTT for ALDO were 4454 and 3 minutes, respectively; while for ILA mean of MU was 2322 and mean of OTT was 1.6 min-

utes.

Conclusions: ALDO and ILA give good results in terms of target coverage, OARs sparing and low doses at healthy brain. However, ALDO uses lower prescription isodoses to obtain similar results to ILA, leading to a D2%>150% Dp, which could correlate with a higher risk of radionecrosis. In SRS planning expert hands, the clinician and physicist might choose between ALDO-ILA to customize treatments based on histology, BMs size and number, proximity to OARs, performing treatment plan optimization tailored on the patient.

CO022

HYPOFRACTIONED RADIOTHERAPY FOR HIGH GRADE GLIOMAS WITH CONCOMITANT AND ADJUVANT TEMOZOLOMIDE: OUTCOME AND PROGNOSTIC FACTORS AT TOR VERGATA UNIVERSITY

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Aims: In this retrospective study we aimed to evaluate results and prognostic factors in patients with high grade gliomas treated with hypofractionated Radiotherapy (HYPO-RT).

Methods: Patients with histologically confirmed high grade gliomas not fit for standard radiotherapy (RT) and Temozolomide (TMZ), underwent to HYPO-RT + TMZ. Un-eligibility for standard treatment was age (≥70 years) or performance status (KPS<70). HYPO-RT was administered as 36Gy/12 fx or 40Gy/15 fx alone or concomitantly with TMZ. Adjuvant TMZ was administered in fit elderly patients. Overall survival and Progression Free Survival were recorded and evaluated along with neutrophil/lymphocyte ratio (NRL), MGMT methylation, age, KPS, type of resection.

Results: From January 2013 to January 2020, 41 patients with high grade gliomas and median age of 75 years and median KPS of 80 were observed and treated at our institution. Among these 41 patients, 36 were Glioblastoma, 2 Anaplastic Astrocytoma and 3 had no histological diagnosis. Ten patients had complete resection, 27 partial, one a biopsy. MGMT methylation was recorded in 25 patients with 7 methylated MGMT promoter, and 8 without. Thirteen patients have an NRL ≤ 4, twenty-seven >4 and for 1 it was not possible to determine the blood count values. Twelve pts received HYPO- RT only, 29 HYPO- RT+TMZ. One patient rapidly progressed during HYPO- RT with fatal event; 24 pts received adjuvant TMZ and 16 did not due to the rapid decline of the general conditions or disease progression. Median OS was 7.9 mo, while median PFS was 4 mo. Patients who had MGMT methylation had significantly longer overall survival than those without MGMT methylation [9.7mo (95%CI 8.2-14.2) vs 3.4mo (95%CI 1.7-7.9), p=0.002]; pts who had complete resection had significantly longer survival than those who had a partial resection [11.3mo (95%CI 1.1-309 vs 7.4mo (95%CI 4.4-9.6), p=0.016]. In the NLR <4 group no statistical difference in OS vs the NLR>4 was found [7.4mo(95%CI 2.4-11.3) vs 9.5mo(95%CI 4.1-10) p=0.78]. Also in the KPS ≥70 group no statistical differences in OS vs KPS <70 was recorded [8.2mo(95%CI 5.2-9.7) vs 5.4mo (95% CI 2.4-10)p=0.48]. For age younger than 70 years survival was better [9.5mo (95%CI 5.9-11-3) vs 5mo(95%CI 2.4-9.7) p=0.014]. No factor affected PFS.

Conclusions: This cohort confirmed the results of HYPO-RT in older patients and in those with poor KPS. An impact of resection and MGMT methylation was observed too. NLR did not have any impact on OS

CO023

PROTON THERAPY RE-IRRADIATION OF INTRACRANIAL MENINGIOMAS FAILING AFTER PREVIOUS RADIATION THERAPY

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Aims: Re-irradiation of intracranial meningiomas (MS) is often difficult due to the limited radiation tolerance of the surrounding tissue. Aim of this analysis is to report safety and efficacy of proton therapy (PT) for re-irradiation of recurrent MS.

Methods: Between March 2015 and June 2019, 25 patients (pts) with 29 intracranial MS were re-irradiated with PT. Location of the primary lesion was skull base (n = 21) and convexity (n = 8). All but two pts had histologically proven diagnosis of MS (80% were WHO grade II). Median age was 66 years (range, 38-83). Median Karnofsky Performance status was 80 (range, 70-100). All pts failed after previous RT: 33% after Gamma-knife, 43% after Cyber-Knife, 10% after Tomotherapy, 14% after Linac-based stereotactic radiotherapy. Median time from initial irradiation to re-irradiation was 36 months (range, 18-60). Treatment planning was based on MRI with contrast enhancement medium administration. All pts received also 68-Ga-DOTATOC-PET to identify the so-called Biological Tumor Volume. Clinical target volume ranged from 7 to 176 cc. All but one pts (who received 60 Gy in 30 fractions) were treated with 54 GyRBE in 30 fractions. All the pts was treated with active beam scanning PT using 3-4 fields with single or multiple field optimization technique. Toxicity was assessed according to Common Terminology Criteria for Adverse Events version 4.0. Median follow-up time was 18 months (range, 3-52)

Results: All the pts completed the treatment without breaks. The treatment was well tolerated, no registered acute and late grade 3 or higher toxicities were reported. During follow-up two pts (7%) developed radionecrosis (diagnosed at imaging) with no symptoms and no need of steroids. Another pts (5%) developed hydrocephalus that needed ventriculoperitoneal drain. Currently, abso-

lute treated site tumor control is 80%, while absolute tumor control is 76%. Median time to local or distant tumor progression was 19 months. Disease specific absolute survival after re-irradiation is 95%, while absolute overall survival is 81%: three pts died of other causes than MS after re-irradiation. Moreover, relief of symptoms recorded before irradiation occurred in 35% of pts.

Conclusion: Reirradiation with PT of MS progressing after previous RT appears to be feasible with promising clinical outcomes and an acceptable toxicity profile. Longer follow-up is necessary to assess definitive efficacy.

CO024

RADIOSURGERY FOR PITUITARY ADENOMAS: MONOINSTITUTIONAL ANALYSIS

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Aims: Pituitary adenomas (PA) represent one of the most common intracranial pathologies, accounting for 10-20% of intracranial tumors. PA are traditionally classified as functioning and non-functioning according to the hormone secretion. Although PA are histologically benign, the neurological and physiological consequences can be devastating, particularly if these tumors compress the optic apparatus. Microsurgery is the primary recommendation for nonfunctioning and most of functioning adenomas. However, about 30% of patients require additional treatment after microsurgery for recurrent or residual tumors. Radiosurgical treatment (SRS) is represents a viable option as adjuvant treatment following incomplete surgical resection, tumor recurrence, or failure of medical therapy. The SRS literature data reports tumor control greater than 90% at 10 years. However, single fraction SRS is not recommended for tumors located close to the optic apparatus due to the restricted radiation tolerance of the optic pathway. Published series have demonstrated the advantage of multisession SRS (mSRS) in both tumor and hormonal control, with low rates of adverse events. The aim of this study is to retrospectively evaluate the efficacy and safety of mSRS for patients with diagnosis of PA in terms of local control and toxicity.

Methods: Forty-two patients treated by means of mSRS between 2011 and 2019 have been analyzed. A regular follow-up with endocrinological evaluation, ophthalmological examinations and MR imaging were scheduled at 4–6 month intervals after mSRS procedure. The radiosurgical procedures were performed using a CyberKnife® system.

Results: The median age at the time of mSRS was 54 years. Twenty-six (62%) patients had evidence of partial or total hypopituitarism before mSRS. Visual defects were present in 66.7% of patients. The median follow-up was 29.5 months (range 6-110 months). The median tumour volume pre-mSRS was 7070 mm^3 (range, 1339 - 74530 mm^3). The mean prescription dose was 25 Gy in 5 fractions. Only one patient developed a recurrence, 33 (73.3%) showed stable disease, 7 (16.7%) partial response and one patient (2.4%) had a complete response. No patients showed new or worsen hypopituitarism after treatment. One patient (2.4%) developed mild visual deterioration.

Conclusions: mSRS seems a safe and effective treatment, both in adjuvant and salvage approaches, for patients diagnosed with recurrent or residual pituitary adenomas.

CO025

CLINICAL AND DOSIMETRIC PARAMETERS CORRELATED WITH ACUTE CHEILITIS IN ANTERIOR ORAL CAVITY CANCER (AOCC) PATIENTS TREATED WITH INTENSITY-MODULATED RADIOTHERAPY (IMRT) WITH AND WITHOUT CONCURRENT CHEMOTHERAPY (CCT)

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Aims: The lips are an essential aspect of the human face and play a critical role in facial expression, phonation, sensation, mastication, physical attraction, and intimacy. We investigate the clinical and dosimetric factors correlated with radiation cheilitis in patients (pts) with anterior oral cavity cancer (AOCC), treated with IMRT+/- CCT.

Methods: 29 pts with AOCC treated with IMRT from 2011 to 2020 were reviewed retrospectively, median age 64 years (range 53-88), 89% males and 11% females, ECOG PS 0-2.The primary tumor sites were 44% oral tongue, 34% floor of mouth, 10% upper gum, 7% retromolar trigone 3% cheek mucosa; 75% received postoperative RT and 25% radical RT, 48% with concurrent CDDP-based chemotherapy. Total dose was 54-66 Gy Gy, 1.8-2.25 Gy/fr. Acute toxicity was weekly evaluated using the CTCAE v 4.0. The maximum toxicity score was used. Lips were contoured a posteriori, thus no attempt was done to spare them. Dmean, Dmax, V10, V20, V30, V40, V50, V60 and the patient baseline clinical characteristics were calculated. Receiver operator characteristic (ROC) analysis was used to analyse function of acute cheilitis and to determine the optimum cut-off point. Youden index were calculated and the largest value was defined as the cut-off point of dose constraints.

Results: The rates of acute cheilitis grades 0, 1, 2, and 3 were 62.5%, 8.3%, 16.6% and 12.5%, respectively. There was no grade 4 or 5 toxicity. The median Dmean, Dmax, V10, V20, V30, V40, and V50 were 36.35 Gy, 61 Gy, 100%, 87%, 65.5%, 35.5%, 17.5%

and 0%, respectively. In univariate analysis we reported a statistically significant correlation between acute ≥ G2 cheilitis and Dmean ($p<0.05$) and V40 ($p<0.05$) and V50 ($p<0.05$) whereas age, size of PTV, gender ,CCT, daily dose, Dmax and total dose were not. The ROC analysis and Youden index found that the optimal constraints of doses tolerated by lips were Dmean < 38.5 Gy and Dmax < 62.3 Gy, and the area under the curve was 0.630 and 0.667, respectively. According to the cut-off of mean dose, by using area under the curve, we determined that the optimal dose–volume constrains to lips was V40< 36%. The area under the curve was 0.615.

Conclusion: ROC method successfully produced thresholds for dose-volume constraints for lips. We suggest that lips should be routinely contoured in AOCC and when does not be possible reduce Dmean under 20 Gy any attempt should be done to reduce Dmean <40 Gy, V40 <35%.

CO026

IMPACT OF LOW SKELETAL MUSCLE MASS AND QUALITY ON OUTCOMES IN PATIENTS WITH HEAD AND NECK CANCER UNDERGOING CHEMORADIATION: PRELIMINARY RESULTS

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Aims: To explore the impact of low skeletal muscle mass and quality on disease free survival (DFS), overall survival (OS), treatment tolerance in patients undergoing radical chemoradiation (CRT) for head-and-neck squamous cell carcinoma (HNSCC) given the growing interest for sarcopenia as possible negative predictive/prognostic factor for disease progression and survival.

Methods: Pretreatment CT scans of HNSCC patients undergoing CRT between January 2010 and December 2017 at our Institution were retrospectively reviewed. By using manual segmentation, skeletal muscle area, normalized for height to obtain skeletal muscle index (SMI), skeletal muscle density (SMD), and intramuscular adipose tissue area (IMAT) were measured at the level of L3 vertebra. Low SMD and SMI were defined according to population-specific cut point analysis, and previously reported threshold values (SMD <41 Hounsfield Unit (HU) for BMI<25, <33 HU for BMI>25; SMI <41 in women, <41/<43 in men with different BMI levels). Clinical morphofunctional parameters, Charlson Comrbidity Index (CCI), baseline nutritional markers with known or suspected impact on HNSCC treatment outcomes and sarcopenia were also collected.

Results: Preliminary data on the first 69 consecutive patients (among 225 patients included in total) were analyzed. Table 1 summarizes population characteristics. Median age was 70(59.4-80.7) years, median CCI was 4(3-7). Patients were planned for 66 to 70 Gy in 30-33 fractions, all but 2 with rotational intensity-modulated Radiotherapy. Median SMD was 35(22-45) HU for BMI<25, 37(20-50) HU for BMI>25; median SMI was 46(37-52) for women, >50(28-70) for men, respectively. Median IMAT was 13(3-150) cm^2. 1-y and 2-y DFS were 81% and 79%, 1-y and 2-y OS 80% and 65%, respectively. Patients with SMD <35 HU had lower 1-y and 2-y DFS (both 65%; p=0.003) and 1-y and 2-y OS (68% and 48%; p=0.001). CRT suspension was more frequent for SMD <36 HU (p=0.08). IMAT and SMI did not have an impact on survival. Multivariate analysis showed male sex to correlate with sub-threshold SMD (p=0.02), sex and BMI with SMI < median (p=0.01).

Conclusions: Despite elderly and locally advanced disease at presentation, preliminary results showed good treatment tolerance and response after CRT for HNSCC. Low muscle quality seemed to worsen survival outcomes and male patients may be at higher risk for such negative impact. The analyses completion of all the recruited patients will clarify our promising findings.

Table 1. Population in study characteristics.

	n.	%		n.	%
Sex			**Tumor site**		
Male	51	73.9	Oral cavity	3	4.3
Female	18	26.1	Oropharynx	36	52.2
BMI			Nasopharynx	4	5.6
<18	3	4.3	Hypopharynx	14	20.3
18-25	26	37.7	Larynx	10	14.5
25-30	35	50.7	Occult primary	2	3.1
>30	5	7.3	**TNM stage (2010 VII Ed.)**		
Baseline weight loss			I	0	0
<10%	13	18.8	II	1	1.5
≥10%	9	13.0	III	17	24.6
Smoke habit	46	66.7	Iva	46	66.7
Alchol abuse	2	2.9	IVb	5	7.2
Tumor grading			**Concurrent CHT regimen**		
G1	4	5.6	Platinum-based (CDDP)	51	73.9
G2	17	24.6	Cetuximab	18	26.1
G3	30	45.2	**Acute Toxicity (CTCAE v4.0)**		
Gx	17	24.6	<G3	43	62.3
HPV (p16) status			≥G3	26	37.7
Positive	15	21.8	**CHT interruption**	14	20.3
Negative	17	24.6	**Treatment response**		
Undetermined	32	46.4	Complete	64	92.8
Treatment program			Persistence	5	7.2
Induction CHT plus CRT	7	10.1	Progression	0	0
Chemoradiation	62	89.9	**Local Recurrence**	19	27.5

CO027

IGRT PROTOCOLS OPTIMIZATION IN IMRT TREATMENTS FOR H&N CANCER

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Aims: Re-organization of the study protocol of head and neck (H&N) cancer with SIB IMRT, according to the new ESTRO ACROP guidelines (01/2017) to evaluate the patient set-up error and to assess the optimal planning target volume (PTV) margin to the clinical tumour volume (CTV).

Methods: From January 2015 to July 2018, 30 pts with stage III-IV, histologically confirmed, H&N cancer were treated with SIB IMRT: Group A (15 pts) treated before ESTRO Guidelines publication) with 2 radiation therapists involved in thermoplastic mask construction, kV CBCT images acquired during first 3 days of irradiation and every two weeks, kV OBI images every two days; Group B (15 pts) treated after ESTRO Guidelines publication, with 3 radiation therapists involved in thermoplastic mask construction (the mask was removed and refitted prior to CT scanning to ensure right fit and adequate immobilization), PET/CT images fusion used for target delineation, kV CBCT images acquired during first 3 days of irradiation and weekly thereafter and kV OBI images every day. Our retrospective statistical study was conducted to evaluate patient set-up errors along the 3 translational directions (VRT,LONG,LAT), calculated as shift values confirmed through pre-treatment portal images obtained during first treatment day. For each patient, the mean and standard deviation (SD) of all recorded errors were calculated. Van Herk's formula (2.5Σ + 0.7r) was used for CTV-PTV margin estimation.

Results: We analysed 210 CBCTs and 270 OBIs. The mean of set-up errors in group B was less than 3 mm in any direction compared to group A (5 mm). The CTV-PTV margin calculated with Van- Herk was about 3 mm (Group B) in the 3 directions and 5 mm (Group A), confirming our retrospective analysis.

Conclusions: The re-organization performed in group B (simulation, contouring and IGRT protocol) reported a reduction of set-up errors, with a 95% confidence interval. Finally, 3mm PTV margin appears more adequate and safe in order to overcome the problem of set-up errors.

CO028

SHOULD COMORBIDITIES DISCOURAGE CLINICIANS TO ADD CETUXIMAB TO DEFINITIVE RADIOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED HEAD AND NECK CANCER PATIENTS UNFIT FOR CISPLATIN? AN ITALIAN RETROSPECTIVE MULTICENTER STUDY

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Aims: Concurrent Cisplatin and Radiotherapy is the gold standard treatment for locally advanced head and neck squamous cell carcinoma (HNSCC). Cetuximab (Cet) is employed in patients unfit for chemotherapy in concurrent regimens with Radiotherapy. The aim of this study is to assess the impact of comorbidities in tolerance, toxicity and outcome in HNCa patients treated with radiotherapy and concurrent Cet.

Methods: A multicentre retrospective analysis of patients unfit for Cisplatin treated between 2010 and 2020 was performed. The burden of comorbidities was calculated with Charlson Comorbidity Index (CCI). A subgroup analysis between patients with low and high CCI (defined by median CCI value, group A=low CCI and group B=high CCI). Tolerance was defined as number of total cycles of Cet administered and duration of concurrent treatment in days. Toxicity was collected according to CTCAE scale v4.0. The comparison of baseline characteristics was made with Chi square test or Fisher exact test. Survival probabilities were calculated according to the Kaplan-Meier method.

Results: A total of 56 patients were enrolled in this study. Median age was 73 years (range 44-85) and 46 (83%) were male. Median follow up was 15.9 months (range 2.6-107.5). CCI ranged from 2 to 4 and from 5 to 9 in group A and B, respectively. Among baseline characteristics, median age was higher in the subgroup with high CCI (76 vs 68 years, p=0.009). Tolerance was similar in both groups with median 6 cycles of Cet administered and median 49 days of treatment duration in each group. No difference for the prevalence of acute toxicity was found in both groups: Mucositis G≥3 in 15 pts (71,4%) and 17 pts (81%) in grup A and B (p=0.46) and Dermatitis G≥3 in 6 pts (40%) and 12 pts (66,7%) in group A and group B (p=0.12), respectively. Survival in terms of Progression Free Survival, Overall Survival and Cancer Specific Survival were comparable in both subsets of patients. Two-years OS was 52% and 63% in group A and B (p=0.3), respectively.

Conclusions: Our preliminary results suggest that concomitant treatment with Cet and radiotherapy is

well tolerate also in older patients with high CCI. On these grounds clinicians should not be discouraged in prescribing Cet in patients with HNCa not eligible for concomitant cisplatin in presence of a high burden of comorbidities.

CO029

ABSTRACT WITHDRAWN

CO030

CLINICAL EVALUATION OF LATE DYSPHAGIA AFTER CONCOMITANT RADIOCHEMOTHERAPY: INITIAL RESULTS OF A LONGITUDINAL PROSPECTIVE MULTICENTER STUDY ENDORSED BY THE ITALIAN HEAD AND NECK RADIOTHERAPY STUDY GROUP

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Aims: To investigate changes in patient-reported dysphagia as measured by M.D. Anderson Dysphagia Inventory (MDADI) in patients affected with head and neck cancer after definitive radiochemotherapy (RTCT).

Methods: Eligibility criteria included all patients affected with naso and oropharyngeal cancers (Stage III-IVA TNM 7th ed) who were candidates for RTCT with curative intent requiring bilateral neck irradiation. MDADI questionnaires were prospectively collected at baseline and at 6 and 12 months after treatment. Only patients who completed the 3 time intervals questionnaires were included in the analysis. MDADI composite and subscale scores were categorized into three different categories (>80 "optimal", <80 and >60 "adequate" and <60 "poor function") and dicotomized as "optimal" vs "adequate/poor function" for the intent of analysis. Moreover, a mean difference of 10 points in MDADI scores was considered as minimum clinical interest difference (MCID), according to literature data. The study was registered in ClinicalTrials.gov (ID. NCT03448341).

Results: Between February 2018 and May 2020 we enrolled 61 patients of whom 56 completed the study. A total of 43 patients filled out all the questionnaires and was considered for the analysis. At baseline evaluation, 22 patients (51%) were classified as "optimal group" while 21 (49%) as "adequate/poor function group". Results are reported in Table 1. An overall clinical meaningful worsening of both composite (p= 0,003) and all subscale (p<0,005) MDADI scores from baseline to after treatment was reported for "optimal group" while a clinical meaningful improvement of both composite (p= 0,009) and subscale (p<0,005) MDADI scores was reported for the "adequate/poor function group". Mean baseline MDADI composite was 93.3 dropping to 80.8 at 6 months and slightly rising to 85.6 at 12 months after treatment for the "optimal group". On the contrary, mean baseline MDADI composite was 64.3 rising to 77.4 at 6 months and stabilizing at 76, after 12 months.

Conclusions: Patients with a baseline "optimal function" seem to suffer from detrimental effect of RT while those with a certain degree of baseline disability appear to benefit from the tumor volume reduction due to RT. Therefore, our results seem to unravel that the beneficial effect of RT on "Cancer-Related Dysphagia" overcomes its detrimental effect (also known as "Treatment-Related Dysphagia") in patients experiencing a certain degree of swallowing dysfunction at baseline.

Table 1.

MD Anderson Dysphagia Inventory (MDADI) scores results						
Categoria al basale	**Variabili**	**N**	**Mean**	**SD**	**p-value***	**p-value****
≥80	Tot_Iniz	22	93,18	6,84	0,002	<0,0001
	Tot_6m	22	80,55	14,92		
	Tot_12m	22	85,45	13,30		
<80	Tot_Iniz	21	64,10	12,80	0,008	
	Tot_6m	21	77,43	11,25		
	Tot_12m	21	75,95	12,92		
≥80	G_Iniz	28	91,43	10,08	0,033	<0,0001
	G_6m	28	78,57	21,03		
	G_12m	28	85,00	20,82		
<80	G_Iniz	15	44,00	11,21	0,002	
	G_6m	15	73,33	26,90		
	G_12m	15	70,67	22,51		
≥80	E_Iniz	23	92,83	7,80	0,007	<0,0001
	E_6m	23	82,91	14,84		
	E_12m	23	87,17	14,00		
<80	E_Iniz	20	64,50	12,44	0,013	
	E_6m	20	77,65	11,86		
	E_12m	20	76,35	12,42		
≥80	F_Iniz	29	92,97	8,19	0,015	<0,0001
	F_6m	29	83,59	15,61		
	F_12m	29	86,76	13,05		
<80	F_Iniz	14	62,57	12,51	0,008	
	F_6m	14	80,00	11,53		
	F_12m	14	80,00	12,84		
≥80	P_Iniz	21	92,24	8,35	0,011	<0,0001
	P_6m	21	78,79	15,33		
	P_12m	21	82,69	15,69		
<80	P_Iniz	22	61,14	13,84	0,033	
	P_6m	22	73,52	14,87		
	P_12m	22	72,73	16,46		
≥80	Comp_Iniz	22	93,32	7,03	0,003	<0,0001
	Comp_6m	22	80,86	14,64		
	Comp_12m	22	85,64	13,09		
<80	Comp_Iniz	21	64,36	12,95	0,009	
	Comp_6m	21	77,49	10,84		
	Comp_12m	21	76,00	12,57		
*Intra-assay; **Inter-assay						
ANOVA for repeatead measures, stratified for category						

CO031

DEPTH OF INFILTRATION (DOI) IN ORAL CAVITY TUMORS: STAGE MIGRATION FOR PT3 CANCERS AND IMPACT ON INDICATIONS TO POSTOPERATIVE RADIOTHERAPY

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Background: The 8th edition of the AJCC (American Joint Committee on Cancer) Staging Manual has introduced the parameter "depth of invasion" (DOI) as a key criterion for staging oral cavity squamous cell carcinomas (OCSCCs). We hypothesize that a significant proportion of tumors previously staged as pT1-pT2 may be upstaged to pT3 becoming eligible for postoperative radiotherapy (PORT). The aim of the present study is to quantify the amount of pathological T stage migration.

Methods: All consecutive patients (pts) treated at two Italian Radiation Oncology facilities for OCSCC between 2014 and 2019 were re-classified according AJCC 8th Ed. Only those with pT3 per the 8th AJCC classification were selected. Second primary/recurrent tumors and previous surgery and/or radiotherapy in the head and neck region represented exclusion criteria. Risk factors for indication to PORT were: positive margins (R1), perineural invasion (PNI), lymph vascular invasion (LVI), more than 1 positive lymph node (>pN1 7th Ed.) and extracapsular extension (ECE). The study was approved by the Ethical Committee of the European Institute of Oncology, Milan, Italy (notification number: IEO 225 and IEO 254).

Results: A total of 153 pts with pT3 (8th Ed) OCSCC were analyzed. Of them, only 42 (27%) did not undergo staging modification (T maximum size >4 cm), while 43 (35%) previously classified as either pT1 or pT2 (11 and 42, respectively) were upstaged to pT3 due to DOI> 10 mm; finally, 58 (38%) pts formerly staged as pT4 (extrinsic tongue muscle invasion) were downstaged to pT3. R1, PNI, LVI, pN1>1 and ECE were present in 4 (7.5%), 28 (53%), 5 (9.5%), 21 (40%), 12 (23%) cases, respectively. Overall, 139 pts (91%) would have presented at least one indication for PORT besides pT3-DOI. Indeed, both size-pT3 (27%) and ex-pT4 (38%) would have been PORT candidates. Conversely, pT1 and pT2 cases without any risk factor to PORT were 14 (26%). The number of risk factors (besides DOI) in patients with pT1-pT2 are summarized in Table 1.

Conclusion: The number of pts within the pT3 category increased by more than 4-fold (from 42 to 135) when introducing the AJCC 8th Ed. classification. Nevertheless, the number of pts for whom PORT would have been indicated was only slightly increased (9%) due to the widespread presence of pathological risk factors. However, 26% of pts previously staged aspT1-pT2 may have skipped indication to PORT due to the absence of risk factors other than DOI.

Table 1. Number of risk factors (besides depth of infiltration-DOI) in patients with pT1-pT2 (7th AJCC).

Number of risk factors	Patients	(Tot=53)
0	14	26%
1	18	34%
2	15	28%
3	3	6%
4	2	4%
5	1	2%

CO032

RADIOTHERAPY IN ELDERLY PATIENT WITH HEAD AND NECK CANCER: TOXICITIES AND SURVIVAL OUTCOMES

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Aims: The aim of this multicenter retrospective study is to evaluate toxicities and survival outcomes in a series of elderly patients with head and neck cancer treated with Radiation therapy (RT) +/- Chemiotherapy (CHT).

Materials and Methods: Between January 2015 and December 2019, 150 patients were treated with RT at Radiotherapy Department of Sant'Andrea Hospital in Rome and Fatebenefratelli Hospital-Isola Tiberina in Rome. The median age was 78 years (range 70-95 ys). Patients were evaluated for comorbidities and classified according to Charlson Index Score (CCI): 122 pts (81.3%) had comorbidities, 93 pts (62%) had a CCI score ≤6 and 57 pts (38%) had CCI ≥6. Fifty-three pts (35.3%) were affected by oral cavity cancer, 48 pts by oropharynx cancer, 35 pts (23.3%) by larynx-hypopharynx cancer and 14 pts (9.3%) by cancer in other head and neck sites. One hundred-twentytwo pts (86%) had squamous cell histology. Patients were divided into three groups depending of fields of treatment: the first group included 37 pts (N0 pts; 25.3%) receiving RT only on the tumor primary site (T), the second group

with 85 pts (57.3%) received RT on T and positive node levels (N+) and the third group with 28 pts (39%) on T, N+ and negative node levels. Eighty-seven pts received a curative treatment (58%) and 63 pts (42%) received an adjuvant treatment after surgery. Only 22 pts received concomitant CHT (14%).

Results: Median RT dose was 66 Gy (range 50-70 Gy). The median one-year overall survival (OS) was respectively not reached for the first group, 31.2 months for the second group, 49.6 months for the third group. Toxicities were reported according to RTOG. Forty-one pts (27.3%) experienced grade 1 (G1) acute toxicities (erythema, disphagia, mucositis), 82 pts (54.6%) had G2 acute toxicities and G3 toxicities in only 13 pts (8.6%). Fourteen pts (9.3%) reported no acute toxicity. Late toxicities (disphagia, mucositis) were observed in 21 pts (14.6%). No G3 late toxicity was observed.

Conclusion: RT in elderly patients seems to be associated with a minimal acute and late toxicity and with a good overall survival. As there is no significant difference in acute and late toxicity in the three analyzed subgroups, a more aggressive radiotherapy treatment can be considered even in elderly patients. Our study showed that a treatment extended not only to the primary site of the disease but also to the lymph nodes, kept a feasible high safety profile.

CO033

4D CT ANALYSIS OF ORGANS AT RISK (OARS) IN STEREOTACTIC RADIOTHERAPY

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Aims: OARs, like target volumes, can be propagated to obtain an internal organ at risk volume (IRV). To our knowledge no one has tested the IRV in a clinical setting. This work aims at studying the IRVs in a retrospective database of lung SABR.

Methods: Sixty consecutive patients that underwent 4DCT for thoracic stereotactic radiotherapy were analyzed and IRVs for heart, trachea, esophagus, bronchial tree, great vessels and spinal cord were calculated. IRVs were then tested for the respect of dose constraints.

Results: IRVs were significantly bigger than standard OARs (p-value<0,001 for all the IRVs). IRVs that did not respect the dose constraints were, respectively, 7/60 (11,7%) for Heart IRV, 6/60 (10%) for Esophagus IRV, 11/60 (18,3%) for Trachea IRV, 16/60 (26,6%) for Bronchial Tree and 0/60 (0%) for great vessel and spinal cord IRV.

Conclusions: IRVs could be useful to understand the real volume of irradiated OARs. Our results need validation in prospective trials.

CO034

30 GY SINGLE DOSE STEREOTACTIC BODY RADIATION THERAPY (SBRT): REPORT ON OUTCOME IN A LARGE SERIES OF PATIENTS WITH LUNG OLIGOMETASTATIC DISEASE

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Aims: To evaluate local control (LC), long term adverse effects and survival in a series of patients with oligometastatic to the lung disease who received 30Gy in single dose with stereotactic technique.

Methods: Between December 2008 and March 2020, a total of 186 lung metastases in 147 patients affected by oligometastatic disease were treated, at our Institution, with stereotactic body radiotherapy (SBRT) delivered in a single dose of 30 Gy. The primary tumors in most cases were non small-cell lung cancer and colon-rectum cancer (48.2% and 30.7%, respectively). Prognostic factors were also assessed.

Results: The median follow-up was 56 months. 26 (13.9%) lesions in 25 patients progressed locally. Intrathoracic progression (new lung lesions or thoracic lymph node metastases) occurred in 67 (36%) patients. Distant progression occurred in 49 (33.3%) patients after a median time of 21 months. The 3- and 5-year local relapse-free survival (LPFS) were 80.3% and 79.5% (median not reached), respectively. Late toxicity was evaluated in 141 patients (follow-up >6 months): 58 (41.1%) had grade ≤2 fibrosis, 11(7.8%) experienced grade 3 fibrosis. Two (1.4%) cases of rib fracture occurred. One case of toxic death (grade 5) has been reported. Prognostic factor at the univariate analysis was: lesion diameter ≤18 mm correlated significantly with a longer LPFS (p=0.001). Prognostic factors at the multivariate analysis was only lesion diameter.

CO035

LUNG CANCER RADIOTHERAPY AND FUNCTIONAL IMAGING: A MONOINSTITUTIONAL EXPIERENCE

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Aims: Lung cancer radiotherapy (RT) is associated with potential risk of serious lung injury due to vascular damage. Lung Perfusion can be considered a new parameter to avoid lung toxicity in RT treatment. The inclusion of Lung Perfusion SPECT(L-P-SPECT)

information in the planning process could be useful to better spare normal functional lung tissue (FLT) switching from an anatomical to functional base planning.

Methods: From 03/2017 to 12/2018, 41 patients (pts) (16 women, 25 men) with lung cancer and 47 lesions were treated with Tomotherapy (TT). Thirty-eight pts had I-IIIB stage NSCLC (26 adenocarcinoma (adk), 8 squamous cell carcinoma, 1 Large cell carcinoma, 3 PET+ lesions NOS) and 3 pts had lung metastasis; 28 pts had central cancer whereas 13 pts had periferic lesion. All pts underwent L-P-SPECT and PET before TT. According to the literature, FLT was defined as two volumes with a cut-off of 20% (T20) and 30% (T30) perfusion threshold. Median PTV was 174 cc (25cc-567cc), median BTV was 11 cc (1cc-175cc). In 21 pts (51%) PTV also included mediastinum. V5, V10, V20 and mean dose were evaluated for whole and unilateral lung considering parameters of T20, T30. 23 pts (56%) were treated with conventional fractionation, median delivered dose was 60 Gy (60-70Gy) (1,8-2,0 Gy/fr); 18 pts (44%) received hypofractionated RT, median delivered dose was 60 Gy (2.65-9 Gy/fr in 6-25 fr). Toxicity was assessed by CTCAE 4.0 criteria.

Results: 34 pts (83%) showed G0 acute toxicity; 5 (12%) pts reported G1-G2 toxicity (cough 68% and dyspnea 62%). Two chemo pretreated pts (5%) (1:CBDA+Pemetrexed 1:CDDP) had G3 acute toxicity (bacterial pneumonia) resolved with antibiotic drugs. A G3 late toxicity (bilateral interstitial pneumonia) was registered six months after the end of TT, probably related to immunotherapy started 4 months before. V5,V10,V20, mean dose were similar in FLT and in whole lung.

Conclusions: Despite more than half of pts received the radiation therapy on mediastinum and despite the median PTV volume was considerable (174cc) we registered only one G3 late lung toxicity. In our experience, L-P-SPECT can be included in the planning process in order to reduce significantly lung toxicity. The next step will be try to find a specific constraint for FLT allowing the full implementation in the plan optimization together with respiratory function tests.

CO036

THORACIC RADIOTHERAPY IN EXTENSIVE DISEASE SMALL CELL LUNG CANCER: A PROSPECTIVE MULTICENTRIC OBSERVATIONAL STUDY

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Aims: Consolidative thoracic radiotherapy in lung extended microcytoma with complete or partial response after first-line chemotherapy has demonstrated advantages in terms of survival and disease control with low toxicity rate. Although it is clinical practice, much variability in terms of patient selection, dose, fractions and treatment volumes has been reported. The aim of the work is to report the preliminary results of multicentric retrospective of patients undergoing thoracic consolidation radiotherapy

Methods: Eight Italian radiotherapy centers participated to present prospective multicenter observational study. From November 2017 to May 2020 stage IV small cell lung cancer patients, who underwent to thoracic radiotherapy after complete (CR) or partial response (PR) to first line chemotherapy, were enrolled. The aim of this study is to describe the pattern of care of consolidative thoracic radiotherapy and to evaluate the treatment response in terms of disease control, PFS, OS and toxicity.

Results: Fifty seven patients where included in this interim report, of which 14 (24.6%) patients were in CR after chemotherapy. Six (10,5%) cases did not complete CT: 2 for clinical disease progression and 4 for severe pulmonary or esophageal toxicity. All patients underwent consolidative thoracic radiotherapy with a median thoracic RT dose of 34,37 Gy (range 9-60). Thirty four (59,6%) patients also underwent Prophylactic Cranial Irradiation. Follow-up data are not currently available for all patients. Median follow up was 9,1 months (range 1 – 19,8). None of the patients who concluded CT showed greater toxicity than G2. Three months after treatment 10 patients (17,5%) developed thoracic and systemic progression, 4 (7%) had thoracic PR, but developed distant metastasis. After one year, 8 patients are alive, including 3 with thoracic SD, 6 with thoracic and extrathoracic PD. Only one patient had a complete response to treatment and remained alive without disease until the last visit.

Conclusions: The results of this prospective multicenter observational study are still preliminary. Thoracic consolidation radiation therapy appears to play a controversal role in maintaining long-term thoracic control after chemotherapy in stage IV lung cancer. Therefore, definitive results are needed to clarify doubts about this therapeutic approach, in particular identifying a subgroup of patients could benefit from it, which arouses increasing interest.

CO037

ACUTE TOXICITY OF SBRT TO CENTRALLY LOCATED LESION OF THE LUNG: A MULTICENTRIC RETROSPECTIVE ANALYSIS

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Background: Stereotactic body radiotherapy (SBRT) delivers high doses of radiation to small and well-defined targets in an extreme hypofractionated schedule. SBRT seems to be associated with a higher probability to develop severe acute side effects when used for central lung lesions (CL). The aim of this multi-institutional study is to retrospectively evaluate acute toxicity and efficacy of SBRT in this setting.

Methods: CL were defined as tumors located within 2 cm around the proximal bronchial tree. From March 2012 to June 2019,a total of 60 patients with LC were treated with SBRT in four Italian radiotherapy institutions. Median age was 73.5 years. Male patients were 45 (75%), female patients were 15 (25%). All patients were staged with total body CT and/or 18FDG-PET-CT scan before SBRT. Biopsy samples of the pulmonary lesions were obtained in 44 patients. SBRT was used for 42 patients (70%) with primary or recurrent NSCLC, while 18 treatments (30%) were for metastatic lesions.

Results: All patients finished the treatment without any interruptions. 44 patients (73%) were treated with 7-7.5 Gy/fraction to 56-60 Gy, 8 patients with 10-12Gy/fx to 30-36 Gy and the last 8 patients with other schedules. At a median follow up of 16.5 months, 26 pts (43%) reported an acute adverse event (AE) according to CTCAE scale v4.0: 10 pts (16.6%) had respiratory toxicities (7 G1, 2 G2 and 1 case of G3), 5 (8%) had G1 cutaneous toxicity, 5 (8%) G1 esophageal toxicity (3 G1 and 2 G2). Ten (16.6%) cases developed lung toxicity (seven G1 and three G2); no G3 or higher grade AEs were reported. Late toxicitiers were found in 23% of patients: G3 dyspnea and pneumonitis were reported in 1 and 3 patients, respectively. G4 or more AEs were reported. At time of analysis, 5 patients were lost during follow up; 41 patients were still alive and 56% did not have evidence of disease. One and 3-year overall survival were 83.9±4.9 ES and 56.8±8.7 ES, respectively. One and three-year local control rate was 82.3±5.4 and 50.9±9.0 ES. Twenty patients developed loco-regional progression, 14 controlateral or extra thoracic metastases.

Conclusion: Our analysis confirmed that SBRT to CL seems to be an effective and well tolerated treatment. We reported a relatively low rate of serious treatment related AEs and no death treatment-related occurred.

CO038

SAFETY AND EFFICACY OF RADIOTHERAPY AND IMMUNOTHERAPY COMBINATION: A MULTICENTRIC RETROSPECTIVE STUDY IN ADVANCED NSCLC

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Aims: Preclinical studies suggest a synergistic effect of RT-ICIs combination. This retrospective multicentric study evaluates the efficacy and safety of this concomitant association.

Methods: We collected data of advanced NSCLC (aNSCLC) patients who received concomitant RT and ICIs in eight Italian centers. All patients received RT ≤ 4 weeks before or after the first/last administration of ICIs, and the RT delivery occurred within 2 consecutive cycles of ICI. Survival curves at one and three years were calculated with Kaplan-Meier method, adverse events (AEs) were graded according to the CTCAE version 4.0.

Results: From September 2015 to December 2018, 187 aNSCLC patients were treated in 8 different cen-

ters. Median age was 66 years; males were 116 (62%), females were 71 (38%). At the time of analysis, 131 (69.7%) patients received palliative RT. Bone was target of RT treatment in 76 patients, and 23 patients were treated on brain; other targets were lung, lymphnodes and soft tissues. SBRT was administered in 57 patients (30.3%). Nivolumab, pembrolizumab and atezolizumab were the systemic treatment for 131 (70.7%), 47 (25%) and 7 (4.3%) patients, respectively. ICIs was the upfront therapy in 43 patients, the second line treatment in 105 and were administered subsequently in 37 patients. After a median follow up of 23 months, the median and the mean overall survival (OS) were 16.5 and 29.8 months, respectively. OS at one and three years were 75.5% and 38.3%, respectively. Of the entire cohort, 43 patients (22%) developed immune related AEs. The most frequent AE was thyroid dysfunction. Ten (5.6%) patients experienced a grade 3 or more side effect. Other side effects were pneumonia, gastrointestinal symptoms, liver dysfunctions and neurological signs.use RT related AEs were developed in 13 (10,2%) patients, but none was grade ≥ 3.

Conclusions: Our retrospective analysis showed that the concurrent association of systemic ICIs and local palliative or ablative RT for the management of aNSCLC patients is safe and effective. These results must be validated in prospective trials.

CO039

OVERALL SURVIVAL PREDICTION IN NON-SMALL CELL LUNG CANCER: A RADIOMIC APPROACH WITH A MULTI-VOI ANALYSIS

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Aims: This study aims to predict the Overall Survival (OS) of patients with lung cancer who underwent a chemoradiotherapy treatment using a radiomic approach. Moreover, we evaluate how an accurate segmentation impacts the results using three incremental segmentations of the same lesion.

Methods: For this retrospective study 97 CT images of patients with NSCLC lung cancer treated with chemoradiotherapy were included. Images were acquired with a Siemens Somatom Emotion, with 140 Kv, 80 mAs, and 3mm slice thickness. Patients were divided into two classes according to their OS (53 patients died, 44 survived after median follow-up of 18.55 months. For each patient three segmentations were considered: the Gross Tumor Volume (GTV), the Clinical Target Volume (CTV) and the Planning Target Volume (PTV). All volumes were manually segmented by a radiation oncologist who included in the GTV all the macroscopic disease seen at CT, in the CTV the GTV plus a margin for sub-clinical disease and in the PTV, the CTV plus of a 0.5 cm safety margin. Totally 242 radiomic features: First order, 3D Gray Level Co-occurrence Matrix and Three Orthogonal Planes-Local Binary Patterns, were extracted with an inhouse developed MATLAB code. For features selection, we ran a wrapper based approach using three machine learning (ML) algorithms; AdaBoost (Ada), Decision Tree (DT) and Random Forest(RF). In the classification stage, the same ML algorithms were used.

Results: Totally 9 different experiment were performed, combining three ML algorithms and three segmentations for each patient. Performance was evaluated through accuracy and AUC. We obtained the following results: Ada-GTV:70.1%,70.1%, Ada-CTV:83.5%, 82.8%, Ada-PTV:71.1%,70.1%, DT-GTV:70.1%, 70.1%, DT-CTV:60.8%,61.1%, DT-PTV:63.9%,64.1%, RF-GTV:73.2%,71.8%, RF-CTV:78.4%,77.3%, RF-PTV:77.3%,76.6%.

Conclusion: Results reported an accuracy of 83.5% and an AUC of 82.8% in predicting the OS. The best result was obtained with the intermediate segmentation, which includes margin for sub-clinical disease and increases the prediction accuracy. This result could be the first try to change the knowledge about the segmentation step in radiomics. The result showed that it is possible to predict the OS of patients giving the opportunity to change treatment options. Moreover, it showed some aspects of relevance for segmentation.

CO040

STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN UNRESECTABLE LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (LA-NSCLC): THE DISCOVERY OF A PRECIOUS TREASURE INTHE BOTTOM OF PACIFIC TRIAL

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Purpose: In this trial we report feasibility and safety of extreme hypofractionated stereotactic body radiotherapy (SBRT) in locally advanced non-small cell lung cancer (LA-NSCLC) patients (pts) treated with radical intent based on PACIFIC trial.

Methods: Between June 2015 and December 2019, 50 unresectable and unfit to concurrent chemo-radiotherapy (ChT-RT) LA-NSCLC pts were recruited in a phase II trial of extreme hypofractionated SBRT. Neoadjuvant ChT was prescribed only in fit pts. After PACIFIC trial, pts who had not progression of disease after ChT and SBRT, received immunotherapy with Durvalumab as consolidation therapy. From September 2018 Durvalumab was administered only if block programmed death-ligand 1 (PD-L1) was expressed in > 1% of tumor cells. The gross tumor volume (GTV) included primary tumor (GTV-T) and CT-PET positive node/s (GTV-N). The co-primary study endpoints were

local control (LC) and safety. Co-secondary endpoints were thoracic nodal-recurrence (tnR) free survival, distant-progression free survival (d-PFS) and overall survival (OS).

Results: Of 50 enrolled patients, 19 (38%) received also neoadjuvant ChT and 6 (12%) Durvalumab as consolidation therapy. Considering only the sub-group of Durvalumab patients, cancer stage was IIIA and IIIB in 5 and 1 case, respectively, 3 and 3 had squamous cell carcinoma (SCC) and adenocarcinoma (ADK). All cases had PTV overlapping the major airways. Median prescribed dose was 45 Gy (range, 40-50) and 40 Gy (35-45) in 5 fractions to GTV-T and GTV-N, respectively. Median PTV was 95 cc (range, 55-139). At a median follow-up of 27 months (range, 6-31), only 2 pts had experienced local recurrence (LR) and discontinued Durvalumab 9 months after SBRT. They had a IIIA and IIIB stage, an ADK and a SCC, submitted to 50 Gy and 40 Gy, and 40 Gy and 35 Gy to T and N, respectively. At last follow-up, all patients were alive, 2 started ChT after local recurrence and 4 are continuing Durvalumab in absence of disease progression. No patient developed distant metastases. The median duration of Durvalumab administration lasted for 8 months (range, 4-24) in all patients and 15 months (range, 4-24) in no progressive patients. No adverse events of ≥G3 grade was recorded.

Conclusions: Although our experience is limited to a small number of cases, extreme hypofractionated SBRT and Durvalumab in LA-NSCLC resulted feasible, safe and effective. This association should be verified in other studies and could represent a precious treasure in the bottom of PACIFIC trial for selected unresectable LA-NSCLC pts.

CO041

MOLECULAR SUBTYPE IMPACT ON LOCAL CONTROL IN 1325 CONSECUTIVE EARLY STAGE BREAST CANCER PATIENTS TREATED WITH HYPOFRACTIONATED ADJUVANT RADIOTHERAPY WITHOUT BOOST

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Aims: Intrinsic subtypes of breast cancer (BCa) decisively influence the evolution of disease and have a very important role for systemic therapy recommendations. This is to report the molecular subtype impact on 1325 consecutive early BCa pts treated with whole breast hypofractionated (WBH) adjuvant forward-planned intensity modulated radiotherapy (F-IMRT) without boost after breast conservation surgery (BCS).

Methods and Materials: From 02/2009-05/2017 1325 pts with pTis-pT2, pNx-N1a(≤ 3 positive lymph-nodes)cM0 BCA who underwent BCS were treated with WBHF-IMRT, to a total dose of 40 Gy/15 fr delivered in 3 weeks, without boost. Median age was 62 (interquartile range-IR-:51.14-70.53) years. Histology was: 8% of pts had ductal carcinoma *in situ* (DCIS), 8.8% invasive lobular carcinoma (ILC), 72.5% invasive ductal carcinoma (IDC), 3.2% invasive mixed carcinoma (ILC+IDC), and 7.5% other histology. Molecular subtypes were: 45.9% Luminal A, 30.4% Luminal B Her 2 neu negative(-), 5.7% Luminal B Her 2 neu positive(+), 3.3% Erb 2 overexpression, and 6.5% Triple negative. In two patients only the presence of hormonal receptors was available (0.2% RO+). Ductal carcinoma in situ (8%), being non-invasive, was analyzed as it is. Chemotherapy (CT) was prescribed in 28% of patients, hormonal therapy in 80.3%, monoclonal antibodies (MAb) in 86.8% of Luminal B Her 2 neu+ and 97.7% of Erb B 2 overexpression pts (4 refused MAb, others had comorbidities).

Results: Median follow up was 72.43 (IQR: 44.63-104.13) months. The 5-year Kaplan-Meier estimates of local-, regional-, distant-relapse-free survival and overall survival (OS) were: 97.8%, 98.6%, 96.6% and 95.5% respectively. When considering molecular subtypes, the 5-year local relapse-free survival was: 99.8% for Luminal A, 96.7% for Luminal B Her 2 neu-, 94.1% for Luminal B Her 2 neu+, 87.9% for Erb B2 overexpression, 95.1% for Triple negative and 99.1% for in situ carcinoma, respectively.

Conclusion: While the overall estimated probability of local relapse within 5 years of 2.2% after WBHF-IMRT without boost is good, molecular subtype has a strong impact on estimated probability of local relapse - with good results for Luminal A, Luminal B Her 2 neu- and DCIS pts (0.2%, 3.3% and 0.9%, respectively), but insufficient for Luminal B Her 2 neu+ and Erb B2 overexpression (5.9% and 12.1%), despite MAb therapy, and for Triple negative pts (4.9%)- and should be used as a parameter to decide the boost prescription.

CO042

LOW DOSE TO HEART SUBSTRUCTURES AND HEART DAMAGE RELATIONSHIP: ANALYSIS OF SAFE TRIAL (NCT2236806)

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Aims: Risk of cardiovascular comorbidities increase with adjuvant radiotherapy in breast cancer patients (ARBC). Patients undergoing ARBC in SAFE trial in our Radiation Oncology Unit aimed to reduce cardiovascular morbidity and based on periodic follow

up with heart speckle tracking ultrasound US. Our aim is to evaluate the relationship between dose received by heart substructures and occurrence of subclinical heart damage.

Methods: 17 left sided BC patients are included in this analysis. The cardiac substructures were delineated according to a pre-existing contour guideline and with 3d conformal radiotherapy (3dCRT). We extracted data on, Dmax, Dmean D2% and D98% and then obtained the doses for the whole heart (WH) and each of the four heart chambers. While for left ventricle, the doses for each component were collected: Anterior (Ant), Lateral (Lat), Apical (Api), Inferior (Inf) and Septal (Sep). Follow up was expected at 6, 12 and 24 months from enrollment by 2D and 3D echocardiographic, evaluating the variations of ejection fraction of the 3D left ventricle (LVEF), final diastolic volume index (EDVI), volume index final systolic (ESVI) and global linear deformation (GLS) between the baseline and the latest US available. For predict a possible subclinical cardiac damage, we had calculated curves of the recipient operator (ROC) to evaluate the accuracy of the different doses for each of cardiac substructure.

Results: A significant variation in 3D LVEF, EDVI, ESVI and GLS observed in 12, 9, 9 and 8 patients, respectively. 3d LVEF was significantly conditions by LV D98%, Lat D2%, Inf D98%, Inf Dmean, Lat Dmean and Lat Dmax. A significant impact on EDVI and ESVI was found for WH Dmean, WH Dmax, RV Dmean, RV D98%, RV D2%, RA Dmean, Lat Dmean, Inf Dmean, Sep D98%, Api D98%. GLS was affected only by LA Dmax. Dose significantly related to decrease in 3D LVEF, EDVI, ESVI and GLS are also reported (Table 1).

Conclusions: We showed a significant correlation between dosimetry data and early subclnical cardiac toxicity. Further analysis are warranted within the context of SAFE trial.

Table 1.

Receiver Operator Characteristics curves results for parameter significantly associated to heart function deterioration

Parameter	Outcome	Sensibility	Specificity	Dose	p
LV D98%	3D LVEF	75%	100%	≤48 cGy	0,006
Lat Dmean	3D LVEF	66,7%	100%	≤139,3 cGy	0,013
	EDVI	88,9%	71,4%	≤182,cGy	0,04
	ESVI	88,9%	71,4%	≤182,cGy	0,04
Lat Dmax	3D LVEF	91,7%	75%	≤649,7 cGy	0,018
Lat D2%	3D LVEF	91,7%	75%	≤481 cGy	0,002
Inf Dmean	3D LVEF	66%	100%	≤56,2 cGy	0,013
	EDVI	88,9%	71,4%	≤ 57,4	0,01
	ESVI	88,9%	71,4%	≤ 57,4	0,01
Inf D98%	3D LVEF	83,3%	75%	≤67 cGy	0,015
WH Dmean	EDVI	77,8%	85.7%	≤135,9cGy	0,01
	ESVI	77,8%	85.7%	≤135,9cGy	0,01
WH Dmax	EDVI	77,8%	85.7%	≤3849,3 cGy	0,0015
	ESVI	77,8%	85,7%	≤3849,3 cGy	0,015
RV Dmean	EDVI	55,6%	100%	≤125,4 cGy	0,02
	ESVI	55,6%	100%	≤125,4 cGy	0,02
RV D98%	EDVI	66,7%	85,7%	≤ 50 cGy	0,01
	ESVI	66,7%	85,7%	≤ 50 cGy	0,01
RV D2%	EDVI	77,8%	85,7%	≤338,37 cGy	0,02
	ESVI	77,8%	85,7%	≤ 338,37	0,02
RA Dmean	EDVI	77,8%	83,3%	≤44,5 cGy	0,03
	ESVI	77,8%	83,3%	≤44,5 cGy	0,03
Sep D98%	EDVI	100%	71,4%	≤ 70 cGy	0,002
	ESVI	100%	100%	≤ 70 cGy	0,002
Api D98%	EDVI	55,6%	100%	≤ 63 cGy	0,04
	ESVI	55,6%	100%	≤ 63 cGy	0,04
LA Dmax	GLS	100%	62,5%	≤ 123,8 cGy	0,02

CO043

DEEP BREATH INSPIRATION HOLD RADIOTHERAPY. OUR EXPERIENCE OF ORGAN PRESERVATION

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Aims: To match treatment planning in free breathing (FB) vs deep inspiration breath hold (DIBH) for patients with left side breast cancer valuating dosimetric difference to heart, left anterior descending artery (LAD) and ipsilateral lung .

Methods: Fifty patients with left breast carcinoma and candidate to radiotherapy were enrolled consecutively from 01/12/2018 to 30/06/2020. A CT scan in FB, the study of respiratory motion and then a DIBH TC were performed for all patients. During DIBH TC it was used SentinelTM to have a reference surface. Gating window was initially defined as 4 mm and then personalized on respiratory study. For visual feedback of the breathing position, the patients wear video glasses Epson Moverio BT200. During DIBH treatment it was used CatalystTM and portal imaging with iViewTM to evaluate target position. Tangential fields were used with field in field technique to optimize the dose distribution. Hypofractionated schedule of 20 fraction was used. Medium dose, V25, V10, V5 of heart, average dose and V20 of LAD, V20,V10, V5 of ipsilateral lung were valuated. A subgroup analysis of respiratory cycle excursions was done in order to identify a population with a possible benefit. It was considered variation of β/α (α=max excursion FB; β=min excursion DIBH) choosing arbitrarily a cut-off of 3.5. The time of the individual sessions for each patient was calculated and analysed at the start and 4 time until the end of treatment.

Results: All 50 patients were treated with DIBH with good compliance and no interruption. The mean heart dose was 2.72 Gy in FB vs 1.35 Gy in DIBH with an average reduction of 50%. The mean LAD dose was 12.18 Gy in FB vs 4.62 Gy in DIBH with an average reduction of 62%. Analyzing DVHs the mean values of V5, V20 and V25 at the heart and V20 at the LAD were decreased with the DIBH vs FB. The exposure of the ipsilateral lung dose were analyzed. The analysis by subgroup showed that 12 patients had an excursion with a $\beta/\alpha<3.5$ related to variation of dosimetric parameters at the heart (V20 and V25) and LAD (Dmax and V20) not statistically significant. The timing analysis shows a decreasing execution mean time (from 23 min at T1 to 10 at T4).

Conclusions: DIBH is an excellent heart-saving technique, allowing adequate coverage of the target and without major obstacles in timing management in a modern radiotherapy department

CO044

DOSIMETRIC IMPACT OF DIBH IN LEFT SIDED WHOLE BREAST RADIOTHERAPY

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Purpose: Late cardiac toxicity induced by whole breast radiotherapy (WBRT) is now recognized as rare but relevant sequelae. The aim of this work is the evaluation of the dosimetric impact of deep inspiration breath hold (DIBH) in cardiac and lung dose reduction.

Materials and Method: Patient selection included women undergoing WBRT after lumpectomy for left sided breast cancer. The respiratory gating systems were optical surface scanning devices: Sentinel for simulation and Catalyst HD for treatment. Respiratory signal has been monitored in the lower part of the sternum at the height of the xiphoideus process. The chosen gating window was between 3-5 mm. The patient training was carried out with electronic eyeglasses (video coaching). Only patients (pts) able to follow the training to find their individual deep inspiration level and to retain breathing for at least 20 seconds have been included. Pts underwent CT simulation in the supine position with the acquisition of both Free Breathing (FB) and DIBH image sets. Contouring and treatment planning were realized on both CT studies with Monaco TPS. From March 2019 to May 2020, 59 pts (median age: 54 years, range: 24-74) successfully completed DIBH simulations. Fifty-two pts were treated with 40 Gy in 15 fractions (fr) and 7 patients with 50 Gy in 25 fr. The following dosimetric parameters were evaluated and compared for statistically significant differences using the Wilcoxon-Test in both FB and DIBH plans: mean heart dose (MHD), D2cc and V13, left mean lung dose (MLD) and V18 in hypofractionation or V20 in conventional treatments.

Results: For 7 patients treated with standard fractionation, 2 plans were realized with VMAT modality and 5 with 3DCRT planning. For 52 patients treated with hypofractionation, 7 plans were realized with VMAT modality and 45 with 3DCRT planning. All cardiac dosimetric parameters were significantly improved with DIBH in all patients: MHD and D2cc decreased of 33% (1.39 Gy FB vs 0.87 Gy DIBH; $p<0.0001$) and 55% (19.48 Gy FB vs 7.96 Gy DIBH; $p<0.0001$) respectively. For left MLD the average dose reduction was 3% with DIBH ($p=0.014$). Pts treated with VMAT modality experienced a significantly larger reduction in MLD (12%).

Conclusions: DIBH with surface tracking systems results to be an effective option for cardiac dose sparing. This benefit could potentially reduce long term major coronary events. Clinical correlations are expected.

CO045

INDICATORS OF RISK OF ADDITIONAL POSITIVE AXILLARY NODES IN BREAST CANCER PATIENTS WITH POSITIVE SENTINEL NODE BIOPSY AFTER NEOADJUVANT CHEMOTHERAPY

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Aim: To develop a nomogram based on preoperative tumor features to assess the probability of having additional positive nodes in the axilla in case of positive sentinel node (SLN) after neoadjuvant chemotherapy (NAC) in breast cancer (BC) patients. The question is whether in patients with positive SLN biopsy axillary dissection (ALND) can be safely avoided in favor of axillary radiotherapy (RT), based on the expectation of low residual nodal burden.

Methods: From 2000 to 2015, 689 BC patients treated with NAC followed by surgery were retrieved from our Breast Cancer database. BC stage included cT1-cT3, cN0-N1 M0. All patients had received SLN biopsy and the study population consisted of subjects with positive SLN biopsy who underwent ALND (n° 220). The dissected axilla was analyzed and patients were separated into those with (ypN+) and without (ypN0) residual nodal disease. The variables associated with pre-chemotherapy tumor biology and the presence of additional positive axillary nodes were analyzed in order to build the risk framework. In addition, the axillary levels involved were identified in order to suggest the extension of axillary RT according to risk categories. The study was notified to the Ethical Committee (nr725).

Results: Risk stratification based on biomolecular, histopathologic and clinical variables is provided. The ongoing analyses are briefly described. Overall, 92 (41.8%) patients with positive SLN have additional nodal metastases at ALND. The positive SLN was micrometastatic, macrometastic, or with isolated tumor cells in 38 (17.3%), 177 (80.5%) and 5 (2.2%) of the

cases, respectively and according to the above classification s the rate of further axillary nodes was 12 (31.6%), 77 (43.5%) and 3 (60%) respectively. There was no difference in the percentage of additional positive axillary nodes between women younger or older than 40 years old. Additional involved nodes were seen in 28 (45.9%) of the Luminal A, in 2 (22.2%) of the triple negative, in 32 (42.7%) of the Luminal B Her2 negative, in 8 (15%) of the Luminal B Her2 positive, and in 7 (50%) of negative hormonal status Her2 positive patients.

Conclusion: A nomogram is under way to help the decision-making on axillary treatment, especially in case of SLN low-volume disease, while waiting for the randomized trials. Analysis on the involved axillary levels may give useful information on the extent of the RT (limited to the I-II levels or enlarged to include the III-IV levels).

CO046

IDENTIFICATION OF PATIENTS AT HIGH RISK OF RECURRENCE AFTER MASTECTOMY WITHOUT RADIOTHERAPY FOR BREAST CANCER T1-2 N0-1

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Aims: Postmastectomy radiotherapy (PMRT) reduces the risk of locoregional relapses and improves overall survival in breast cancer (BC) patients. PMRT is highly recommended in T3/4, ≥4 positive nodes, and positive resection margins. To date, there are no consensus on PMRT in pT1-2 N0-1. The aim of this study is to identify patients presenting pT1-2 N0-1 who could benefit from radiation therapy due to the high incidence of relapse after mastectomy alone.

Methods: BC patients with pT1-2 N0-1 who underwent mastectomy from 1998 to 2008 in our centre were retrospectively evaluated. None of them received PMRT. This study was approved by the internal review board/ethics committee. A number of variables were considered to build the risk frame: age, first degree family history, breast/ovarian cancer, tumor size, grade, histology, peritumoral vascular invasion, molecular subtype, type of systemic therapies. The study endpoints consisted of ipsilateral breast tumor recurrence (IBRT) and Cancer specific survival (CSS). Cumulative incidence functions were estimated according to Kalbfleisch and Prentice while Gray's test was used to test difference of the cumulative incidence between patients' subgroups.

Results: 2387 BC patients were identified: 1306 BC patients with pT1-2 N0 and 1081 BC patients with pT1-2 N1. Median follow-up time was 8.2 years in pT1-2 N0 and 7.7 years in pT1-2 N1. The 5-year and 10-year IBRT rates were 2.7% (95% CI 1.9-3.7) and 5.6% (95% CI 4.3-7.1) in the node-negative group. Very young age (<35) and PVI increased 10-year IBRT rates (14.6%, 95% CI 7.3-24.4 and 10.0%, 95% CI 6.2-15.5). These factors were also associated with lower 10-year CSS (<85%). The 5-year and 10-year IBRT rates were 4.5% (95% CI 3.4-5.9) and 7.7% (95% CI 6.0-9.6) in the nodal positive group. Again, statistical analysis showed that very young age increased significantly the 5-year and 10-year IBRT rate (9.8%, 95% CI 4.5-17.4 and 17.0%, 95% CI 9.6-27.3). Triple negative presented significantly worse outcome (p=0.004). CSS was significantly reduced in presence of pT2 (p=0.005),G3 (p<0.0001), PVI (p=0.001), triple negative BC (p<0.0001) and in those who did not received hormone therapy (p=0.0002) or received chemotherapy (p=0.01).

Conclusions: Waiting for the results of the SUPREMO, the study has identified additional risk factors which increased relapse rate and which might require PMRT to improve the outcome.

CO047

SKIN TOXICITY FOLLOWING RADIOTHERAPY IN PATIENTS WITH BREAST CARCINOMA: IS ANTHOCYANIN SUPPLEMENTATION BENEFICIAL?

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Aims: The ATHENA project, stems from an observational study suggesting that moderate wine consumption reduced the side-effects of radiation therapy. And we evaluate the role of anthocyanins in the prevention of RT skin side effects in breast cancer patients.

Methods: A randomized, controlled, double-blinded clinical trial was designed.The patients received either a forward planned intensity modulated radiation thera-

py(IMRT) for 3 weeks (40 Gy + 4 Gy simultaneous boost, over 16 fractions), or for 5 weeks (50 Gy + 10 Gy simultaneous boost, over 25 fractions).Each patients was separated randomized to receive three times a day a dose (125 mg anthocyanins) of water-solubleextract of corncob, in anthocyanins (test treatment) or not (placebo). The supplementation startedone week before and lasted untill the end of RT. Skin characteristics were detected in the irradiated breast areas by a standardized, non-invasive instrument (Cutometer® dual MPA580) which provides quantitative indices of skin maximal distensibility (R0), elasticity (R2, R5, R7) and viscoelasticity (R6). The Mexameter® MX18 probe evaluates the skin colors erythema (Er) and melanin (M). All measures were performed before (T0), at the end, and 1, 6 and 12 month safter RT (T1-T4). Acute and late skin toxicity were also grade according to the RTOG/EORTG scoring scale.

Results: 193 patients were randomized to either anthocyanin (97) or placebo (96) supplementation; 74 and 119 of them had been previously assigned by clinical criteria to 3- or 5-week RT schedules, respectively. RT induced different changes in skin parameters: R0, R2, R5 and R7 decreased, while R6 increased; the changes in R0 and R6 continued in the same direction up to one year, while the other parameters recovered towards basal values; Er and M peaked at T1 and T2, respectively, and returned to basal values at T4. Similar skin changes were reported in the anthocyanin and placebo groups; acute and late skin toxicity by RTOG/EORTG scores confirmed no difference between the two supplementation arms.

Discussion and conclusion: Our study did not show a beneficial effect of anthocyanin. The cutometer-mexameter, used for the first time in this type of study, documented the skin response to RT and may be proposed as an objective and quantitative marker of skin toxicity in response to a stress condition such as RT and of the potential modulation by an anthocyanins.

CO048

ACCELERATED PARTIAL BREAST IRRADIATION (APBI) USING 3D CONFORMAL RADIOTHERAPY (3D-CRT): SINGLE-CENTRE EXPERIENCE WITH LONG-TERM FOLLOW-UP

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Aims: To evaluate long-term local and nodal recurrence, survival (OS), late toxicity profile of a consecutive cohort of patients with low-risk stage I breast cancer, treated with APBI delivered to the lumpectomy cavity, after breast-conserving surgery (BCS). Our previous paper, published in 2013, evaluated cosmetic outcome and APBI toxicity. We report our experience, with extended follow-up.

Table 1. Eligibility criteria and Patient, tumor and treatment characteristics.

Eligibility criteria	
Post-menopausal woman	
≤3 cm invasive ductal carcinoma	
Absence of an extensive intraductal component (EIC).	
No skin involvement, and no Paget's disease of the nipple	
Surgery consisting of a wide local excision with negative surgical margins by at least 2 mm	
Negative sentinel node biopsy and/or axillary dissection	
The placement of radiopaque surgical clips delineating the extent of the lumpectomy cavity. A total of 6 clips were positioned after tumor removal delineating the planes of an ideal cube representing the surgical cavity.	
Patient, tumor and treatment characteristics	
Variable	**Number (%)**
Age	
Median Age (years)	66 (range 51-87)
Breast side	
Left	37 (44)
Right	46 (55)
Bilateral	1 (1)
pT Stage	
pT1mi	4 (4.8)
pT1a	9 (11)
pT1b	32 (38.1)
pT1c	38 (45.2)
pT2	1 (1.2)
Histology	
Ductal N.O.S.	72 (85.7)
Mucinous	7 (8.3)
Tubular	3 (3.6)
Intracystic papillary	2 (2.4)
Grading	
1	30 (35.7)
2	34 (40.5)
3	18 (21.4)
not available	2 (2.4)
Tumor estrogen receptor status	
Positive (≥1%).	84 (100)
Radiation dose	
34 Gy	60 (71.4)
38.5 Gy	24 (28.6)
Endocrine therapy	83(98.8)
Chemotherapy	0

Methods: Between 2005 and 2011, a total of 84 women were treated with 3D-CRT APBI. Eligibility criteria of APBI, patients, tumor and treatment characteristics are shown in Table 1. The prescribed dose was 34/38.5 Gy delivered in 10 fractions twice daily over 5 consecutive days. Four to 5 no-coplanar 6MV beams were used; 3D-CRT was performed in accordance with the technique and dose-volume constraints specified in the NSABP/RTOG protocol. Late toxicity was evaluated according to the RTOG grading scale.

Result: Median patient age was 66 years (range 51-87). Median follow-up was 120 months (range 24-180). The incidence of skin late toxicity was: G1 16.7%, G2 2.4% and G3 3.6%. The most pronounced G2 late toxicity was telangiectasia in 3 cases; moderate fibrosis was observed in 4.8% cases. Radiological evidence of fat necrosis, in absence of any clinical symptom, was detected in 70% of cases. In 1 patient we observed recurrent breast abscesses (fat necrosis area), clinically evident 12 years after the end of the treatment. Actuarial 5-year overall (OS), cancer-specific (CSS) and disease-free survival (DFS) were 92.8%, 98.5% and 96%,

respectively. Ten-year OS, CSS and DFS were 82%, 98.5% and 94%, respectively. Three patients developed loco-regional recurrence (LRR): 1 in breast (out-of RT field), 1 in regional nodes, 1 in both sites (out-of RT field), [time range: 37-99 months]. In these patients salvage radical surgery was performed and they are currently alive with no evidence of disease. All relapses were observed in patients who received a radiation dose of 34 Gy. One patient had bone metastases, without LRR, 16 months after the end of RT.

Conclusion: Our clinical results support the use of APBI as a safe and effective RT option in patients at low risk of relapse submitted to BCS. Long-term oncological outcomes are in line with those reported in the literature. Furthermore, we'll update our data taking in account new patients, new RT techniques and biological features.

CO049

PRE-TREATMENT PRIMARY TUMOR STAGE IS A RISK FACTOR FOR RECURRENCE IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA AND ADENOCARCINOMA WHO ACHIEVE PATHOLOGICAL COMPLETE RESPONSE AFTER NEOADJUVANT CHEMORADIOTHERAPY

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Aims: Although pathological complete response (pCR) after multimodal treatment for esophageal cancer (EC) is associated to the best prognosis, recurrence may occur in 20-40% of cases. The present study aims at investigating recurrence pattern and predictive factors of recurrence after pCR in patients with esophageal cancer.

Methods: 427 patients received preoperative treatment for either esophageal squamous cell carcinoma (SCC) or adenocarcinoma (AC) at our Center between 2000 and 2018; of these, 145 patients (34%) achieved a pCR. Long-term prognosis, recurrence pattern and risk factors for relapse in pCR patients were analysed.

Result: During a median follow-up of 52 months, 37 relapses (25.5%) occurred, mostly at distant level (28/37, 75.7%). Nearly all loco-regional relapses (8/9, 88.9%) were detected in SCC cases. The 5-year Overall Survival (OS) and Cancer Related Survival (CRS) were 71.7% (95% CI 62.6-78.9%) and 77.5% (95% CI 68.5-84.2%) respectively. Male sex, higher BMI, and cT4 were significant risk factors for recurrence at univariate analysis. The multivariate analysis confirmed the role of cT4 as predictor of recurrence in both SCCs and ACs.

Conclusion: Esophageal cancer recurs in about one fourth of pCR cases. A fair number of local recurrences occurs in SCCs, but the main problem is the systemic disease control. According to our analysis patients with cT4 stage have an increased risk to recur, so they should be differently managed by a personalized approach in terms of adjuvant treatment and follow-up.

Table 1. Multivariate analysis for recurrence risk factors in pCR population.

Parameter	HR	95% CI	P value
Age (per 10 year increase)	0.89	0.49-1.63	0.714
Histotype (SCC vs AC)	0.71	0.26-1.92	0.501
BMI (over vs normoweight)	2.34	0.82-6.63	0.109
cT (T4 vs T1-3)	3.14	1.07-9.18	*0.037**
cN (N+ vs N-)	0.97	0.34-2.78	0.950

Hazard Ratios (HR) were derived by Cox regression model. P values were computed by the Wald test. BMI: Body Mass Index; HR: Hazard ratio; CI: Confidence Interval. *indicate significant correlation

CO050

HYPOFRACTIONATED STEREOTACTIC BODY RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST AND SIMULTANEOUS INTEGRATED PROTECTION IN PANCREATIC DUCTAL ADENOCARCINOMA

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Aims: To evaluate the safety and feasibility of stereotactic body radiation therapy (SBRT) with simultaneous integrated boost (SIB) and simultaneous integrated protection (SIP) in borderline resectable (BR) and locally advanced (LA) pancreatic ductal adenocarcinoma (PDAC).

Methods: Patients receiving SBRT following induction chemotherapy from January 2017 to December 2018 were included in this observational analysis. SBRT was delivered in 5 consecutive daily fractions by administering 30 Gy to the planning target volume (PTV) while simultaneously delivering a 50 Gy SIB to the tumor-vessel interface (TVI). SIP was created by lowering the dose to 25 Gy on the overlap area between the PTV and the planning organ at risk volume. Primary endpoint was acute and late gastrointestinal grade ≥ 3 toxicity. Secondary endpoints were freedom from local-progression (FFLP), overall survival (OS) and progression-free survival (PFS).

Results: Fifty-nine consecutive patients (27 BRPC and 32 LAPC) were evaluated, with a median follow-up time of 15.1 months. Fifty-eight patients (98.3%) completed the SBRT planned treatment and 35 patients (59.4%) received surgical resection after SBRT. No acute or late grade ≥ 3 adverse events SBRT-related were observed. 1-/2-year FFLP rates were 85% / 80% versus 79.7% / 60.6%, in resected versus non-resected patients, respectively (p=0.33). Median OS and PFS were 30.2 months and 19 months from diagnosis and 10.2 months and 10 months from SBRT, respectively, for the entire cohort. Resected patients had improved 2-year OS rate (72.5% versus 49%, p=0.012), and median PFS (13 months versus 5 months; p < 0.001), respectively, compared with non-resected patients. There was no survival difference between the BRPC and LAPC patients.

Conclusions: The SBRT with SIB/SIP had an excellent toxicity profile and could be administered safely on PC patients, even in a total neoadjuvant setting.

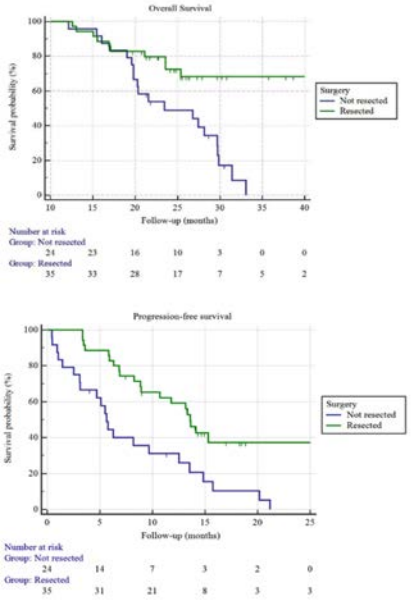

Figure 1. Kaplan-Meier survival curves show overall survival from diagnosis (a), and progression-free survival from SBRT (PFSsbrt, b).

CO051

CHEMORADIOTHERAPY IN UNRESECTABLE BILIARY CANCERS: A SYSTEMATIC REVIEW

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Aim: In advanced biliary tract cancer, international guidelines recommend the use of chemotherapy alone as a primary option. The role of concurrent chemoradiation is still being discussed. The aim of this report was to perform a systematic review on concurrent chemoradiotherapy for unresectable, non-metastatic biliary tract cancers.

Materials and Methods: A literature research based on Pubmed, Scopus, and Cochraine Library was performed. Only English-written papers published over the last 12 years (from 2008 to July 2020) were screened. Only papers separately reporting outcomes after concurrent chemoradiation in unresectable biliary cancers were included in the analysis.

Results Fourteen papers for a total of 1766 patients with primary or locally recurrent unresectable biliary tract cancers were included in the analysis. Median radiotherapy (RT) dose ranged from 45 to 72.6 Gy, with conventional fractionation. Chemotherapy schedules were different. Median follow-up ranged from 9 to 27.6 months. From the analysis of selected studies median overall survival and progression-free survival were 13.5 and 8.1 months, respectively.

Conclusions Concurrent CRT is a safe and effective option in unresectable BTC with results almost comparable to the standard approach, based on chemotherapy alone. Moreover, a significant benefit compared to chemotherapy alone was recorded in three trials included in our analysis. Few data are available about the potential advantages of modern IGRT techniques. Prospective randomized trials directly comparing systemic and local treatments are still lacking.

Table 1. Outcomes.

Reference, year	Median FU (months)	Median OS (months)	1-Year OS (%)	Median PFS (months)	1-Year PFS (%)	Tumour Response Evaluation	Acute Toxicity G≥3, % (scale)	Local Control (LC)
Hong et al, 2020[21]	16 (3-36)	20.6	NR	12.1	NR	NR	HE 21.7 (CTCAE 4.0)	1Year LC 88%
Sebastian et al, 2019[22]	17	14 (11-20)	NR	NR	NR	NR	NR	NR
Verma et al, 2018[23]	9 (0-123) *	12.9 (11.0-14.7)	NR	NR	NR	NR	NR	NR
Bisello et al, 2018[24]	NR	13.5	58.1 2Y-OS 25.8	10	43.4 2Y-PFS 9.4	NR	GI 13.2 HE 8.1 (RTOG)	NR
Verma et al, 2017[25]	1003-1141 *	13.6 (12.3-15.7)	NR	NR	NR	NR	NR	NR
Kim et al, 2015[26]	14.2 (2.4-114.6) *	NR †	2Y-OS 52.1	NR †	2Y PFS 53.5		0.0 GI (CTCAE 4.03)	60.9% local and distant failure
Jackson et al, 2016[27]	11.3 *	12.7	2Y OS 25.8	NR	NR	NR	NR	NR
Lee et al, 2016[28]	NRS	9.6 (5.4-30.4)	NR	6.8 (4.5-19.8)	NR	(RECIST) CR 0.0 PR 27.8 SD 72.2	GI 5.6 HE 50.0 (NCI CTC 4.0)	NR
Chen et al, 2015[29]	9.4 (2.4-47.4) *	13.5 (9.6-17.7)	NRS	8.8 (5.2-10.7)	NR	NR	13% all group	NR
Yi et al, 2014[30]	NRS	42.6 (8.3-320.1)	36.8	29.9 (22.9-36.8)	NR	CR 0.0 PR 19.8 SD 69.8 PD 10.4	GI 9.4 HE 21.7 (NCI CTC 3.0)	NR
Philip et al, 2014[31]	27.9 *	13.5 (7.8-22.6)	NR	7.5 (2.8-12.5)	NR	NR	GI 11.8 HE 23.0 (NCI CTC 4.0)	NR
Moureau-Zabotto et al, 2013[32]	12 (1-83)	NRS	66.7± 11.7	NRS	44.4±11.7	NR	(NCI CTC 3.0) GI 22.0 Systemic 15.0 ‡	66% disease progression: 13% local, 30% systemic, 3% both
Habermehl et al, 2012[33]	NR	13.6 (4.0-34.8)	NR	3.1 (2.3-24.8)	NR	NR	NR	66% Local and distant failure
Bainden et al, 2008[34]	NR	13 (3.4-24.2)	NR	Median DFS 10.5 (1.4-22.2)		NR	0.0 (RTOG)	NR

*Legend: CR complete response, DFS disease free survival, FU follow-up, GI gastrointestinal, HE Haematological, NCI CTC National Cancer Institute -Common Toxicity Criteria, NR not reported, OS overall survival, PD progression disease, PFS progression-free survival, PR partial response, RECIST Response Evaluation Criteria in Solid Tumours, RTOG Radiation Therapy Oncology Group, SD stable disease, *all population included in the trial; †median OS all group 18.4 (4.4-114.6); median PFS all group 15.5 (1.6-114.6). patients with OS > 5Y were in CRT group only; ‡ pain, fever, asthenia*

CO052

STEREOTACTIC RADIOTHERAPY VERSUS TRANSARTERIAL (CHEMO) EMBOLISATION IN HEPATOCELLULAR CARCINOMA: A PHASE III TRIAL

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Background: Hepatocellular carcinoma (HCC) is the most common primary liver tumor and the third cause of cancer death in the world. In unresectable HCC patients with intermediate-stage disease, transcatheter arterial (chemo-)embolization (TAE/TACE) has shown partial responses in 15–55% of cases. Though multiple TAE/TACE can be administered in principle, Stereotactic body radiotherapy (SBRT) emerged as an alternative option in case of local relapse following one or more TAE/TACE courses.

Methods: This a multicentre, prospective, randomised controlled, unblinded, parallel-group superiority trial of SBRT versus standard TAE/TACE for the curative treatment of intermediate stage of HCC after incomplete response following one TAE/TACE cycle (NCT02323360). Primary endpoint is 1-year Local Control (LC). Secondary endpoints are 1-year Progression Free-Survival (PFS), Distant Metastases-Free Survival (DMFS), Overall Survival (OS) and incidence of acute and late complications.

Results: At the time of our analysis 40 patients were enrolled, 19 (49%) in the TAE/TACE and 21 (51%) in the SBRT arm respectively. One and 2-year LC rates were 57% and 36%. Use of SBRT resulted in superior LC as compared to TAE/TACE (median not reached versus 8 months, p=0.0002). PFS was 29% and 16% at 1 and 2 years, respectively. OS was 86% and 62% at 1 year and 2 years, respectively. No grade >3 toxicity was recorded.

Conclusions: In patients affected by inoperable HCC experiencing incomplete response following ≥1 cycle of TAE/TACE, SBRT was correlated to significantly higher LC rates as compared to rechallenge with TAE/TACE. (NCT02323360; https://clinicaltrials.gov/ct2/show/NCT02323360)

CO053

MODELING OF DOSIMETRIC PARAMETERS FOR TOXICITY REDUCTION OF RADIOTHERAPY IN UPPER GASTRO-INTESTINAL TUMORS - THE MODERATOR STUDY

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Aim: Upper gastro-intestinal (GI) toxicity is a limiting factor in radiation therapy (RT) for abdominal neoplasms. Constraints for treatment planning in abdominal RT mostly derive from scientific publications of pelvic tumors. The aim of our study is evaluate dosimetric and clinical parameters about toxicity outcome in upper GI cancer RT patients (pt).

Materials and Methods: During the first phase we retrospectively analyzed pt with upper GI cancer treated since 2009 to 2018. They may have received 3D-conformal or intensity modulated radiotherapy, with concurrent chemotherapy or not, and after abdominal surgery or not. During the treatment, acute upper GI toxicities were coded according CTCAEv5.0 scale. In all patients stomach, bowel bag (BB), single small bowel loops and liver, were delineated by radiation oncologists on simulation CT. Dose Volume Histograms were extrapolated and analyzed for detecting the Vdose related to organs at risk (OARs) and the impact of further clinical factors that better predict the toxicity rising during the treatment. In the second phase, in order to proceed with the external validation of the developed model, we studied pt treated in a second RT center. They have been selected so that their treatments are consistent with the characteristics of the pt included in the first training dataset.

Results: We analyzed the records of 276 pt. Primary tumors were located in upper GI tract: gallbladder, junction, pancreas, stomach, biliary tract. Median prescription dose was 50.4 Gy with median fractionation 1.8 Gy. The V24 Gy is the best predictor of toxicity. The AUC of ROCs for training and validation sets are respectively 0.731 and 0.771, with not significant difference at De Long test (p-value 0.627). The calibration doesn't show significant deviation for both training and validation sets.

Conclusion: Our analysis shows a strong correlation between toxicity grade and Vdoses on BB. The most significant result is given by the model using V24 Gy for CTCAE toxicity grade ≥ 2. Model prediction can be considered reliable and prediction can be performed by using a specific nomogram.

CO054

PREOPERATIVE RADIOTHERAPY WITH INTENSITY-MODULATED SIMULTANEOUS INTEGRATED BOOST (SIB) FOR LOCALLY ADVANCED RECTAL CANCER: A SYSTEMATIC REVIEW OF PATHOLOGICAL COMPLETE RESPONSE OUTCOME

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Aims: The present review investigates the impact of preoperative radiotherapy (RT) with simultaneous integrated boost (SIB) on pathological complete response (pCR) in locally advanced rectal cancer.

Methods: A systematic review according to PRIS-

MA model was performed. A literature search via PICO in MEDLINE/PubMed and EMBASE databases was independently conducted by two authors in May 2020. The following keywords were used with different arrangements: (P) Rectal cancer/adenocarcinoma, (I) Preoperative/neoadjuvant radiotherapy AND boost/SIB, (O) Pathological complete response. Clinical trials enrolling patients aged >18 years, affected by rectal adenocarcinoma, in clinical stage cT2-T4 cN0-N2 and suitable for preoperative chemoradiation were specifically included. Furthermore, only studies assessing intensity modulated (IMRT/VMAT) RT were included. The primary outcome was pCR; data on survival outcomes, toxicity, sphincter preservation rate and R0 resection were also collected and analyzed.

Results: A total of 64 studies were identified. After the PRISMA-based study selection, 8 clinical trials (prospective/phase II) were included in a qualitative synthesis. A total of 297 patients received preoperative RT to the pelvis with a SIB to the primary tumor. Different daily fractionation schedules were used: total dose to the pelvis ranged between 41.8 Gy (1.9 Gy/fr) and 50.6 Gy (2.3 Gy/fr) while SIB total dose ranged between 55 Gy (2.2 Gy/fr) and 58.75 Gy (2.35 Gy/fr). Different chemotherapy schemes and surgical approaches were admitted. Median follow up in 5 of 8 included studies ranged between 16 and 61 months. Pathological complete response was assessed according to different Tumor Regression Grading scales (Mandard's, Dworak's, ypT0N0 rates), reaching the maximum observed value of 38%. Good survival outcomes (1-, 3- or 5-year DFS, OS) were observed. Sphincter preservation was improved (up to 66%), with a 100% R0-resection rate achieved in 3/4 studies. Satisfactory toxicity profiles were observed, with only one study stopped for G3 toxicity (gastrointestinal, anemia, fatigue, pain).

Conclusion: The encouraging rates of pCR combined with satisfactory toxicity outcomes may support the use of preoperative intensity modulated-SIB to primary rectal tumor in clinical practice. Further considerations on the appropriate timing for post-RT surgery and anatomo-pathological results assessment are still required.

CO055

METABOLOMICS AS POTENTIAL PREDICTION OF NEOADJUVANT CHEMORADIATION TREATMENT RESPONSE IN LOCALLY ADVANCED RECTAL CANCER PATIENTS

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Aims: The identification of biomarkers of tumor response to neoadjuvant chemoradiotherapy (CRT) in locally advanced rectal cancer (LARC) patients is an interesting and promising topic. The feasibility of collecting metabolites from blood without invasive procedures could be well accepted by patients. The aim of our study is to identify potential aminoacids, acyl-carnitines and ceramides able to predict response, in order to personalize treatments.

Methods: Between March 2013 and January 2019, 40 LARC patients were treated with neoadjuvant CRT at the Radiotherapy Department. Sera (7.0 μL) were collected during routine chemistry tests before starting treatment (T0), at day 14 (T14), at day 28 (T28) of CRT and after finish CRT, at day 45 (T45). They were subjected to a targeted tandem mass spectrometry (MS/MS) analysis for the detection of the analytes. Tumor response was evaluated according to Mandard tumor regression grade (TRG).

Results: Twenty-seven reported TRG1-2 and were considered responder patients (RP) whereas the remaining 13 were no-responder (NRP) (TRG3-5). The LC-MS/MS lipid profiling showed that among the analytes, lysophosphatidylcholines (LPC) were identified as variable important for the projection (VIP > 1) and significantly different expressed between NRPs and RPs at T0 (p value < 0.05). Some aminoacids (citrulline, alanine and ornithine) and acyl-carnitines (C18:2OH and C26) also resulted as major discriminant variables. In particular, we focused the attention on 3 out of 4 lysophosphatidylcholines (C20:0-LPC, C22:0-LPC, C24:0-LPC) that were altered in our analysis. These LPCs have good sensitivity and specificity in discriminating from RP group with lower serum levels in NRP before CRT. More interestingly, the same lipidomic study revealed that C22- and C24-ceramides followed their respective LPC trend, due to lower expression in NRP before CRT. Finally, we analysed ceramides at T14, T28 and T45: sphinganine-1-phosphate and sphingosine-1-phosphate increased at T14 only in RP (Table 1). These metabolites are described as important in cell migration, survival and differentiation.

Conclusions: The analysed aminoacids, acyl-carnitines and ceramides resulted able to predict response with lower levels in NRP before CRT (T0). In addition, ceramides levels were increased during CRT (T14) in RP. The potential role of these analytes could permit to personalize treatment. The study is still ongoing in order to validate a larger number of analytes.

Table 1. Aminoacids, acyl-carnitines and ceramides able to predict tumor response between responder and no-responder patients.

	Metabolites	Responder patients	No-responder patients	Time
Lysophosphatidylcholines (LPC)	C20:0-LPC	>	<	T0
	C22:0-LPC	>	<	T0
	C24:0-LPC	>	<	T0
Aminoacids	Citrulline	>	<	T0
	Alanine	>	<	T0
	Ornithine	>	<	T0
Acyl-carnitines	C18:2OH	>	<	T0
	C26	>	<	T0
Ceramides	C22-ceramides	>	<	T0
	C24-ceramides	>	<	T0
Ceramides	Sphinganine-1-phosphate	>	<	T14
	Sphingosine-1-phosphate	>	<	T14

LPC: Lysophosphatidylcholines; >: higher serum levels; <: lower serum levels; T0: before starting treatment; T14: at day 14 during treatment.

CO056

DOES RADIOMIC OF RESTAGING MRI IMPROVE PREDICTION OF PCR AFTER NEOADJUVANT CHEMORADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER?

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Aims: A 18-38% of locally advanced rectal cancer (LARC) reach pathological complete response (pCR) after neoadjuvant chemoradiotherapy (nCRT). Sometimes the clinical response could be uncertain; radiomic features could help in the detection of pCR.The aim of this study is to evaluate the benefit of the addition of radiomic features from restaging magnetic resonance imaging (MRI) to morphological and functional MRI features,endoscopy and digital rectal examination (DRE) information in the prediction pCR in LARC patients (pts) with a near-complete response (nCR) or complete clinical response (cCR).

Methods: We retrospectively evaluated LARC pts who underwent nCRT followed by TME from January 2010 to September 2019 in our institution,with CR and nCR at restaging MRI plus all pCR at surgery.The response to nCRT was established by multidisciplinary tumor board (MTB) considering DRE,T2- and DW-MRI and endoscopy information.Radiomics features selection was done in three steps: Boruta features selection,non-correlated variables with a Pearson correlation value less than 0.9, stepwise logistic regression based on Akaike Information Criterion value.The radiomic model (RM) was compared with a univariate logistic regression with MTB outcome (yMTB). Furthermore,a combined model (CM) was trained including the selected radiomics features and the yMTB covariates.De Long test was performed to assess the differences in terms of performance between the different models.The analyses were conducted for both pCR and Tumor Regression Grade (TRG)1-2 outcomes. Significance level for tests p-value was set at 0.05. All statistical analysis was performed in R version 3.4.

Results: The analyses was conducted on 144 LARC pts (M:89, F:55). 117 (81.2%) and 129 (89.6%) pts obtained pCR and TRG 1-2, respectively.For pCR, yMTB, RM and CM showed an AUC of 81.9, 73.4 and 84.1, respectively. The ROC comparison was not significant (p=0.6) between yMTB and CM. For TRG, yMTB, RM and CM showed an AUC of 80.2, 62.9 and 81.5, respectively. The ROC comparison was not significant (p=0.8) between yMTB and CM.

Conclusions: Radiomics features from post-treatment MRI seems not to add information to current clinical and radiological evaluation,especially when validated and objectified by a MTB.This result could be related to the small residual tumor volume after nCRT.It may be useful,in the future, to investigate if the radiomics features variation before and after nCRT (Delta) may improve MTB evaluation in LARC pts.

Table 1. Patient characteristics.

Age		62 (range 26-82)
Sex	Male	89 (61.80%)
	Female	55 (38.20%)
Clinical T stage	cT1	1 (0.69%)
	cT2	16 (11.11%)
	cT3	97 (67.36%)
	cT4	30 (20.83%)
Clinical N stage	cN0	17 (11.80%)
	cN1	71 (49.30%)
	cN2	56 (38.88%)
Clinical T re-stage	ycT0	63 (43.75%)
	ycT1	10 (6.94%)
	ycT2	47 (32.64%)
	ycT3	18 (12.50%)
	ycT4	4 (2.78%)
Clinical N re-stage	ycN0	102 (70.83%)
	ycN1	37 (25.70%)
	ycN2	5 (3.47%)
ROI yGTV-T		4.95 cc (range 0,1- 42,35 cc; median 2,58 cc)
DRE	Complete Response	25 (17.36%)
	Major Response	38 (26.39%)
	Partial Response	55 (38.19%)
	Unvaluable/Unknown	26 (18.06%)
Endoscopy	Scar	20 (13.89%)
	Ulcer	7 (4.86%)
	Residual disease	10 (6.94%)
	Unvaluable/Unknown	107 (74.31%)
yMTB	3 (Complete Response)	59 (40.97%)
	2 (Major Response)	34 (23.61%)
	1 (Partial Response)	49 (34.03%)
	0 (Non-Response)	2 (1.39%)
Pathologic T stage	ycTx	2 (1.39%)
	ypT0	117 (81.25%)
	ypT1	6 (4.17%)
	ypT2	16 (11.11%)
	ypT3	5 (3.47%)
	ypT4	0
Pathologic N stage	ypNx	32 (22.22%)
	ypN0	103 (71.53%)
	ypN1	6 (4.17%)
	ypN2	3 (2.08%)
Correlation yMTB-stage and pathologic stage	ycT0→ypT0	36 (25%)
	ycT≠0→ypT0	81 (56.25%)
	ycT0→ yp≠T0	27 (18.75%)
TRG	1	114 (79.17%)
	2	15 (10.42%)
	3	12 (8.33%)
	4	1 (0.69%)
	NA	2 (1.39%)

CO057

FACTORS PREDICTING ACUTE AND LATE GASTROINTESTINAL AND GENITOURINARY TOXICITY IN PROSTATE CANCER

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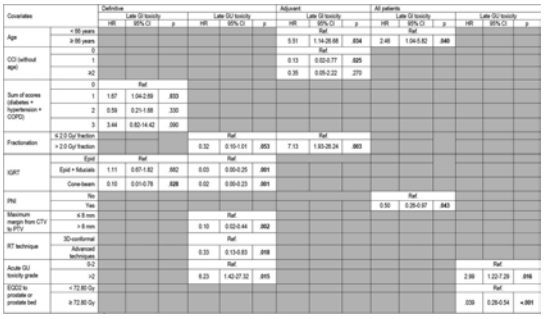
Aims: Radiation therapy (RT) for prostate cancer (PC) can result in gastrointestinal (GI) and genitourinary (GU) toxicity worsening patient's (pts) quality of life. Side effects depend by delivery of RT as well as by pts lifestyle and comorbidities (CO). Literature mainly reports studies evaluating separately impact on RT-induced toxicity. Based on this background, we evaluated in a retrospective observational study the mixed effect of CO and RT delivery on both acute and late GI and GU toxicity in PC.

Methods: We included 1617 PC pts: 1027 underwent definitive RT (dRT), and 590 adjuvant RT (aRT). RTOG-EORTC scales were used for toxicity assessment. We evaluated age, BMI, CO, Charlson Comorbidity Index (CCI), lifestyles and parameters related to RT delivery. Univariate and multivariable analysis were assessed with Chi-square test and logistic regression model, Kaplan-Meier method, and Cox regression model, for acute and late toxicity respectively.

Table 1.



Results: A correlation between greater minimum margin CTV-PTV and lower acute GI toxicity was observed at multivariable model (p<0.001) for dRT pts. Furthermore, multivariable analysis confirmed that age ≥66 years is associated with higher rate of late GI toxicity in the whole cohort of pts (p=0.022) and in the aRT cohort (p= 0.021). A higher dose per fraction (>2.0 Gy) was associated to GI late toxicity G<2 in pts undergoing aRT (p=0.003). A higher incidence of late GI toxicity was also observed in pts undergoing aRT, in case of greater CCI score incorrect for age (p=0.025). The same relation was observed for pts undergoing dRT, with the diabetes-hypertension-COPD score (HR: 1.67, 95% CI 1.04-2.69, p=0.033). Furthermore, for dRT pts late GI toxicity was lower using cone-beam CT (p=0.031). and greater in case of acute toxicity ≥2 (p=0.015). GU toxicity was reduced for dRT pts if treated with IGRT (fiducial markers: p= 0.001 or cone beam CT: p=0.001) or with RT advanced modulated techniques (p=0.018), as well as in case of greater CTV-PTV margin (p=0.002). In the overall population late GU toxicity <2 was observed in case of delivery of ≥72.8 Gy to prostate or prostate bed, while acute GU toxicity G >2 was predictive of late GU toxicity ≥2 (p=0.016).

Conclusion: Our analysis demonstrate that age and comorbidities have a significant impact on RT toxicity for PC, as well as use of IGRT and advanced technique of delivery. On the contrary, significant correlations with lifestyles have not emerged, according to multivariate model.

CO058

A DELPHI CONSENSUS ON SALVAGE STEREOTATIC BODY RADIOTHERAPY FOR INTRAPROSTATIC RELAPSE AFTER PROSTATE CANCER RADIOTHERAPY, AN ESTRO ACROP STUDY

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Aim: Up to 52% of patients treated with definitive radiotherapy (RT) for prostate cancer are at risk of intraprostatic recurrence during their life. Among the different options, including surgery and hormonal therapy, re-irradiation with stereotactic body RT (SBRT) is emerging as a feasible and safe therapeutic alternative in patients with local recurrence. So far, no consensus or guidelines exist on this topic. The purpose of this project, endorsed by the ESTRO ACROP Committee, is to investigate the expert opinion on salvage SBRT for intraprostatic relapse after RT.

Methods: A reviewing committee, a panel of leading radiation oncologists plus an urologist (suggested by EAU society) expert in prostate cancer management, structured and approved a final version of a dedicated questionnaire on the topic. The final version was implemented online and sent to experts on prostate re-irradiation (authors of eminent scientific papers on this topic). The questionnaire included 40 questions divided in three sections: (1) patient selection criteria for prostate salvage SBRT (19 questions); (2) imaging and biopsy-based tests for diagnosis of recurrence (7 questions); (3) dosimetric issues on both clinical target volume (CTV) and organs at risk (OARs) (14 questions). Following the procedure of a consensus, 3 rounds of questionnaires have been sent to the panel. A percentage of 80% agreement has been established as the threshold for reaching the consensus.

Results: Among the 30 contacted authors of studies on prostate salvage SBRT, 18 agreed to participate in the study and to fill in the three rounds of questionnaires. At the end of the 3 rounds consensus was reached in 14/40 questions (35% overall). For instance, in section 1 consensus was found on some criteria for patients' selection (e.g. age, previous hormonal therapy), in section 2 on the number of biopsies needed for partial gland treatment, in section 3 on type of fractionation. For conciseness, the main results are summarized in Table 1.

Conclusion: The main areas where disagreement persists are patients' selection and staging, imaging necessary for diagnosis and dosimetric issues concerning both the CTV and the OARs indicating knowledge gaps for future research. This low consensus suggests that further activities should focus on evidence which supports best practice in order to provide an useful tool to guide the decision-making for salvage SBRT.

Table 1. Summary of most relevant discussion points with the level of agreement

DISCUSSION POINT	RESPONSE	AGREEMENT LEVEL
Section 1 - Patient characteristics and general status		
Age	Not important	Consensus
Previous ADT	No contraindication	Consensus
Maximum T-classification at primary treatment	Any T	Divided opinion
Maximum T-classification at relapse	T2	Divided opinion
Maximum Gleason score at primary treatment	9 - 10	Divided opinion
Maximum Gleason score at relapse	9 - 10	Divided opinion
PSA level at primary treatment	No limit	Divided opinion
PSA level at relapse Maximum level Divided opinion	< 10 ng/dl	Divided opinion
Clinical target volume (CTV)	Gross tumor volume (GTV) plus adaptive margin	Consensus
Section 2 - Diagnostic tests		
Evaluation of metastatic disease	Yes	Consensus
Imaging for metastatic disease evaluation	Choline-PET	Consensus
Biopsy at relapse	Not needed	Divided opinion
Number of biopsies at time of recurrence for whole gland	Between 12 and 18	Major agreement
Number of biopsies at time of recurrence for partial gland	Between 12 and 18	Consensus*
Section 3 - Salvage treatments		
Minimum interval between initial RT and salvage therapy	2 years	Major agreement
ADT delivery concomitantly with re-irradiation	No	Consensus
Primary dose taken into account when planning salvage dose	Always	Consensus
Salvage SBRT fractions	5	Consensus
Dose prescription	At the Isodose	Major agreement
Fractionation schedule	35 Gy - 5 fractions	Divided opinion
Dose level to OARs	Adjusted dose constraints, dependent on previous dose	Divided opinion
Recommendable dose to rectum (first RT + salvage SBRT)	95 - 105 Gy	Divided opinion
Recommendable dose to bladder (first RT + salvage SBRT)	95 - 105 Gy	Divided opinion
Recommendable dose to femoral heads (first RT + salvage SBRT)	No maximum	Divided opinion
Recommendable dose to penile bulb (first RT + salvage SBRT)	No maximum	Divided opinion

List of abbreviations: ADT = androgen deprivation therapy; CTV = clinical target volume; GTV = gross tumor volume; OAR = organ at risk; PET = positron emission tomography; PSA = prostate specific antigen; RT = radiotherapy; SBRT = stereotactic body RT

CONSENSUS	≥ 80%
MAJOR AGREEMENT	65% ≤ x < 80%
DIVIDED OPINION	< 65%

CO059

DOSE ESCALATED PELVIC RADIOTHERAPY FOR PROSTATE CANCER IN DEFINITIVE OR POSTOPERATIVE SETTING, A RETROSPECTIVE STUDY

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Aims: Given the absence of standardized planning approach for clinically node-positive (cN1) prostate cancer, we collected data about use of prophylactic pelvic irradiation and nodal boost. The aim of the present series is to retrospectively assess clinical outcomes after this approach to compare different multi-modal treatment strategies in this scenario.

Methods: Data from clinical records of patients affected by cN1 PCa and treated in 6 different Italian institutes with prophylactic pelvic irradiation and boost on pathologic pelvic lymph nodes detected with CT, MRI or choline PET/CT were retrospectively reviewed and collected. Clinical outcomes in terms of Overall survival (OS) and biochemical relapse free survival (b-RFS) were explored. The correlation between outcomes and baseline features (ISUP pattern, total dose to positive pelvic nodes </> 60 Gy, sequential or simultaneous boost administration and definitive vs postoperative treatment) was explored.

Results: ISUP pattern < 2 and total dose > 60 Gy to positive pelvic nodes were significant predictors of improved b-RFS (HR=0.3, 95% C.I. 0.1220 – 0.7647, p=0.0113 and HR=3.59, 95% C.I. 1.3245 – 9.741, p=0.01, respectively). Conversely, treatment setting (postoperative vs definitive) and treatment delivery technique (SIB vs sequential boost) were not associated with significant differences in terms of b-RFS (HR=0.85, 95% CI 0.338 - 2.169, p = 0.743, and HR= 2.39, 95% CI 0.93 - 6.111, p=0.067, respectively). Overall, one G2 and 1 G3 acute GI toxicities were reported. Two G2 and 1 G3 acute GU toxicities occurred. Only 1 G2 late GU adverse event was recorded.

Discussion: Data from the current analysis confirmed that WPRT and IMRT/VMAT boost on positive pelvic nodes is an effective and promising approach, with limited toxicity, both in postoperative and definitive setting. Interestingly, upfront surgical approach was not associated with better clinical outcomes in these patients, while higher RT dose delivered as a boost to macroscopic nodal evidence of disease apparently yielded superior biochemical control. Finally, cN1 patients would significantly benefit from modern IMRT based approach tailored on novel diagnostic imaging (e.g: PSMA or Choline PET/TC), while upfront RP could be avoided in this setting without compromising main clinical outcomes.

CO060

THE ROLE OF RADIOTHERAPY IN OLIGOPROGRESSIVE MCRPC PATIENTS DURING ARTA: A REAL LIFE EXPERIENCE AT TOR VERGATA UNIVERSITY

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Aims: The aim of the study is to evaluate in real life results of Androgen Receptor-Targeted Agents (ARTA) in metastatic castration resistant prostate cancer (mCRPC) and how the addition of radiotherapy in oligoprogressive patients could improve drug's results.

Methods: Patients with mCRPC have been evaluated and treated with ARTA at our institution. Patients with PSA progression during ARTA have been evaluated by choline PET-CT and those with oligoprogressive disease add ablative radiotherapy (aRT) to site of progression. Progression Free Survival 1 (PFS1) was calculated from the start of ARTA up to its end or the start of aRT, while PFS2 from irradiation for oligoprogressive disease up to change or definitive end of systemic treatment.

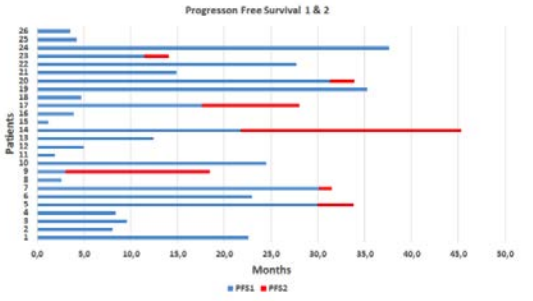

Figure 1. PFS1 (blue) and PFS2 (red) for each patient.

Results: From August 2016 to April 2020, 26 patients with histologically confirmed prostate cancer and mCRPC disease have been evaluated and treated at our institution. According to Classification ISUP 2016, 2/26 patients were Grade Group 1 (7.7%), 3/26 Grade Group 2 (11.5%), 10/26 Grade Group 3 (38.5%), 8/26 Grade Group 4 (30.8%) and 3/26 Grade Group 5 (11.5%). All patients maintained LHRH-analogue during castration resistant phase, 16 received Abiraterone Acetate plus Prednisone (AAP) and 10 Enzalutamide (ENZA). The mean time from the start of androgen deprivation therapy (ADT) and the beginning of ARTA was 34 months. The mean age at initiation of ARTA was 77 years (67-89). Seven out of twenty-six patients (25%) presented PSA progression during ARTA, and based on 18F-Choline PET-TC were defined as oligoprogressive. These patients received RT with ablative

intent (4 bones, 2 lymph nodes, 1 local recurrence) concomitantly with ARTA (3 ENZA, 5 AAP). Only one patient recorded a Grade 1 toxicity (CTCAE v.5). Median PFS1 was 30 months; while PFS2 for the seven patients treated with aRT plus ARTA was: 3.8 months (pt 5),1.4 months (pt 7), 15.5 months (pt 9), 23.5 months (pt 14),10.4 months (pt 17), 2.6 months (pt 20), and 2.6 months (pt 23). The swimming plot below illustrates these results (Figure 1).

Conclusions: This experience confirms the feasibility of ARTA in unselected patient's population and shows the role of aRT in oligoprogressive mCR PC patients. Furthermore, the observed PFS (30 months) is higher than those of pivotal trials (16.5 months for APP and 20 months for ENZA). Even if oligoprogression is quite unusual, these patients could benefit of aRT.

CO061

TRIAL PROSPETTICO DI FASE II "GIVE ME FIVE" RADIOTERAPIA AD ALTA PRECISIONE CON BOOST SIMULTANEO SULLA LESIONE INTRAPROSTATICA DOMINANTE PER TUMORE DELLA PROSTATA IN STADIO INIZIALE: IMPATTO DELLA TOSSICITÀ SULLA QUALITÀ DI VITA (AIRC IG-13218)

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Aims: As part of the AIRC IG-13218 (NCT019 13717), we analysed data from 65 prospectively enrolled patients with low and intermediate risk prostate cancer treated with extreme hypofractionated radiotherapy (RT) in order to identify clinically meaningful information through the analysis of validated questionnaires testing gastrointestinal (GI) and genitourinary (GU) RT related toxicities and their impact on quality of life (QoL).

Methods: At the end of RT treatment, clinical assessment and prostate-specific antigen (PSA) measurements were performed every 3 months for at least 2 years and GI and GU toxicities were evaluated contextually. QoL of enrolled patients was assessed by International Prostatic Symptoms Score (IPSS), Quality Life Questionnaire - Core 30 (QLQ-C30), QLQ prostate specific (QLQ-PR25) and sexual activity by International Index of Erectile Function (IIEF-5). Patients score changes were calculated at the end of RT, at one month after RT and at 12 and 24 months. This study was part of the research notified to our Ethic Committee (nr N79).

Results: Extensive analysis of different QoL assessments showed that patients' tolerance was satisfactory across all the considered time points, with no statistically significant change of QoL from baseline compared to that before RT (Figure 1). Overall survival and biochemical progression-free survival at 2-years were of 98% and 97%, respectively.

Conclusions: Low toxicity of extreme hypofractionation and the encouraging tumour outcome were observed, however a longer follow up is necessary to confirm these findings. The increasing dose to the dominant intraprostatic lesion does not worsen the RT toxicity and consequently does not affect patients' QoL, thus opening the room for further dose escalation.

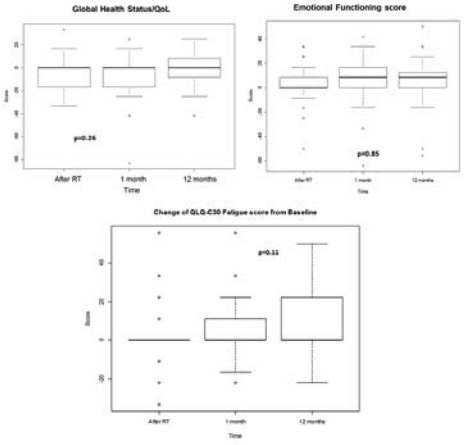

Figure 1. Change of QLQ-C30 from Baseline. Legend: p-values are from linear mixed models for repeated measures evaluating, respectively, the effect of time on the change of QoL score, Emotional Functioning score and Fatigue score from baseline.

CO062

IMPROVEMENT IN CLINICAL STAGING USING 18-F-CHOLINE PET/TC FOR PATIENTS WITH UNFAVORABLE INTERMEDIATE, HIGH-RISK AND METASTATIC PROSTATE CANCER

M. De Angeli, C. Sciommari, D. Giovenco, S. Loprete, M. Bottero, V. Cirnigliaro, C. Demofonti, S. Pietrosanti, A. Iadevaia, L. Cedrone, M. Leprai, R.M. D'Angelillo

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Aims: The role of 18F-fluorocholine positron emission tomography-computed tomography (18FCh-PET/TC) in the upfront staging of patients with intermediate and high risk prostate cancer remains controversial. ASCO guidelines suggest the use of 18FCh-PET/TC when conventional imaging is suspicious or

equivocal. The aim of this study is to evaluate the potential role of 18FCh-PET/TC in improving the staging of Prostate Cancer (PC) patients.

Methods: This is a retrospective observational study conducted in our center, including patients with intermediate and high-risk PC disease, treated at our hospital between November 2017 and March 2020, and who underwent 18FCh-PET/TC in pretreatment phase. All patients with confirmed adenocarcinoma of the prostate with Gleason Score assessment received clinical examination, PSA serum test, standard imaging with MRI/CT and bone scan and were classified according to D'Amico risk classes. A 18FCh-PET/TC has been done in order to evaluate nodal and/or distant metastases even with negative standard imaging. The decision to perform PET/TC was made after multidisciplinary discussion, including urologists, medical oncologists, radiation oncologists, radiologists and nuclear medicine specialist. A Sankey diagram was applied to show patients' flow throughout risk classification.

Results: Between November 2017 and March 2020, 57 patients with intermediate, high-risk or metastatic PC, underwent to standard imaging recording: 10 intermediate unfavourable, 29 high risk, 13 N+, 5 M+. After 18FCh-PET/TC, all 10 unfavourable intermediate risk patients were confirmed. Among 29 high-risk one's, 16 were confirmed as high-risk, while in 12 a Node+ and in one a metastases were recorded. All but 3 patients with N+ disease were not confirmed by 18FCh-PET/TC, with one metastatic disease and two negative nodal disease (confirmed high risk only disease). Finally, for 5 M+ patients, just in one case metastatic disease was confirmed. A Sankey diagram shows these results.

Conclusions: These preliminary results show how 18FCh-PET/TC could improve staging in high risk, N+ and M+ PC, and eventually change management of disease.

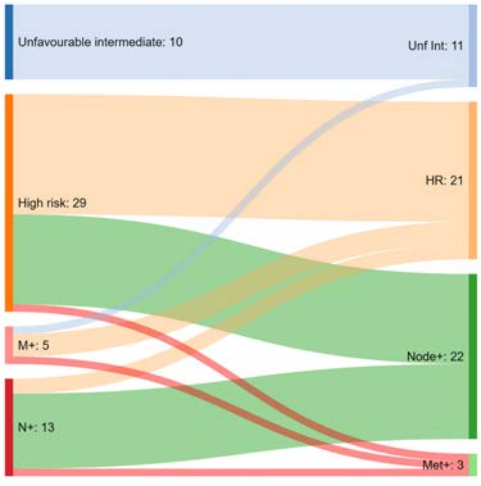

Figure 1.

CO063

SBRT ALONE OR IN ASSOCIATION WITH TARGET THERAPY: A POTENTIAL TREATMENT OPTION IN LUNG METASTASIS FROM RENAL CELL CARCINOMA

F. Zerbetto[1], S. Foti[2], A. Fodor[1], C.L. Deantoni[1], M. Pasetti[1], A. Chiara[1], F. Borroni[1,3], R. Tummineri[1,3], S. Villa[1,3], S. Baroni[1,2], S. Broggi[4], C. Fiorino[4], N.G. Di Muzio[1]

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Aim: The introduction of new target therapy in metastatic renal cell carcinoma RCC has improved the prognosis of these patients (pts). Recently the role of robotic Stereotactic Body Radiotherapy (SBRT) in oligometastatic setting is emerging as a promising treatment option. Our aim is to evaluate toxicity and local control (LC) of SBRT with CyberKnife® (Accuray, Sunnyvales, CA-CK) in the management of lung metastasis (LM) from RCC as monotherapy or in combination with new target therapy.

Materials and Methods: From 02/2018 to 02/2020, 22 LM in 17 RCC pts were treated with CK in our Institute. Median maximal diameter of the lesions was 1.75 cm (0.6-3.3 cm). Maximal number of lesion treated for patient was three. Median prescribed dose was 45 (30-60) Gy in 1-5 fractions, at a median isodose of 80% (73-85%). The Biologically Effective Dose (BED), considering an alpha/beta ratio of 10 was 112.5 (48-120) Gy. Five patients underwent SBRT only, while in the other 12 pts radiation treatment was associated to immunotherapy (Nivolumab) or Thyrosine Kynase Inhibitors (TKY: Sunitinib, Pazopanib or Carbozatinib).

Results: Median follow-up was 7.3 months (3-27.3). No acute toxicity was registered. Only one patient presented G2 asymptomatic early-late radio-induced pneumonia computer tomography (CT) documented 16 weeks after the end of SBRT and subsequently solved with steroid therapy. In this case three LM were concomitant treated with SBRT and Nivolumab, for a cumulative PTV of 65,22 square cm. No other late toxicities were recorded. Six LM (27,2%) presented complete CT or 18F-FDG-PET/CT response, four LM (18.2%) were in partial response, while stable disease was observed in 12 LM (54,6%). In the six cases with complete response, five were treated with concurrently TKY (4 with Sunitinib and 1 with Pazopanib). No local progressive disease were observed.

Conclusion: In our experience robotic SBRT in LM from RCC cancer is a feasible treatment with excellent local short-term control. Apparently the concomitant use of immunotherapy or TKY doesn't increase the toxicity, except in case of high volumes of treatment. Longer follow-up is necessary to verify the toxicity and

the stability of the complete local response over time and to better evaluated if the early stable disease will become a complete response.

CO064

ACUTE AND LATE TOXICITY AFTER IMAGE-GUIDED ELECTIVE NODE IRRADIATION WITH SIMULTANEOUS INTEGRATED BOOST (SIB) RADIATION THERAPY FOR HIGH RISK PROSTATE CANCER. A TWO INSTITUTIONAL ANALYSIS

P.R. Cicco[4], E Serpetti[1], M. Di Staso[3], M. Parisi[4], F. Rossi[1], A. Chalaszczyk[1], G. Grimaldi[1], F. Puce[1], S. Ridolfi[1], I. Mihoci[1], C. Sorce[1], F. Vittorini[2], P. Franzese[3], V. Ruggieri[3], E. Varrassi[3], R. Gimenez De Lorenzo[2], V. Tombolini[4], F. Marampon[4], D. Musio[4], F De Felice[4], C. Masciocchi[5], G.L. Gravina[1]

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Aims: To evaluate the acute and late toxicity (1-year) of elective nodal irradiation using moderately hypofractionated, intensity-modulated radiotherapy (IMRT) or VMAT with a simultaneous integrated boost (SIB) and daily IGRT for patients with high risk for prostate cancer.

Methods: A retrospective cohort of 46 men with treatment-naïve prostate cancer and a risk of lymph node involvement of more than 20% were selected. IMRT-VMAT plans were designed to deliver 45Gy in 25 fractions (1.8 Gy/fraction) to the pelvic nodes (WPRT) while simultaneously delivering 55 Gy in 25 fractions (2.2 Gy/fraction) to the seminal vesicles and 68,75 Gy in 25 fractions (2.75 Gy/fraction) to the prostate. Androgen deprivation therapy (ADT) was administered for a minimum of 2 months before radiotherapy continuing for at least 24 months. Acute toxicity was assessed during treatment and at 2 weeks after the end of radiotherapy and every 12 weeks thereafter. Late toxicity was analyzed 6-12 months after RT completion. The GI and GU toxicities were rated according to the Radiation Therapy Oncology Group (RTOG) scale for early and late side effects. Differences in the incidence of toxicities were evaluated by the Fisher's exact test or Chi-squared test. A p-value lower than 0.05 was considered statistically significant.

Results: Two weeks after RT a non-significant lower incidence of any grade GI acute toxicity (>Grade 1 or greater) was observed in the entire study cohort with respect to acute GU toxicity [GI>G1: 24/46 (52,2%) vs GU>G1: 32/46 (69,6%); p=0,13)]. A similar incidence of Grade 2 GI and GU toxicity was observed (p=0.38) (11% (5/46) and 19.6% (9/4 respectively) No grade 3 of greater acute toxicity was reported. At a mean follow-up of 22,7 months (95% CI 16,5 to 28,9), a significant higher incidence of any grade (>Grade 1 or greater) late GU toxicity [35% (15/43)] was observed with respect to GI toxicity [14% (6/43)] (p=0.043). Grade 2 late GU and GI toxicity was not significantly different [GI: 2/43 (4.7%) vs GU: 5/43 (12%); p=0,43)].

Conclusions: Men undergoing elective nodal irradiation using moderately hypofractionated, IMRT or VMAT with a simultaneous integrated boost (SIB) and daily IGRT experienced a favorable safety profile. Longer follow-up and increased sample size will provide more definitive evidence concerning this important topic.

CO065

THE ROLE OF 0-7-21 HYPOFRACTIONATED RADIOTHERAPY IN THE MELANOMA METASTASIS TREATMENT

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Aims: The aim of this study is to evaluate Response Rate (RR), Progression Free Survival (PFS) and Overall Survival (OS) as second point in patients treated with 0-7-21 hypofractionated radiotherapy in the melanoma metastasis treatment.

Methods: Of the 45 patients treated from January 2013 to December 2019, we retrospectively analysed 9 patients with melanoma metastases who underwent 0-7-21 hypofractionated radiotherapy.

Results: The median age at the time of treatment was 78 years (range 56-86 years). Lymph node metastases were treated in 5 patients and in 4 a skin localization. The delivered dose was 24 Gy in 3 fractions, at day 0-7-21, 8 Gy for fraction, one fraction to week. One patient had the BRAF V600K mutation, the other eight were BRAF Wild Type. All patients were treated also with immunotherapy. Three with Pembrolizumab alone, three with Nivolumab, one with Pembrolizumab and Ipilimumab, one with Ipilimumab and Nivolumab and one with Vemurafenib, Pembrolizumab, Ipilimumab and Dabrafenib associated with Trametinib. RR was 100%, median PFS was 11,5 months (range 4-13 months) while local progression has not been observed in any patient. Median OS from the end of radiotherapy at 6 and 12 months was 100% and 77,8% respectively.

Conclusions: 0-7-21 regimen has shown to obtain responses in the treatment of malignant melanoma, particularly affecting long-term local control. The clinical results obtained encourage the use of this fractionation in melanoma palliative treatment.

CO066

ELECTRON BEAM RADIOTHERAPY FOR NON-MELANOMA-SKIN-CANCER: OUR EXPERIENCE

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Aims: Nonmelanoma skin cancer (NMSC) represents the most common cancer in Caucasians, with continuing increase in incidence worldwide. Basal cell carcinoma (BCC) accounts for 75% of cases of NMSC, and squamous cell carcinoma (SCC) accounts for the remaining majority of NMSC cases. The majority of patients (pts) are over 80. Radiotherapy is an effective option for extensive lesions that would require demolithic surgery and as salvage treatment after non-radical surgery.

Methods: Between January 2011 and December 2019, 267 patients (median age 82, range 41- 99) and 360 lesions were treated with electron beam RT for NMSC. Lesions were localized in most cases on head and neck district (80%). In 220 cases RT was the unique treatment, in 160 cases RT was delivered after surgical exscission. The treated lesions histology were BCC in 111 lesions, SCC in 194, others in 33, untyped in 22 cases. The most common schedule was 60 Gy in 10 daily fractions (6 Gy for fraction) in definitive treatments and 30, 48 or 60 Gy in post-operative cases. An electron beam of 4, 6 or 12 MeV was selected based on the thickness of the target. Results were evaluated every 2 months for the first 6 months after the end of RT and then every 6 months.

Results: 236 pts (88%) were evaluated for response. Median follow up was 15,8 months (range 0,5- 74), complete response was in 87% lesions and partial response in 10%. Marginal recurrence occurred in 28 lesions (7,7%), 4 pts showed lymph node recurrence and 1 patient lung metastases. Treatment was safety and aesthetic result was good: grade 3 toxicity was observed in only 5 cases, no grade 4 toxicity was detected.

Conclusions: In our experience hypofractionated electron beam radiotherapy for NMSC is effective providing excellent local control (87%). Moreover low toxicity and excellent cosmetic results indicate that this therapy could be a valid alternative to surgery for limited lesions and first option in lesions that would require demolytic surgery.

CO067

PROTON BEAM RADIOTHERAPY OF LOCALLY ADVANCED OR RECURRENT CONJUNCTIVAL SQUAMOUS CELL CARCINOMA: EXPERIENCE OF THE CATANA CENTER

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Aims: Conjunctival squamouscell carcinoma (SCC) is a rare tumor of the ocular region and microscopic surgical radicality is difficult. There are no single guidelines for therapeutic management. The role of radiation therapy is not yet clearly defined and conventionally photon or electron beams are used, Proton beam radiotherapy (PBRT) is a new option for conservative approaches and allows a good saving of organs at risk.

Methods: After surgical resection, we collected the 15 cases treated by our institution with PBRT. The dose delivered was between 48-60 GyRBE, with fractions of 12-15 GyRBE.

Results: After an average period of 48 months, the patients achieved excellent disease control (OS and DFS: 86,6%), with minimal acute and late toxicity.

Conclusions: In this work, we present our experience about the use of Proton beam radiotherapy technique in SCC treatment. A larger sample of patients is nedeed to draw conclusions about the impact of this treatment on disease recurrence and overall survival.

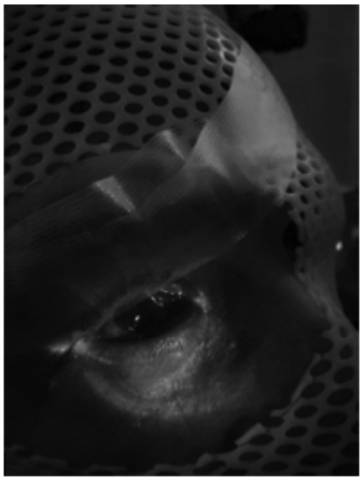

Figure 1.

CO068

RADIOTHERAPY FOR SKIN CANCER NON-MELANOMA: AN ITALIAN SURVEY

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On the behalf of the Italian Association on Oncological RadiotherapyAIRO Emilia Romagna and Marche Working Group.

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Aims: According to AIRT1 data, a yearly average of 119.4 new non-melanoma skin cancers per 100,000 males and 90.7 per 100,000 females were diagnosed. Basal cell carcinoma (BCC) and Squamous cell carcinoma (cSCC) were respectively 66% and 17% out of all cases. A variety of treatment options are available including surgical excision, cryotherapy, radiation therapy (RT), and topical agents. RT plays an important role in both definitive and adjuvant settings (PORT). Recently, ASTRO performed a systematic literature review on this topic publishing a practice guideline2. Aims of this survey were to assess the role of RT and the adherence of Italian Centers (Cs) to ASTRO guidelines.

Methods: During July 2020, we performed a 23-question online survey among all Italian RT Cs, asking for an only one answer from each center, using the SurveyMonkey platform3. The role of multidisciplinary team, RT modalities and some specific statements from the ASTRO guidelines were addressed to the panelists. Responses were recorded anonymously, and standard descriptive statistics used to evaluate the response distribution.

Results: Responders to the survey, homogeneously spread all over Italy, represent Cs treating >10pts/year in 61.5%. The answers highlighted a missing of a specific tumor board in most Cs (90%). Globally the panelists considered RT as a highly effective alternative to surgery, most using electrons (70%) for lesions < 2 cm and MV photons (88%) for bigger ones. RT was confirmed the treatment of choice in case of positive (100%) or close (71%) surgical margins and pT3/pT4 lesions (51.6%). Nodal RT is used in PORT setting if multiple positive regional lymph nodes and/or extracapsular extension (96.3%) or as curative treatment in pts unfit for lymphadenectomy (81.5%). Heterogeneity in techniques and dose/fractionation schedules was observed. Only 4.4% of Cs have electronic brachytherapy and 13% superficial roentgen machines. Conventional fractionation (CF) is used for curative RT with 50-60 Gy total dose in 33% and >60 Gy in 42%; hypofractionation with 40 Gy in 8 fractions is also used by 36% of Cs. CF is preferred by 80% of panelists in PORT. Histologic confirmation is mandatory for 76% of Cs in primary lesions and in 42% in the recurrence setting.

Conclusions: Data from the survey showed a quite good adherence to ASTRO guidelines even if within a certain heterogeneity in the management of pts with BCC and cSCC, suggesting the need of controlled trials focusing techniques, doses, margins of RT.

CO069

LATE CARDIAC COMPLICATIONS FROM CHEMOTHERAPY AND RADIOTHERAPY IN PATIENTS WITH LYMPHOMA (HODGKIN AND NON HODGKIN)

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Aims: The primary endpoint of this multicenter prospective observational study is to survey the prevalence of late cardiovascular toxicity in patients with lymphoma (Hodgkin and no Hodgkin) treated with chemotherapy antracycline-based and 3D conformal radiation therapy (3D-CRT) on the mediastinum, off therapy for five years. Secondarily, we aim to correlate clinical and / or subclinical cardiac damage to dosimetric data, in particular the dose of radiation therapy delivered to the cardiac substructures.

Materials and Methods: Patients undergo cardiovascular screening with: cardiological examination, complete blood chemistry tests, blood thyroid function, blood troponin and NT proBNP o BNP, electrocardio-

gram, echocardiogram, cardio-pulmonary exercise test and supraortic trunk echocolor-doppler. Specifically, the following parameters are retrospectively evaluated: total dose, dose by fraction and technique used for cardiac, pulmonary, thyroid and carotid structures. The assessment of toxicity is obtained through the contouring of the heart chambers and cardiac structures, lungs, thyroid and carotids and the dose volume histogram (DVH) evaluation. Based on the expected prevalence of the primary endpoint of 16%, after 5 years, a sample of 207 patients was estimated assuming a margin of error of 5% and a confidence interval of 95% (CI 95%). For time to event endpoints the survival curve will be estimated using the Kaplan Meier method and the comparisons will be based on the log-rank test.

Results: The expected duration of the study is 24 months, starting in November 2019, so it is still ongoing.

Conclusions: The results of this study could have an impact on daily clinical practice, proposing a specific cardiological screening program reserved for a selected category of patients considered at risk of developing late cardiotoxicity.

CO070

LONG-TERM RESULTS OF RADIOTHERAPY FOR STAGE I-II LOW-GRADE NON-HODGKIN LYMPHOMAS

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Aims: To evaluate long-term results in low-grade non-Hodgkin lymphoma(NHL) staged with 18F-FDG PET-CT and treated with radiotherapy (RT).

Methods: From September 2002 to December 2019, 18 patients (pts) with histologically confirmed low-grade NHL treated with RT ± chemotherapy (ChT) were retrospectively reviewed.

Results: Considering that 2 of 18 patients were subsequently treated in 2 different sites, the number of sites submitted to RT were 20. Patient characteristics were as follows: median age 62 years (range, 35-77 years), female/male ratio 5/13, median KPS 90% (range 90-100%). Histological subtype was grade I-IIIA follicular lymphoma in 13 (72%) and marginal zone lymphoma in other 5 (28%) cases. Lesion sites were inguinal nodes (45%), soft tissue (20%), orbit (20%) and other localizations (15%). Staging was done with echography and computed tomography (CT) in all cases, 12 pts (67%) were submitted also to 18F-FDG PET-CT. 13 pts (83%) were stage I and 5 (17%) stage II. In 7/18 pts (38%) ChT with Clorambucile, Rituximab or R-CHOP was done prior to RT obtaining partial response in 1, stable disease in 2 and complete response in 4 pts. Median dose was 36 Gy in 18 fractions of 2 Gy (range, 26-50 Gy). After a median follow-up of 90 months (range, 6-215 months), 15/18 pts (83%) were alive without disease, 2 were died for other disease, one for local and systemic progression. The 5- and 10-year local control (LC), progression-free survival (PFS), and overall survival (OS) rates were 100%, 100%, 65% and 88%, 75%, 65%, respectively. Radiotherapy was well tolerated without acute or late grade 3-5 toxicities.

Conclusions: RT is an effective and curative local treatment for early-stage low-grade NHL at conventional doses. Our experience confirms the role of RT in "true" localized, stage I-II low-grade NHL. As suggested in recent papers, 18F-FDG PET-CT is the more accurate diagnostic tool for staging pts and choosing the better therapeutic approach.

CO071

TREATMENT PATTERNS OF ELDERLY SOFT TISSUE SARCOMA PATIENTS

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Objectives: Soft-tissue sarcomas (STS) are a group of rare and heterogeneous neoplasms. Nowadays, data regarding management of STS in elderly patients are still needed. In this study we present a single center experience in terms of clinical outcome in elderly patients treated for STS

Methods: In this retrospective study data of patients older than 65 years affected by locally advanced STS were collected and analyzed, all patients were underwent surgery, radiotherapy and/or chemotherapy. Primary endpoints were Overall Survival (OS) and Distant Metastatis Free Survival (DMFS).

Results: Among 111 elderly patients, 105 (94%) underwent surgery, 91 (82%) received radiotherapy, 23 (20%) received radio-chemotherapy and 20 (18%) chemotherapy was administered as a single treatment. At a median follow-up of 4.1 years (0.1-17.7), 24 (22%) patients showed local or distant recurrence; 3- and 5-year local-recurrence free survival were 80% and 75%, respectively. Our analysis showed that frequency of local recurrence was not statistically correlated neither with type of treatment nor baseline characteristics. Fifty-five (52%) patients developed distant metastasis, with 3- and 5-year DMFS being 59% and 44%, respectively. Univariate analysis showed a higher risk of distant metastasis in patients who did not receive either adjuvant radiotherapy or surgery($p=0.043$ and $p=0.002$). On multivariate Cox Regression analisys, both undifferentiated-pleomorphic sarcoma histology and Charlson Comorbidity Index (CCI) > 7 were independent factors associated with worst DMFS ($p=0.026$ and $p=0.0001$). Overall survival (OS) was 62% and 46% at 3 and 5 years, respectively. At Multivariate Cox regression analisys, surgery and CCI <7 were independent factors associated with worse OS ($p=0.006$ and $p=0.0001$).

Conclusions: In elderly STS patients a tailored treatment (consisting of surgery, radiotherapy and/or chemotherapy) is feasible resulting in high rate of local control. Comorbidities should be considered in order to offer the best treatment in this frail setting of patients.

CO072

NEOADJUVANT RADIOTHERAPY IN SOFT TISSUE SARCOMAS OF THE EXTREMITIES: LONG-TERM RESULTS FROM A LARGE MONOCENTRIC SERIES

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Aim: To evaluate outcomes in a large series of patients treated with neoadjuvant radiotherapy (RT) for primary localized soft tissue sarcomas (STS) of the extremities.

Methods: One-hundred and twelve patients (median age: 53 years, range: 16-87) with primary high grade STS and treated with neoadjuvant external beam RT and surgery +/- chemotherapy (CHT) were retrospectively analyzed. Selection criteria were localized high grade STS and bulky diseases or tumor in close proximity of critical structures such as nerves or vessels. All patients underwent CT and MRI scan of the region of interest, chest TC +/- 18F-FDG-PET-CT before and after RT, and during the follow-up (FU). Eight patients, treated in the first year of this study received 44 Gy PTV dose delivered in 22 daily fraction. Thirty-two patients treated between 2006 and 2009 received a dose of 46 Gy (23 daily fractions), while the prescribed dose was 50 Gy to the PTV delivered (25 daily fraction) for patients treated between 2009 and 2019. Treatment was delivered with multiple beams technique to allow the best PTV coverage while reducing OARs irradiation and avoiding contralateral limb irradiation.

Results: With a median follow-up of 47.9 months (range 4-176), only five patients (4.5%) had local relapse, with 94.7% 5-year local control (LC). Twenty-six patients (23.2%) developed metastases and 5-year metastasis-free survival and disease-free survival were 73.9% and 70.5%, respectively. Seventeen patients died (15.2%) with 85.8% 5-year overall survival (OS) rate. Twenty patients (17.9%) received an adjuvant RT-boost due to marginal or intralesional margins. Nevertheless, a statistically significant impact of margin status was recorded being 5-year LC 95.2%, 96.6% and 80.0% in patients with wide, marginal, and intralesional margins, respectively (p=0.021). Eighty-two patients (73.2%) with chemo-sensitive histological subtypes received also neoadjuvant and/or adjuvant CHT. Younger patients (<52.8 years old) showed a trend for improved 5-year OS (88.0% vs 83.9%; p=0.066).

Conclusions: A high LC rate was recorded in this large series of patients treated with preoperative RT. Prospective studies on STS neoadjuvant setting are still needed to improve these results.

CO073

METASTASIS-DIRECTED THERAPY (SBRT) GUIDED BY PET-CT 18F-CHOLINE VERSUS PET-CT 68GA-PSMA IN CASTRATION SENSITIVE OLIGORECURRENT PROSTATE CANCER: A COMPARATIVE ANALYSIS OF EFFECTIVENESS

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Aim: New metabolic tracers has improved sensitivity and specificity for the real extent of tumor burden in prostate cancer increasing the attractiveness for local approaches in the oligometastatic patients with the aim to postpone the start of systemic therapies. The present analysis aims to compare the impact of 18F-Choline and 68Ga-PSMA PET-CT guided metastases-directed therapies (MDT) in castration-sensitive oligorecurrent prostate cancer (PC) patients.

Methods: Inclusion criteria were: i) histologically-proven prostate adenocarcinoma, ii) evidence of biochemical relapse after primary tumor treatment, iii) ≤3 hypermetabolic oligorecurrent lesions detected by 18F-Choline or 68Ga-PSMA PET-CT, iv) PET-CT imaging performed in a single Nuclear Medicine Department, v) patients treated with upfront-SBRT without hormonetherapy, vi) SBRT delivered with a dose per fraction ≥5 Gy. In the case of oligoprogression (≤3 lesions outside the previous RT field) after MTD, further SBRT course was proposed; otherwise, androgen deprivation therapy (ADT) was administered.

Results: 118 lesions in 88 patients were analyzed. Forty-four (50%) patients underwent 68Ga-PSMA PET-guided SBRT, and the remaining underwent Choline PET-based SBRT. The median follow-up was 25 months (range, 5-87), for the entire cohort. Overall Survival and Local Control were both 100%. Distant progression occurred in 48 patients (54.5%), for a medi-

an DPFS of 22.8 months (14.4-28.8). Median pre-SBRT PSA was 2.04 ng/ml in the Choline PET cohort and 0.58 ng/ml in the PSMA-PET arm. Disease-free survival rates were respectively 63.6% and 34% in the 68Ga-PSMA and Choline PET group (p=0.06). The ADT administration rate was higher after Choline-PET guided SBRT (p=0.00) due to the higher incidence of polymetastatic disease after first-course SBRT compared to 68Ga-PSMA-based SBRT.

Conclusion: In the setting of oligorecurrent castration-sensitive PC, PSMA-PET-guided SBRT produced a higher rate of ADT-free patients when compared to the 18F-Choline-PET cohort. The impact of metabolic imaging could be crucial for the identification of the real tumor burden that can benefit from a MDT approach, deferring the start of ADT until the evidence of a poly-metastatic progression takes place. Randomized trials are warranted.

CO074

SHORT-COURSE RADIOTHERAPY IN PALLIATIVE TREATMENT OF ADVANCED SOLID CANCER (SHARON PROJECT): A POOLED ANALYSIS

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Aims: To evaluate safety and efficacy of patients with symptomatic advanced and metastatic solid cancer treated with palliative hypo-fractionated accelerated radiotherapy (RT).

Methods: Clinical data from three monocentric phase I-II trials and one monocentric phase II trial were pooled for this study. A total dose of 14-20 Gy in 3.5-5 Gy/fraction administered twice a day was delivered. Pain and quality of life were recorded according to the Visual Analogic Scale and the CLAS scales, respectively.

Results: A total of 180 patients were included in this analysis. Fifty-two patients (28.8%) had advanced primary or metastatic H&N tumors, 54 patients (30.0%) locally advanced or metastatic thoracic cancers, 25 patients (13.9%) locally advanced pelvic cancers, and 49 patients (27.2%) complicated bone metastases. The most frequent baseline symptom was pain (63.9%). The overall palliative response rate (complete plus partial) was 88.9% with a median palliative duration of 4 months (Table 1). The response rate for pain was 86.8% (CI 0.95: 79.8%-91.7%). The pre-treatment and post-treatment mean VAS was 5.3 and 2.5 respectively ($p < .00001$). Overall, the majority of patients (92.2%) were able to rank the different aspects of QoL as well-being (CLAS1), fatigue (CLAS2) and ability to perform daily activities (CLAS3) using a visual analogue scale. An improvement of CLAS1, CLAS2, and CLAS3 indices was noted in 80 (48.2%), 70 (42.2%), and 77 (46.4%) of patients. Only 4/180 patients (2.2%) presented ≥ G 3 acute toxicity: 3 patients treated at 20 Gy with mucosal toxicity (n=2) and esophagitis (n=1), and 1 patient treated at 16 Gy with lung toxicity. Only 1 patient (0.5%) with a H&N lesion (total delivered dose: 20 Gy) experienced G 3 late skin toxicity (marked atrophy and telangiectasia) at 20 Gy. No other patients experienced > G 2 late toxicity. The treatment was well tolerated also when administered between systemic therapy courses.

Conclusions: A hypo-fractionated accelerated RT delivered twice a day in two consecutive days is effective in the symptomatic treatment of advanced and metastatic solid cancer. Currently, six multicenter randomized phase III trials comparing this short course regimen to a standard one (30 Gy in 10 daily fractions) in this setting are ongoing to establish the non-inferiority of the experimented treatment.

Table 1. Treatment characteristics and symptomatic response.

Tumor site	RT[a] dose (Gy)	No. patients	CR[b]	PR[c]	NC[d]	PS[e]
Any site	Any dose	180	52	108	14	6
H&N[f]	14	7	0	7	0	0
	16	6	1	4	1	0
	18	6	2	4	0	0
	20	33	10	16	5	2
Lung	16	12	1	11	0	0
	18	7	3	4	0	0
	20	35	10	23	2	0
Bone	14	1	1	0	0	0
	15	3	2	0	0	1
	16	7	1	5	1	0
	18	7	3	2	1	1
	20	31	10	16	3	2
Pelvis	20	25	8	16	1	0

[a]radiotherapy; [b]complete symptoms remission; [c]partial symptoms remission; [d]no changes; [e]progression of symptoms, [f]head and neck.

CO075

CAROTID BLOWOUT SYNDROME (CBO) AFTER REIRRADIATION FOR RECURRENT NASOPHARYNGEAL TUMORS: PRELIMINARY RESULTS FROM A RETROSPECTIVE MULTICENTRIC STUDY

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Aim: Incidence of carotid blow out (CBO) in patients treated with reirradiation (reRT) for recurrent nasopharyngeal tumors (rNPT) is particularly high (from 17 to 31%). When a massive hemorrhage occurs, mortality reaches 75%. Aim of the present study was to investigate risk factors for CBO in a cohort of patients (pts) treated with reRT for rNPT

Methods: We performed a multicentric retrospective study including four Italian centers. Inclusion criteria were: 1) reRT performed with fractionation schedule <3 Gy/day 2) availability of radiation treatment plans from both first the and second radiotherapy courses; 3) minimum reRT dose 40 Gy (EqD2) 4) minimum follow up of 6 months. Internal carotid arteries (ICAs) were retrospectively contoured on simulation computed tomography scans of both RT treatment plans. Cumulative lifetime dose (CLD) to ICA was calculated as EqD2 considering an α/β ratio of 3. The following radiologic risk factors were analyzed: presence of mucosal ulcer before reRT, ICAs encasement > 180°, tumor involving the petrous bone (yes/no). This study was part of the research notified to our Ethic Committee (UID nr. 2125).

Results: A total of 25 pts (20 male, median age 50 years, IQR 45-60 yrs) treated between February 2005 and August 2019 were analyzed. Radiation treatment details are summarized in Table 1. One hundred ICAs have been contoured. Median and maximum CLD (EqD2) to ICAs were 118 Gy and 157 Gy (range 5-157 Gy), respectively. Mucosal ulcer before reRT, ICA encasement> 180° and tumor involving the petrous bone were found in 1 (4%), 13 (52%), 10 (40%) pts, respectively. Two pts (8%) experienced acute CBO after 19 and 31 months, respectively. Both pts were reirradiated with protontherapy and died due to the hemorrhagic event. First patient had a maximum total CLD to ICAs of EqD2 157 Gy with ICA encasement > 180° and tumor involving the petrous bone. This was the only patient with combination of CLD > 150 Gy and two risk factors. The second patients had CLD to ICAs EqD2 138 Gy, but was the only patient with mucosal necrosis before reRT.

Conclusion: Our preliminary results suggest that combination of CLD and radiologic risk factors should be considered to evaluate the risk of CBO in pts treated with reRT for rNPT. More mature results from a wider cohort of pts are being collected to confirm the presented preliminary findings.

Table 1. Treatment characteristics of the first and second course of radiotherapy.

First RT course	RT dose (Gy)	Median 70
		Mean 68
		Range 60-76
		Median number of fractions 33
	RT Technique n. pts (%)	3D conformal 8 (32%)
		IMRT 10 (40%)
		VMAT 7 (28%)
Interval between the two radiation courses		Median 26 months
		Range 11-122 months
Second RT course	RT dose (Gy)	Median 54
		Mean 55
		Range 40-70
		Median number of fractions 26
	RT Technique n. pts (%)	Proton therapy 14 (56%)
		IMRT 6 (24%)
		Tomotherapy 2 (8%)
		Cyberknife 2 (8%)
		Cyberknife and VMAT 1 (4%)

Legend Gy= Gray, IMRT = Intensity Modulated Radiotherapy, pts= patients, RT = radiotherapy, VMAT = Volumetric Modulated Arc Radiotherapy

CO076

OLIGO METASTATIC RENAL CELL CARCINOMA: SABR, IF, WHEN AND HOW?

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Aims: Renal cell carcinoma (RCC) has traditionally been considered radioresistant but since the appearance of stereotactic ablative radiation therapy (SAbR), radiotherapy (RT) has been increasingly employed in the management of metastatic RCC (mRCC). The aim of this study was to evaluate the role of SAbR for synchronous and metachronous oligo-metastatic RCC patients (pts) in terms of local control, delay of systemic treatment, overall survival and toxicity.

Methods: Monocentric retrospective data collection was performed. The inclusion criteria were: (1) oligo-recurrent or oligo-progressive disease (less than 5) in

mRCC pts after local surgery or during systemic therapy; (2) surgery or other local therapies not feasible; (3) any contraindication to receive systemic therapy (such as comorbidities); (4) all the histologies were included; (5) available signed informed consent form for treatment. Tumour response and toxicity were evaluated using the Response Evaluation Criteria in Solid Tumours and the Common Terminology Criteria for Adverse Events version 4.03, respectively. In-field and out-field progression free-survival (PFS) and overall survival (OS) were calculated with the Kaplan-Meier method. The drug treatment free interval was calculated from the start of SAbR to the beginning of any systemic therapy in pts receiving exclusive SAbR. This study was part of the research notified to our Ethic Committee (nr N93/1).

Results: From 2010 to 2018, 61 pts with extracranial and cranial mRCC underwent SAbR on 83 lesions. Forty-five pts were treated for one metastatic lesion. Median RT dose was 25 Gy (range 10-52) in 5-10 fractions. With a median follow-up of 2.3 years (range 0-7.15), one- and two-year in-field PFS was 70% and 55%, respectively. One-year out-field PFS was 40% and one-year OS was 78% (Table 1). Concomitant systemic therapy was used for only 11 pts, for the other 50 the drug treatment free rate was of 70% and 50% at one and two years, respectively. No acute and late toxicities were reported.

Conclusions: The pattern of failure was pre-dominantly out of field, even if the population was negatively selected and the used RT dose could be considered palliative. SAbR seems to be a feasible and safe approach in oligometastatic RCC pts with an excellent in-field PFS and well tolerated. SAbR might play a role in the management of selected RCC pts, allowing to delay systemic therapy (1 out of 2 pts was free of progression and treatment at 2 years after SAbR).

Table 1. In field and out field PFS and OS.

Outcome	% of patients free of relapse (or death) at 1 year	No. of events at 1 year
In field progression-free survival	70	11
Out Field progression-free survival out field	39	29
Overall survival	78	12

Median follow-up (range): 2.3 years (0-7.15)

CO077

STEREOTACTIC ABLATIVE RADIOTHERAPY IN COMBINATION WITH IMMUNOTHERAPY: WHAT IS THE OPTIMAL TIMING IN OLIGOPROGRESSIVE ADVANCED NON SMALL CELL LUNG CANCER (NSCLC)?

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Aim: The combination of immunotherapy(IT) and ablative radiotherapy such as stereotactic ablative body radiotherapy(SABR) or stereotactic (cranial) radiosurgery(SRS) is being actively investigated for their potentially synergistic effects.The aim of this study was to evaluate safety and efficacy of this combination in oligoprogressive metastatic NSCLC.

Material and methods: Data from 57 pts treated from September 2015 to December 2018 were retrospectively analyzed.Median age was 67 years.At time of treatment, all pts had oligoprogressive NSCLC (defined as progression or appearance of no more than 3 metastatis).All pts were treated with IT concomitant to SABR/SRS.SABR/SRS was delivered during, before or after IT (within 30 days from last IT infusion or before the first one) using Image-Guided RT in all cases.

Results: SRS was delivered to brain metastases in 39 pts, SABR was delivered to bone metastases in 8, adrenal gland metastases in 5 and to other metastatic sites in 5 pts.Different dose prescriptions/fractionations were used: single fraction SRS/SABR was used in 22 pts (median dose 24Gy, range 12-25Gy), while fractionated SRS/SABR was used in the remaining pts.Nivolumab was administered in the majority of pts, while pembrolizumab and atezolizumab were used in in 21 and 5 cases, respectively.After a median FUP of 23 months(range 3-88), median PFS was 7.6 months, while median OS was 23.3 months. One- and 2-year OS rates were 75.5±3.2SE and 47.7%±4.0SE, respectively. After the first restaging, 6 pts showed complete response, 25 partial response and 15 responded with stable disease at the treated site, while 11 pts experienced disease progression, resulting in local ORR of 80.7%.During the entire fup, 36(66.7%) pts had to discontinue IT, 3 of whom due to severe toxicity (1 severe asthenia, 1 hypothermia and 1 diarrhea), the remainder for progression.After brain SRS, 1 patient developed

limbic encephalitis, 1 pt had G2 asthenia, in 2 pts intracranial radiation necrosis was observed and 2 pts reported persistent headaches. Only 1 pt developed pneumonitis after SABR.

Conclusions: SABR in combination with IT seems to achieve promising results and could be proposed in patients that become oligoprogressive during first line immunotherapy to postpone a switch to other, potentially on an overall systemic level less effective, pharmacologic therapies.The combination appears safe and well tolerated, but prospective trials are strongly needed to identify oligoprogressive NSCLC pts who benefit the most from adding SABR to IT.

CO078

USE OF STEREOTACTIC RADIOTHERAPY IN LYMPH NODES FOR OLIGOMETASTIC PELVIC TUMORS: AN UPDATE

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Aim: Oligometastatic desease has been defined as a state with 5 or fewer clinically detectable metastases. Patients with oligometastatic or oligorecurrence in lymph nodes could be cured with local therapy such as stereotactic body radiotherapy (SBRT). SBRT represents an emerging strategy. The aim of this retrospective study was to evaluate the oncological outcome and pattern of recurrence in patients treated with stereotactic body radiation therapy (SBRT) to lymph node metastases.

Mmethods: In this mono-institutional analysis, patients with a maximum of three lymph node metastases from prostate cancer, bladder cancer and endometrial cancer treated with SBRT were included. All patients had a positive 18F-Choline PET/CT in case of prostate cancer or a positive 18FDG PET/CT in the other cases. Primary endpoints of the analysis were acute and late toxicities. Secondary endpoints were local control (LC), progression-free survival (PFS) and overall survival (OS).

Results: 36 patients were eligible and treated with SBRT from January 2016 to January 2020 and retrospectively analysed. 18 patients had prostate cancer, 10 bladder cancer and 8 endometrial cancer. 12 patients (66%) with prostate cancer had undergone radical prostatectomy. A total of 43 lesions were treated: 30 patients had one metastasis, while 5 patients had two metastasis and 1 had three metastasis. Patients' median age was 70.9 years (range 51-85). Median follow up was 20 months. The dose delivered to the target ranged from 24 to 35 Gy in 3-5 fractions; 8 Gy daily in 3 fractions, 10 Gy daily in 3 fractions or 7 Gy in five fractions. Toxicity was rare: 31 patients (86%) presented G1 genitourinary acute toxicity, 27 patients (75%) presented G1 gastrointestinal acute toxicity, none had G3 acute toxicity. No patients developed grade ≥2 late toxicity. Local control was achieved in 96%. LC at 1 was 92%. Two-years progression-free survival was 61% and the overall survival was 76%.

Conclusions: SBRT is an effective and well-tolerated treatment option in the management of lymph node metastases. A greater number of cases could help us better stratify patients, that could benefit from a dose or fractionation.

CO079

EFFICACY OF STEREOTACTIC BODY RADIOTHERAPY IN PATIENTS WITH OLIGOMETASTATIC THYROID CANCER

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Aims: Differentiated thyroid cancer is associated with a good prognosis. The development of metastasis in differentiated thyroid cancer adversely affect patients' quality of life and survival. Stereotactic Body Radiotherapy (SBRT) is an effective treatment for metastasis of different histologies. In our study we analysed the effectiveness of SBRT in oligometastatic refractory iodine thyroid cancer patients.

Methods: We retrospectively analysed patients with differentiated oligometastatic thyroid cancer managed with SBRT in our Radiation Oncology Unit from 2011 to 2019. We collected demographics and treatment-related characteristics (total dose, location and number of treatments). Local control, progression free survival and overall survival rates were calculated. Patients with anaplastic histology, incomplete treatment or without follow-up information were excluded.

Results: We retrospective analysed a cohort of 14 adult patients, aged between 47 and 72 years old. 8 (57,1%) patients were males and 6 (42,9%) were females. A total of 41 lesions were treated; 19 lesions of the bone (46.3%), 10 at the lymph node sites (24.4%), 3 visceral (7.3%), 7 of the brain (17.1%) and 2 of the lung (4.9%). SBRT was delivered in 1-8 fractions, with a median dose of 30 Gy (range, 14-60 Gy). 22 lesions (53.7%) had a complete response after treatment, 12 lesions (29.3%) had a partial response, 6 lesions (14.6%) had stable disease and 1 lesion (2.4%) progressed after treatment. The 2-year and 4-year control rates were 89.6% and 65.7%, respectively. The 2-year and 4-year progression free survival was 42.9% and 9.4%, respectively. The overall survival at 2 and 4 years were 84.6% and 76.2%, respectively.

Conclusions: In our experience, SBRT yields satisfying local control in oligometastatic refractory iodine thyroid cancer patients.

CO080

ABOUT SAFETY AND TOLERABILITY OF PEPTIDE RECEPTOR RADIONUCLIDE THERAPY WITH 177-LU-DOTATATE (LUTATHERA) IN PATIENTS AFFECTED BY ADVANCED WELL DIFFERENTIATED GASTROENTERIC NEUROENDOCRINE TUMORS (GEP-NETS): INITIAL EXPERIENCE OF A SINGLE INSTITUTION

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Aims: 177-Lu-DOTATATE therapy (Lutathera®) has been recently approved as second-line treatment for GEP-NETs. Main treatment adverse effects described in literature are gastrointestinal disorders, particularly nausea and/or vomiting, associated with the intravenous amino-acid solution for renal protection, and blood disorders. We reported preliminary data about safety and tolerability of patients who underwent to the Peptide Receptor Radionuclide Therapy (PRRT) in our institution.

Methods: According to ENETS guidelines and Lutathera prescribing protocol, from July 2019-May 2020, the first 17 pts with metastatic GEP-NETs G1-G2 were recruited and started PRRT. Treatment tolerability was assessed on the basis of laboratory tests (blood count, hepatic and renal profiles) and physical examination performed every 15/20 days between administrations. Adverse events grading was assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) scale (version 5.0).

Results: Overall 17 pts (11M-6F; mean age:62 years) were recruited to undergo to 177-Lu-DOTATATE therapy for a total of 4 administrations (activity:7400 MBq-200mCi per administration). Primary tumour site was pancreas in 7/17pts, ileum in 8/17pts, duodenum and right colon respectively in two patients. Metastatic site was liver in 15/17 pts, lymph nodes in 9/17 pts, bone in 2/17 pts, skin in one patient. 9/17 pts completed therapy and one patient stopped treatment at third administration for extra-target disease progression. Until data collection, 6/17 pts have no yet completed therapy. Adverse effect occurred were nausea in 2/17 pts and vomiting in one pts; both were G1 and transient with complete resolution at the end of the infusion. About blood toxicity, we report G1/G2 anaemia in 5/17 pts(29%), G1/G2 thrombocytopenia in 4/17 pts(23%), G1/G2 leukopenia in 4/17 pts(23%), whereas no G3/G4 hematologic events has occurred. No evidence of renal toxic effects except for one patient who showed an increased serum creatinine level (G2) and a clearance of creatinine decrease less than 50 ml per minute which led a 2 months therapy delay and the need to administer half dose at the last administration. Overall, administration procedure has proved to be relatively simple, fast and safe in terms of radiation exposure of the healthcare staff.

Conclusions: Our preliminary results confirm data literature reporting that 177-Lu-DOTATATE therapy is safe and well tolerated. Data collection on treatment response is ongoing.

CO081

COULD A DEDICATED INTERVENTIONAL ONCOLOGY TUMOUR BOARD IMPROVE A PERSONALIZED THERAPEUTIC APPROACH? SINGLE INSTITUTION EXPERIENCE

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Aims: Modern oncology should offer tailored therapeutic strategies. Dedicated multidisciplinary tumor boards called "Inter-board", are meetings in which different specialists are directly involved in patient management. Our aim is to evaluate and report the advantages of Inter-board in terms of waiting-time, medical procedure complications and average hospital stay.

Methods: A retrospective analysis was carried out on patients managed from January 2018 to June 2019 in a single institution. The number of patients managed in each semester, the median time between initial assessment and admission to the hospital, total number of procedures, procedures type, complications and related days of hospital stay were collected and analyzed.

Results: 438 patients were discussed at the Inter-board. The number of discussed patients progressively increased: 82 (18.7%) from January to June 2018, 120 (27.4%) from July to December 2018 and 236 (54.1%) from January to June 2019. Overall 33 different kinds of primary tumors were discussed and 28 different types of procedures were performed. The average waiting-time from Inter-board to hospital admission was 22

days. The overall mean hospitalization days was 4 days (progressively decreased from 5 days in the first semester to 3 days in the last semester) and the overall complication rate was 4%. 223 patients (47.8%) was treated using interventional radiotherapy (IRT).

Conclusions: The Inter-board plays a multifactorial role in bridging the gap between expert consensus panels and choosing the most appropriate care for an individual. It could be extremely useful optimizing patient care through identification of all available options, offering cross-specialty knowledge translation and providing the best evidence and continual updates on innovation among all stakeholders and ensure a low complication rate and reduces waiting and hospitalization times.

CO082

EYE STRUCTURES SPARING BRACHYTHERAPY IN OCULAR MELANOMA BY PERSONALIZED TREATMENT PLANNING

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Aims: To evaluate the impact on dose distribution to eye organs-at-risk (eOARs) of a computed tomography (CT)-based treatment planning in eye plaque brachytherapy (EPB) treatment

Methods: We analyzed 19 ocular melanoma (OMs) patients treated with ruthenium-106 plaques to a total dose of 100 Gy to tumor apex using conventional central-axis-point dose calculation. Treatments were re-planned using the Plaque Simulator (PS) software implementing two different strategies: a personalized CT-eye-model (CT-PS) and a standard-eye-model (SEM-PS) defined by Collaborative Ocular Melanoma Study (COMS). The DICE coefficient and the Hausdorff distance evaluated the concordance between eye-bulb-models. Mean doses (Dmean) to tumor and eOARs were extracted from Dose-Volume-Histograms (DVH) and Retinal-Dose-Area-Histogram (RDAH). Differences between planning approaches were tested by Wilcoxon signed-rank test.

Results: In the analyzed cohort, 8 patients (42%) had posterior tumor location, 8 (42%) anterior, and 3 (16%) equatorial. The SEM did not accurately described the real CT eye-bulb geometry (median Hausdorff distance 0.8 mm, range: (0.4-1.3) mm). Significant differences in fovea and macula Dmean values were found (p=0.04) between CT-PS and SEM-PS schemes. No significant dosimetric differences were found for tumor and other eOARs. From a qualitative evaluation, it can be observed that the planning scheme particularly affects the eOARs closest to the tumor with a general tendency of SEM-PS to overestimate the doses to the eOARs closest to the tumor (Figure 1).

Conclusions: The dosimetric accuracy achievable with CT-PS EPB treatment planning may help to identify those OM patients who could benefit the most from a personalized eye dosimetry with the aim of ensuring the optimal treatment outcome in terms of tumor coverage and eOARs sparing. Further research and larger studies are warranted.

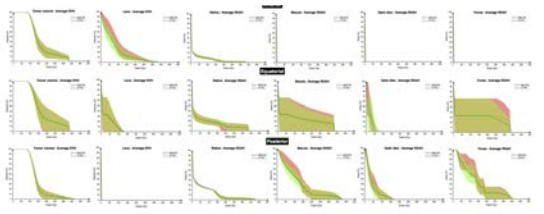

Figure 1. Comparative average Dose Volume Histograms (DVHs) for tumor volume and lens and Retinal Dose Area Histogram (RDAH) for fovea, macula, retina and optic disc for patients grouped according to tumor position: Computed Tomography (CT) versus Standard Eye Model based Pla-que Simulator (PS) planning approaches. The solid spaces indicate the standard error of the mean.

CO083

INTRALUMINAL BRACHYTHERAPY IN UNRESECTABLE EXTRAHEPATIC BILIARY DUCT CANCER: AN ITALIAN POOLED ANALYSIS

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Aim: To evaluate the outcome of patients with unresectable extrahepatic cholangiocarcinoma (CC) treated with external-beam radiotherapy (EBRT) and concurrent chemotherapy (CT) with or without intraluminal brachytherapy (ILBT) boost or with definitive ILBT.

Methods: A pooled analysis of patients with non-metastatic unresectable CC was performed. They were treated in three different institution with EBRT plus CT with or without an ILBT boost. Some patients received only ILBT with curative dose.

Results: Seventy-three patients were included in the analysis. Thirty-nine patients (53%) received EBRT treatment with ILBT boost (18 patients with CT during EBRT), while 28 patients (38%) were treated with EBRT (CT in 26 patients) and 6 patients (8.2%) with definitive ILBT (2 patients with CT). CT was administered including either the use of gemcitabine or 5-fluorouracil. With a median follow-up of 16 month (range=1-94 months), median overall survival (OS) was 16 months. Overall median LC was 16 months and patients who underwent ILBT had a better local control (LC) (p=0.018).

Conclusions: The role of ILBT in unresectable CC is not yet supported by robust evidence in the literature. However, within this limit, preliminary results seem to suggest an improved local control in patients treated with ILBT, almost comparable to the ones of standard chemo-radiotherapy (CRT).

CO084

MONOINSTITUTIONAL COMPARISON OF TOXICITY AFTER HDR BOOST PLUS EBRT AND EBRT ALONE FOR LOCALIZED PC

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Aims: In pts with unfavorable intermediate risk (uIR) and high risk (HR) prostate cancer (PCa), a dose-escalation to the target improved bPFS; however, a further dose increase is limited by a risk of late toxicity to OARs. HDR Brachytherapy boost (BT-HDR) can overcome this problem, by delivering a higher BED to the target, with greater preservation of OARs compared to EBRT. There are currently no randomized clinical trials that compare the HDR boost with exclusive EBRT, delivered with modern RT. The ASCENDE-RT trial showed an improvement in bPFS in the LDR boost arm, against a moderate increase in toxicity, particularly urinary toxicity. The aim of this study is to further support for the potential use of BT-HDR for the treatment of PCa in pts uIR and HR.

Materials and methods: From January 2016 to April 2019, 104 pts with uIR or HR PCa were treated at our Institution with BT-HDR (15 Gy in single fraction) plus EBRT (45 Gy in 25 fractions; 36 pts) or with exclusive EBRT with VMAT-IGRT technique (median dose 77 Gy; 68 patients). The primary endpoint was the evaluation of genito-urinary (GU) and gastrointestinal (GI) acute toxicity and, for pts with at least 12 months of follow-up, also the late one. Toxicities were evaluated according to CTCAE scale v.4.0.

Results: The median follow-up was 13.0 months (range 2-41 months). Details and characteristics of pts are shown in Table 1. The prescribed radiation dose in EBRT group ranged from 60 Gy to 78Gy, with a dose per fraction ranging from 2 to 3.2 Gy. The equivalent dose (EQD2) ranged from 74 to 85.9 Gy, calculated by using a ratio of $\alpha/\beta=1.5$. GU and GI acute toxicity did not differ statistically between the two groups ($p = 0.47$ and $p = 0.41$, respectively). GU late toxicity is worse in the BT-HDR group in G2 grade ($p = 0.038$); there is no statistical difference in GI late toxicity. No acute or late toxicities of grade ≥ 3 were recorded. Furthermore, there is no correlation between dose received by OAR and toxicity grade, both acute and late. In the BT-HDR group, no adverse events were recorded during the surgical procedure.

Conclusion: HDR brachytherapy boost in conjunction with IMRT is a safe treatment with acceptable toxicity, particularly acute, in comparison with EBRT alone. We need to wait for a longer follow-up to further define the toxicity profile and the outcomes.

Table 1. Patients and tumor characteristics.

	BT-HDR	EBRT	*p*-value
Patients	36	68	
Median Age *(range)*	71.5 *(47-79)*	74.0 *(50-84)*	NS
ECOG PS (0/1/2)	33/3/0	49/19/0	*0.02*
Tumor stage			NS
T1c	0	6	
T2a	1	4	
T2b	4	0	
T2c	20	25	
T3a	9	22	
T3b	2	11	
GS			NS
6	2	9	
7	23	31	
8	5	20	
9	6	7	
10	0	1	
Risk group (uIR/HR)	19/17	17/51	*0.005*
Radiation dose (Gy)			NA
45 Gy in 25 fractions	36	0	
74 Gy in 37 fractions	0	3	
76 Gy in 37 fractions	0	2	
78 Gy in 37 fractions	0	10	
60 Gy in 20 fractions	0	16	
64 Gy in 20 fractions	0	37	

CO085

ADJUVANT HDR BRACHYTHERAPY FOR ENDOMETRIAL CANCER WITH MULTICHANNEL CYLINDER: TO REPLAN OR NOT TO REPLAN?

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Purpose: To retrospectively compare the differences between plans obtained prior to each fraction for adjuvant high-dose-rate (HDR) vaginal brachytherapy (BT) with dedicated Multichannel (MCH) cylinders in endometrial cancer (EC) patients and to evaluate the dosimetric advantages of fractional re-planning.

Materials and methods: For our study, two distinct planning modalities were used retrospectively to compare dosimetric differences to vaginal cuff and to organ at risk (OAR): 1) Fractional re-planning (RP): a CT scan was obtained and a 3D-optimized plan was generated for each fraction; 2) First fraction planning only (FP): the plan values of the first fraction were applied to the imaging data set and structures to subsequent fractions without repeat CT planning. Dose-volume-histogram (DVH) analysis was mainly focused on the dose received by the 90% of the clinical target volume (CTV-D90) and the dose received by 2cm^3 of bladder (BD2cc), rectum (RD2cc) and bowel (BoD2cc). Dosimetric differences from the first and the second re-planned fraction (RP1 vs RP2) and from the RP1 and the third re-planned fraction (RP1 vs RP3) were examined. In additions, dosimetric indices of FP plans (FP2 and FP3) were compared to the RP1, and the dosimetric variations compared with RP2 and RP3.

Results: Between September 2016 and January 2019, 24 consecutive patients with early stage EC underwent adjuvant HDR-BT to the vaginal cuff with the MCH cylinder. A total number of 72 plans were retrospectively reviewed. The median percentage dose difference between RP1 and RP2 and between RP1 and RP3 were 0,81% and 0,4% for CTV-D90, 4.19% and 1.63% for BD2cc, 0.06% and 1.87% for RD2cc, 3.48% and 4,60% for BoD2cc, respectively. The median percentage dose difference in terms of CTV-D90, BD2cc, RD2cc and BoD2cc were 4.95%, 5.73%, 0.65% and 2.16% between RP1 and FP2 and 3.95%, 4.06%, 0.41% and 9.11%between RP1 and FP3, respectively. The absolute differences in individual doses for the investigated DVH parameters for a given fraction between the two methods were small for nearly all the 72 plans. Qualitatively, the isodose distributions and DVHs were similar.

Conclusions: A small benefit was found for the customized fractional re-planning used to compensate for inter-fraction difference. The interfractional RP could ensure a higher target coverage and a better bladder and bowel sparing.

CO086

HIGH DOSE RATE BRACHYTHERAPY WITH SURFACE MOLD TECHNIQUE IN PENILE CANCER

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Aim: In penile cancer, radiotherapy (RT) is an alternative to surgery providing good local control (LC) and overall survival (OS) beside benefits in quality of life. RT can be administered by external beam techniques and/or brachytherapy (BRT). For superficial lesions, surface molds is a valid non-invasive approach. Here we report our experience in penile cancer patients treated with high dose rate (HDR)- BRT with surface mold technique, analysing dosimetric parameters and clinical outcomes.

Methods: Seven patients with squamous cell carcinoma of the penis were treated between June 2016 and December 2019. Clinical stage was Tis, T1aN0, T1bN0, T2N0 in 1,3,2 and 1 case, respectively. Treatment was delivered by means of an individualized custom applicator, with catheters at an inter-distance of 10 mm. Two applicators were constructed by using a 3D printer, while the others 5 were customized thermoplastic masks. CT images were acquired for the treatment planning. In 2 patients the clinical target volume (CTV) was the macroscopic lesion with a 0.5 cm margins and in the other 5 the entire glans. The total dose was 57 Gy, delivered in 19 fractions. Patients were evaluated daily before each treatment session, then they were followed at 1, 6 and 12 months after treatment and every 6 months thereafter. Toxicity was graded using the CTCAE v4.02.

Results: The median CTV was 9.82 cc (4.66-12.72). The median CTV receiving 95%, 115% and 150% of the prescribed dose were 93.11% (92.21-98.52), 12% (7.45-32.23) and 0.24% (0-10.85), respectively. The median DHI was 99.7% (88.7-100). The median volumes of urethra receiving 90% and 115% of the prescribed dose were 40.2% (21.02-83.84) and 0.0%(0-0.97), respectively. The median follow-up was 12 months (6-24). All patients achieved a complete remission at a median of 12 months (6-24) after treatment. One patient developed an isolated local failure 12 months after completion of HDR-BRT and underwent salvage penectomy. At the last follow-up all patients were alive in absence of disease. No patient experienced infection. G3 or G4 acute and late toxicities were not observed in any case. All patients developed acute G2 skin reaction. Four patients developed late toxicity, G1 fibrosis in 1 patient and G2 phimosis in 3 patients. No patient experienced urethral stenosis.

Conclusions: Our results show that HDR-BRT with surface mold in penile cancer is a simple technique with a high tolerance profile and good outcome.

CO087

INTRAOPERATIVE RADIOTHERAPY AND BREAST CONSERVING SURGERY FOR BREAST CANCER RECURRENCE: AN OPTION TO AVOID MASTECTOMY

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Aim: Mastectomy is currently recommended for patients with in-breast tumor recurrence (IBTR) after prior whole breast radiation. The normal tissue tolerance does not permit a second full-dose course of whole breast irradiation after a second breast-conserving surgery (BCS). We retrospectively investigated the role of a second BCS followed by intraoperative radiotherapy (IORT) for patients, who refuse mastectomy, with localized breast cancer and prior whole breast radiation compared to salvage mastectomy.

Materials and methods: Patients with IBTR after external beam radiotherapy for breast cancer, treated at our institution, were included. All breast recurrences were pTis, pT1-2. IORT was delivered with the low energy X-rays IntrabeamTM device (Carl Zeiss Meditec AG, Oberkochen, Germany), using a single dose of 6 Gy prescribed to a depth of 1 cm from applicator surface (20-21Gy at applicator surface). Local control (LC) were estimated by Kaplan-Meier estimator.

Results: Between 2009 and 2018, 109 patients with breast cancer recurrences were treated at our istitute. Most patients underwent mastectomy (81/109); 28 patients, who refused mastectomy, successfully underwent BCS and partial breast reirradiation with IORT. The median follow-up from surgery was 53 months (range 2-129 months). In conservative group, three patients with local recurrence underwent salvage mastectomy; one of them had a second local relapse and started chemotherapy. In mastectomy group, four patients had local recurrence and underwent excisional biopsy and chemotherapy, with no more relapse. LC at five years were 93.6% for group underwent mastectomy and 86.5% for conservative group, with no statistical differences (p-value 0.18).

Conclusions: In our retrospective experience, breast-conserving surgery with IORT is a feasible option for breast preservation in patients with localized breast recurrence and prior thoracic radiation. Prospective trials are required to confirm these preliminary findings

CO088

DEMOGRAPHIC, CLINICAL AND TECHNICAL CHARACTERISTICS OF INTRAOPERATIVE RADIOTHERAPY: AN ANALYSIS OF THE ISIORT DATABASE

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Aims: In the past decades, Intraoperative radiotherapy (IORT) has gained interest as an alternative to external beam radiation treatment (EBRT). The increasing number of IORT procedures - the administration of radiation therapy during surgery - required the creation of a joint online database, where each center of the International Society of Intraoperative Radiation Therapy (ISIORT) would have been able to upload demographic, clinical and technical data. The analysis of these information could define the range of IORT techniques and indications encompassed by its member institutions.

Methods: Since 2007, the members of ISIORT have been invited to record demographic, clinical and technical data about the IORT procedures performed in their centers, using a standardized model of collection. Centers have been yearly invited to upload data in a joint online database. The entry of retrospective data and the modification or update of previous uploaded data was

possible. The collected data were analyzed by SPSS statistical software.

Results: The database included 46 centers, 9 of which outside Europe. Data were collected from 13182 IORT procedures performed between 1992 and 2020. The average annual number of procedures performed per institution was 37,7, with two centers performing more than 100 procedures per year. The most frequent tumor was breast cancer with 10373 cases (78.7%), followed by rectal cancer (955 cases, 7.2%), soft tissues sarcoma (731 cases, 5.6%), prostate cancer (190 cases, 1.4%) and uterine cancer (156 cases, 1.18%). The analyzed parameters included mean age, sex, treatment intent, extension of surgery, treatment strategy, number of fields, diameter of applicator, bevel angle, energy, type of radiation, treatment modality, total dose (Gy), bolus, pre or post-operative external beam radiotherapy and chemotherapy administration.

Conclusions: This analysis represents the report on the largest cohort of IORT procedures performed in last decades, highlighting the overall consensus beneath the patient selection and treatment modalities of main tumor types.

CO089

PRELIMINARY RESULTS FROM AN ANONYMOUSLY QUESTIONNAIRE ON PSYCHOLOGICAL IMPACT OF COVID 19 EMERGENCY ON PATIENTS (PTS) SUBMITTED TO RADIOTHERAPY (RT)

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Aims: The COVID19 disease emerged in China, and then widespread. From the end of February it arrived in Italy. Oncological patients mostly continued their treatments. In our Institution a questionnaire was submitted to understand the psychological effect of the emergency.

Materials and methods: From March and June 2020, 62 multiple choice questions were distributed to all pts undergoing RT. The questionnaire was ideated with Psychologist of University and ASST Spedali Civili Brescia. Answers were scored (p) between 1 (rarely; not at all) and 7 (frequently; surely); a scale measuring "anxiety" (SAS) was also submitted (points between 20 and 80).

Results: 201 COVID19 negative pts answered. 181 pts answered at the end of RT; 20 pts during follow-up. 69,7% of pts were >60 years old; 77,6% lived with other people and their major concern was infecting relatives (6-7 points in 59% of pts). The concern was intermediate when the first 2 COVID cases were announced in Rome (1-2 points in 28% of pts, 3-5 in 60% of pts, 6-7 in 12% of pts) and higher when the Lombardy was locked down (1-2 points in 4% of pts, 3-5 points in 45% of pts, 6-7 points in 51% of pts). During RT 20% thought interrupting treatment because the "fear" of being infected. 29 pts (14,4%) thought to be affected by COVID. Regarding the "social" impact of COVID19, the minor part of respondents think that the "negative relations" present in the COVID period will last after it (1-2 points in 66% of pts, 3-5 points in 26% of pts, 6-7 points in 8% of pts); more debated the opinion about the duration of positive relations (1-2 points in 32% of pts, 3-5 points in 35% of pts, 6-7 points in 32% of pts). In the patient's opinion, this period could represent an opportunity for physician's personal growth. Median SAS point was 31. The frequency of insomnia and hands sweat were the highest (4 points 33% and 46% of pts respectively); the other symptoms were less represented (4 points respectively in 0%, 0,5% and 1% for dizziness, headache and gastrointestinal disorders).

Conclusion: The questionnaire has been a simple, cheap and easily administrable method of analysis to understand opinion and feelings of patients. These very preliminary results show that, even if these patients continued RT for their cancer disease, they also had symptoms possibly related to anxiety. SAS points could also be influenced by the patient's mood in relation to their oncologic disease.

CO090

TWO MONTHS OF RADIATION ONCOLOGY IN THE HEART OF ITALIAN "RED ZONE" DURING COVID-19 PANDEMIC: PAVING A SAFE PATH OVER THIN ICE

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Aims: Coronavirus Disease 2019 (COVID-19) pandemic had an overwhelming impact on healthcare worldwide. Nonetheless, the aftermath on neoplastic patients is still largely unknown, and only isolated cases of COVID-19 infections during radiotherapy have been published. In this study, we will report the two-months experience of our Department.

Methods: Data of 402 cancer patients undergoing active treatment from February 24 to April 24, 2020 were retrospectively reviewed; several indicators of the Department functioning were also analyzed.

Results: Dedicated measures allowed an overall limited reduction of the workload. Decrease of radiotherapy

treatment number reached 17%, while the number of administration of systemic treatment and follow up evaluations kept constant. Conversely, new treatment planning faced substantial decline. Considering the patients, infection rate was 3.23% (13/402) and mortality 1.24% (5/402). Median age of COVID-19 patients was 69.7 years, the large majority were male and smokers (84.6%); lung cancer was the most common tumor type (61.5%), 84.6% of subjects were stage III-IV and 92.3% had comorbidities. Remarkably, 92.3% of the cases were detected before March 24. Globally, only 2.5% of ongoing treatments were suspended due to suspect or confirmed COVID-19 and 46.2% of positive patients carried on radiotherapy without interruption. Considering only the last month, infection rate among patients undergoing treatment precipitated to 0.43% (1/232) and no new contagions were reported within our staff.

Conclusions: Although mortality rate in COVID-19 cancer patients is elevated, our results support the feasibility and safety of continuing anticancer treatment during SARS-Cov-2 pandemic by endorsing consistent preventive measures.

CO091

COVID-19 AND RADIOTHERAPY: AN AIRO SURVEY DEPICTING THE ITALIAN LANDSCAPE AT THE DAWN OF PHASE II

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Introduction: Italy was the first European country heavily involved in the COVID-19 pandemic and experienced one of the deadliest outbreaks in the world. However, the massive safety measures adopted had a positive impact on the Italian epidemiologic scenario and allowed the authorities to relax the restrictions and introduce, on the 3rd May 2020, the so-called phase II (P2). This study, which represents the continuation of a previous one carried out during phase I (P1)1, is based on the survey, endorsed by AIRO, which depicts the situation of Italian radiotherapy (RT) departments throughout the two phases.

Materials and Methods: An online questionnaire was readapted from an analogous study conducted in Lombardy during P2 and from other published works1,2. The final version was anonymously sent to Italian RT Directors on the 1st of July 2020.

Results: At the deadline (13-07-2020), 89/174 (51%) contacted Directors (North: 53, Centre: 16, South: 20) responded to the questionnaire. The survey revealed that both in P1 and P2 the RT Director was the main responsible of the management of the pandemic (88.8% and 89.9% centres). The measures put in place to contain the epidemic proved to be particularly effective to reduce cases between staff. The proportion of centres registering positive cases dropped down from 43.8% in P1 to 10.1% in P2, and the maximum reported number of positive staff cases per centre decreased from 18 to 2. Despite the pandemic, during P1 more than 60% centres managed to maintain the activity (<10% reduction of clinical workload). During P2 35 centres (39.3%) experienced an increase in number of treatments, and 22 (24.7%) fully recovered. During the two phases, about one third of Directors who encountered positive patients decided to continue therapy. Follow-up patients' consultations were reactivated in 69 (77.5%) centres. Eleven centres (12.4%) among the few which had cancelled on site first visits during P1 have reopened this service in P2.

Conclusion: The previous P1 investigation revealed

that, despite the shortage of PPE for personnel and important entity of the epidemic, the RT departments were able to contain contagion between patients and staff and continue clinical activity. The current P2 study illustrates how the Italian RT departments are restoring the usual activities, maintaining high safety standards against a possible new spread of infection.

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CO092

HEAD AND NECK CANCER RADIOTHERAPY AMID THE COVID-19 PANDEMIC: PRACTICE RECOMMENDATIONS ON BEHALF OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims: Management of head and neck cancer (HNC) patients amid the COVID-19 pandemic requires dedicated cautions to minimize the risk of cross-infection between patients and health care providers. Aim of the present work is to provide the Radiation Oncology community treating HNCs with a comprehensive set of practical recommendations, encompassing logistic issues, treatment delivery and healthcare personnel's protection in a time of limited resources.

Methods: Under endorsement of the AIRO Executive Committee, a panel of 15 Radiation Oncologists with well-recognized expertise in HNC completed a modified Delphi process consisting of two rounds. A five-point Likert scale was used; the chosen cut-offs for strong agreement and agreement were 75% and 66%, respectively. Items were organized into two sections: 1) General recommendations and 2) Special recommendations. Recommendations were tailored on patients without COVID-19 related symptoms; who were therefore considered as potential carriers. The whole RT workflow was considered; a total of 55 items was circulated and rated using the online survey tool Google Forms. The final consensus was submitted to five senior supervisors and approved by the AIRO Scientific Committee.

Results: The distribution of facilities across the country was as follows: 47% Northern, 33% Central and 20% Southern regions. The majority of participants (60%) was aged between 40 and 50 years; distribution among genders showed a slight female predominance. Seventy-three percent had more than ten years of experience in HNC. There was agreement or strong agreement across the majority (93%) of the proposed items including treatment strategies, use of personal protection devices, set-up modifications and follow-up rescheduling. Examination room sanitization, set-up devices storage (i.e. thermoplastic masks, tongue depressors), use of personal protection devices for healthcare professionals and management of patients who are not resident in the same region as the treating facility were the most debated items.

Conclusions: The need of guaranteeing treatment delivery for HNC patients is well-recognized in Radiation Oncology. Differences in experts' rating can be at least partially explained by differences in local and institutional policies. Our recommendations provide a flexible tool for management both in the pandemic and post-pandemic phase of the COVID-19 outbreak.

CO093

PALLIATIVE RADIOTHERAPY INDICATIONS BY SYSTEMATIC LITERATURE REVISION ALONG COVID-19 PANDEMIC AND FOR FUTURE COMPLEX LOGISTIC SETTINGS: THE NORMALITY MODEL - A DOCUMENT ENDORSED BY AIRO PALLIATIVE CARE AND SUPPORTIVE THERAPIES WORKING GROUP

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The Covid-19 pandemic did challenge over last few months the health care systems worldwide and it is still currently doing. Although some restrictions are being removed it is not sure when the pandemic is actually going to be definitively over.

Aim of this paper is double: 1) to provide a summary of the indications about PRT along Covid-19 period: since some indications can slightly differ and to avoid any possible contradiction, an expert panel of AIRO (Italian Association of Radiotherapy and Clinical Oncology) Palliative Care and Supportive Therapies Working Group (AIRO-Palliative) voted a consensus on that summary; 2) to introduce a clinical care model for PRT (endorsed by AIRO and by a spontaneous Italian collaborative network for PRT, named "La Rete del Sollievo": literally "The Net of Relief"). The proposed model, named "No cOmpRoMise on quality of life by pALliative radIoTherapY" (NORMALITY) is based on an AIRO-Palliative consensus-based list of indication to PRT and on practical indications and materials to manage pt possibly suitable for PRT although dealing within high complexity logistics scenarios (similarly to the ongoing logistics limits for Covid-19).

CO094

COMPLIANCE TO NEW GUIDELINES FOR RADIATION THERAPY ADAPTED TO THE COVID-19 PANDEMIC

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Aims: The emergency situation produced by the COVID-19 pandemic represents a challenge for radiation oncologists (ROs) clinical practice. To reduce the exposure of patients to the hospital environment and minimize the overcrowding of our center we provided to all ROs newly published international guidelines. These guidelines used three potential strategies to reduce the demand for RT during the pandemic: omitting, delaying and shortening the RT course. Our aim was to evaluate ROs compliance in the use of these guidelines.

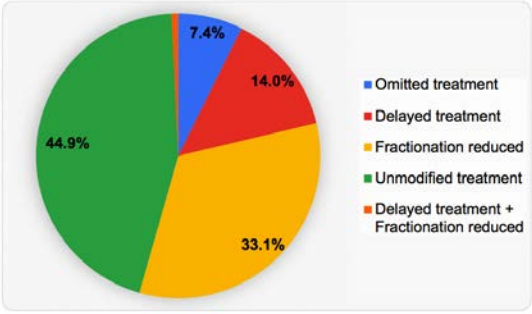

Figure 1.

Methods: All ROs were requested to fill a data form during each patient's first evaluation in May and June 2020. Collected data included: ROs age and gender, patient age and residence, treatment intent, site of disease, dose and fractionation usually prescribed and any changes to treatment (omitted, delayed, shortened). In case of unmodified treatment the motivation was specified. The chi-square test was used to analyse the correlation between treatment prescription and ROs age and gender, patient's age and place of residence, treatment intent, and disease site.

Results: Of 208 treatment prescriptions defined during the period under consideration, 136 were identified for the purposes of this analysis. Seventy-two prescriptions were not included being missing in the guidelines indications to change prescription. Treatment was modified in 54.5% of cases. More specifically, treatment was omitted, delayed, and delivered with a lower number of fractions in 7.4%, 14.0%, and 33.1% of patients, respectively. In one case the treatment was both delayed and shortened. Unmodified treatments were 44.9% of

all prescriptions. A significantly higher compliance in terms of adherence to the new guidelines was recorded in younger (< 40 yrs) and older (> 60 yrs) ROs (p: 0.02), and in older patients (p: 0.01).

Conclusions: In the present emergency situation, the use of COVID-19 specific guidelines were useful to guide ROs in a rational choice of treatment prescription changes. Our analysis showed a reasonably high compliance of ROs to adhere to emergency adapted treatments.

CO095

RADIATION THERAPY FOR HIGH-GRADE GLIOMA IN COVID ERA: SAFE WITH APPROPRIATE PRECAUTION

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Aims: Coronavirus disease (COVID-19) has certainly changed the way of treat oncological patients (pts). High grade glioma (HGG) pts are considered a vulnerable category, in particular for their common advanced age and for their chronic use of steroids. Nevertheless, this study aims to shows that it's possible to preserve an high quality of cures also in COVID era, just taking appropriate precautions.

Methods: To ensure a safe continuum-of-care, we introduced strict regulations to prevent the contagion: triage points at every entrance of the hospital to check the absence of symptoms or contact with SARS-CoV-2 infected; separation between "contaminated" and "clean" area; physical distancing; routinely use of surgical masks. We also introduced a chest CT in pts that had standard CT simulation, even if the cancer was located outside the thorax, to rapidly identify radiological features of COVID disease, even in asymptomatic pts. In case of radiological suspect, the subject was immediately isolated and underwent a nasopharyngeal swab. Every therapeutic decision was evaluated in multidisciplinary way: HGG with MGMT promoter methylation were all treated with temozolomide (TMZ) plus full course radiotherapy (RT); unmethylated pts was considered case-by-case: if was better RT plus TMZ, RT alone, an hypofractionated regimen, or best supportive care (BSC) if poor performance status.

Results: Between March and May 2020, we treated 24 HGG pts, aged between 42 and 80years old. 16 was newly diagnosed and 8 recurrent disease. 4 pts only had radiological diagnosis, 20 underwent neurosurgery. MGMT promoter was methylated in 9 cases. 17pts had concomitant RT-TMZ (71%), 6 had RT alone (25%), 1 patient delayed treatment due to the pandemic, and he progressed, so he only had BSC. During simulation, 1 patient had chest CT suspected for COVID pneumonia and subsequent nasopharyngeal swab positive for SARS-CoV-2 infection. He has postponed treatment until negativization of the swab and he completed RT without side effects. 23 pts took steroids. No pts contracted COVID-19 disease during RT, and all performed the entire therapy without complications.

Conclusions: Even in this difficult scenario, HGG pts can be treated in the most effective way without compromising their safety. In this setting of rapidly progressing tumors, to defer adjuvant therapies beyond the pandemic, can strongly increase the risk of an early progression, and this risk strongly exceeded that of SARS-CoV-2 contagion.

CO096

RADIATION INDUCED PNEUMONITIS IN THE ERA OF COVID-19 PANDEMIC: ARTIFICIAL INTELLIGENCE FOR DIFFERENTIAL DIAGNOSIS.

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Aims: To test the performance of a deep learning algorithm in discriminating radiation pneumonitis (RP) from COVID-19 pneumonia.

Methods: In this retrospective study we enrolled three groups of subjects: Pneumonia-free (control group), COVID-19 pneumonia and RP therapy-related pneumonitis. The CT images were quantitatively analyzed by mean of Artificial Intelligence (AI) algorithm based on a novel deep convolutional neural network structure. Statistical analysis included Mann Whitney U test (significance threshold at $p < 0.05$) and Receiver Operating Characteristic Curve (ROC curve) with fitting performed by using the maximum likelihood fit of a binormal model; the area under the curve (AUC) was calculated with the 95% confidence interval (CI).

Results: The algorithm showed good accuracy in the detection of RP against COVID-19 pneumonia (sensitivity = 97.0%, specificity = 2%, AUC = 0.72). This accuracy increased when an estimated COVID-19 risk probability cut-off of 30% was applied (sensitivity 76%, specificity 63%, AUC = 0.84). The total lung volume ($p = 0.001$), the left lower lobe ($p < 0.001$) and the right lower lobe ($p < 0.001$) involvement resulted increased in COVID-19 group compared to RP.

Conclusions: Deep-learning algorithm was able to discriminate RP from COVID-19 pneumonia, classifying most RP as "Low-risk COVID19" (below the cut off value of COVID-19 risk probability of 30%).

CO097

PROSPECTIVE EVALUATION OF BIOMARKERS (ARV7, ARFL AND PSMA) DETECTION ON CIRCULATING TUMOR CELLS OF MCRPC PATIENTS: PRELIMINARY ANALYSIS OF PRIMERA TRIAL (NCT04188275)

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Aims: The management of metastatic castration-resistant prostate cancer (mCRPC) still remains challenging. The presence of the androgen-receptor (AR) splice variants (ARV7 and ARFL) and the membrane-bound glycoprotein prostate-specific membrane antigen (PSMA) expression in mCRPC patients (pts) has been recently investigated. PSMA ligands were explored to improve prostate cancer imaging by Positron emission tomography (PET). Moreover, Radiopharmaceuticals represent promising therapeutic options for these patients. However, biomarkers to drive both detection and optimal treatment of mCRPC are still missing. Our prospective study testing predictive values of ARV7, ARFL and PSMA combined expression on circulating tumor cells (CTCs), in pts receiving first line Anti andogen Targeted Agents (ARTAs) for mCRPC is ongoing (PRIMERA NCT04188275). This preliminary analysis aims to assess the correlation between prognostic biomarkers expression and the treatment response parameters.

Methods: Pts with mCRPC eligible for ARTA treatment were prospectively enrolled. The combined expression of biomarkers (ARV7 and ARFL variants and PSMA detection on CTC at baseline) on CTCs was collected defining 12 different statuses (table 1). Multiple regression was performed to explore the correlation between status and treatment response features (overall PSA drop, 8 weeks PSA drop, PSA determined at 8 weeks, PSA nadir in CRPC status and time to CRPC).

Results: Overall, 34 pts were enrolled and baseline results are available for 28 pts. CTCs were detected in 15 (53,6%) pts. PSMA, ARV7 and ARFL were expressed in 11, 2 and 9 patients, respectively. ARFL was significantly associated with increased PSA drop and overall PSA drop (P 0.02 and 0.04, respectively). Status 8 (ARFL-/PSMA+) was significantly predictive for higher PSA at 8 weeks (P 0.01) and higher PSA nadir in CRPC status (P 0.01). In addition, Status 6 (ARFL+/PSMA-) was shown to be predictive for reduced time to CRPC development (P 0.02). Status 12 (ARV7-/ARFL+) showed to predict increased PSA drop (P 0.01 and R2 0.2) and overall PSA drop (P 0.02).

Conclusions: These results suggest that PSMA expression on CTCs may help to refine treatment strategy and correct imaging approach in this setting. Development of biomarkers aimed to select patients who benefit from radiopharmaceuticals treatment and/or restaging (e.g PSMA PET/CT) is awaited.

Table 1.

Status	ARV7	ARFL	PSMA
1	-	(+/-)	-
2	+	(+/-)	-
3	+	(+/-)	+
4	-	(+/-)	+
5	(+/-)	-	-
6	(+/-)	+	-
7	(+/-)	+	+
8	(+/-)	-	+
9	-	-	(+/-)
10	+	-	(+/-)
11	+	+	(+/-)
12	-	+	(+/-)

CO098

IS THERE A POTENTIAL ROLE OF FUNCTIONAL IMAGING BOOST TUMOR VOLUME DELINEATION FOR RECTAL CANCER TREATMENT INTENSIFICATION? AGREEMENT BETWEEN RADIATION ONCOLOGISTS AND VOLUMES

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Aims: The gold standard imaging modality for locally advanced rectal cancer (LARC) staging is currently represented by T2 weighted Magnetic Resonance Imaging (MRI). Several studies have suggested a potential benefit of using functional imaging, as Diffusion-Weighted MRI (DWI) and Positron Emission Tomography (PET-CT), in treatment intensification strategies. The aim of this study was to evaluate the inter-observer agreement between two radiation oncologists, and the difference in volumes of Gross Tumor Volume (GTV) delineation in simul-TC, T2-MRI, DWI-MRI and PET-CT, in LARC patients.

Methods: two radiation oncologists retrospectively manually delineated GTVs of 24 patients (20 males and 4 females, mean age: 69.25 years; range: 40–88 years) on simul-TC (TCGTV), T2-weighted MRI (T2GTV), echo planar b1000 DWI (DWIGTV) and PET-TC (PET-GTV), blinded and independently from each other. Observers agreement was assessed using Dice index (ranging from 0 as no spatial overlap, to 1 as spatial overlap) and Wilcoxon test. A p-value < 0.05 was considered statistically significant.

Results: Table 1 reported mean and standard deviation GTV obtained for each imaging methodic for both

radiation oncologists. Mean Dice index was 0.85 for TCGTV, 0.84 for T2GTV, 0.82 for DWIGTV and 0.89 for PETGTV, representative of an almost perfect agreement. Significantly larger volumes delineations were obtained for TCGTV respect to T2GTV ($p<0.001$), for T2GTV respect to DWIGTV ($p<0.001$) and for PET-GTV respect to DWIGTV ($p<0.001$), according to Wilcoxon test.

Conclusions: DWI-MRI resulted in smaller volumes delineation compared to TC, T2-weighted MRI and PET-TC imaging. Almost perfect agreements, as reported through Dice index, were reported for each imaging modality between the two observers, both radiation oncologists. As functional imaging, DWI-MRI obtained smaller volumes compared to PET-CT. DWI-MRI seems to remain the optimal strategy for boost volume delineation in case of dose escalation.

Table 1. Mean and standard deviation Gross Tumor Volume (GTV) for simul-TC (TC_{GTV}), T2-weighted MRI ($T2_{GTV}$), echo planar b1000 DWI (DWI_{GTV}) and PET-TC (PET_{GTV}).

	TC_{GTV} (cm^3)	$T2_{GTV}$ (cm^3)	DWI_{GTV} (cm^3)	PET_{GTV} (cm^3)
First observer	41.3±26.9	25.9 ±15.2	21±14.8	37.7±27.7
Second observer	42.2±27.9	27.6±16.9	19.9±14.9	34.8±24.3

CO099

FDG-PET/CT TARGET VOLUME DEFINITION IN LOCALLY ADVANCED CERVICAL CANCER RADIOTHERAPY

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Aims: Definitive chemoradiotherapy is recommended in locally advanced cervical cancer, particularly in patients with unequivocally involved lymph nodes on imaging. In this kind of patients, 18FDG-PET/CT plays an important role in the pathological lymph nodes detection. In our study, we evaluated the impact of 18FDG-PET/CT acquired before radiotherapy in optimizing radiotherapy dose and volume prescription.

Methods: We analyzed retrospectively 43 patients (pts) affected by locally advanced cervical carcinoma, treated between December 2015 and April 2020. CT was carried out in 35 patients and MRI in 41 patients. All the 43 patients underwent planning 18FDG-PET/CT. Patients received definitive Intensity Modulated Radiotherapy (IMRT) of pelvis +/- para-aortic region, followed by brachytherapy when it was feasible. Weekly Platinum based concomitant chemotherapy was administered. The total dose delivered with external beam was 45-50.4 Gy, 1.8 Gy/fr on the pelvis +/- para-aortic region and 54 Gy (50-56 Gy, 2-2.16 Gy/fr) with simultaneous integrated boost (SIB) on 18FDG-PET/CT positive nodes.

Table 1. Total lymph nodes detection.

	para-aortic LN	common iliac LN	internal iliac LN	Obturator LN	external iliac LN	Presacral LN	Perirectal LN
CT and/or MRI- PET-	30	30	33	29	23	41	39
CT and/or MRI+ PET+	3	6	2	8	13	0	2
CT and/or MRI+ PET-	2	4	4	2	4	2	0
CT e MRI- PET+	8	3	4	4	3	0	2

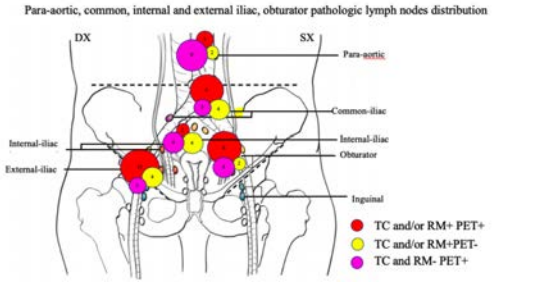

Figure 1.

Results: In 29 out of 43 patients (67%), local lymph nodal involvement was detected. Among them, in 11 patients, 18FDG-PET/CT showed pelvic positive lymph nodes in one or more areas, not detected in the other imaging techniques (CT - , MRI-, PET +,): common iliac lymph nodes (LN) in 3 pts, internal iliac LN in 4 pts, obturator LN in 4 pts, external iliac LN in 3 pts and perirectal LN in 2 patients. Concerning para-aortic region, 18FDG-PET/CT detected metabolically active nodes not evidenced in CT and MRI reports in 8 patients.

Conclusions: In our experience, 18FDG-PET/CT provides a clinical staging optimization. It allowed to modify the clinical target volume in 8/43 (19%) patients with positive para-aortic nodes not detected on CT or MRI and it was useful to intensify dose in involved lymph node areas.

CO100

PET-CT GUIDED CONTOURING IN ANAL CANCER PATIENTS

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Aims: Radiotherapy (RT) with concurrent 5-fluorouracil/mitomycin-C has been established as definitive standard therapy approach for anal cancer (AC). Intensity Modulated Radiotherapy (IMRT) leads to a precise treatment of the tumor, allowing dose escalation on Gross Tumor Volume (GTV), with a surrounding healthy tissues sparing. Our study assessed the impact of PET/CT on the RT contouring process and its contribution to lymphatic spread detection, allowing a per-

sonalization of Clinical Target Volume (CTV) and dose prescription.

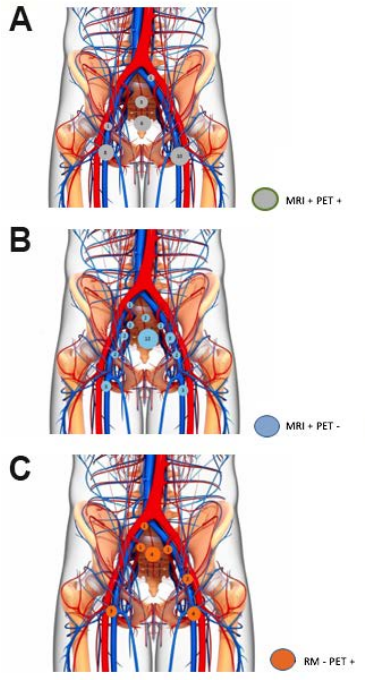

Figure 1. A: PET+ Lymph nodes also detected on MRI. B: MRI detected Lymph nodes otherwise not highlighted on PET TC. C: PET + Lymph nodes not detected on MRI.

Methods: Thirty-one patients (pts), 25 females (81%) and 6 (19%) males, with histologically proven squamous cell carcinoma of the AC were analyzed. They received IMRT and concurrent chemotherapy between May 2012 and September 2020. All pts were evaluated with trans-anal endoscopic ultrasound, MRI of the pelvis, CT scans of the chest, abdomen and pelvis. Simulation was performed by PET/CT imaging with pts in treatment position. GTV and CTV were drawn on CT and PET/TC fused images. RT Target volume included the whole pelvis plus bilateral inguinal lymph node (LN) areas. Common iliac LN were added only when involved. A total dose of 54 Gy (up to 59 Gy) was delivered to the primary tumor and 45 Gy to the elective LN areas; a simultaneous integrated boost of 50-54 Gy was planned on PET/CT positive nodes. A Mapping of the involved LN was carried out, mainly comparing MRI and PET/CT results.

Results: 29 out of 31 (94%) pts presented LN involvement, in 1 or more areas, detected on PET/CT and/or MRI. PET/CT showed positive LN not detected on MRI imaging (PET+, MRI-): 1 in the common iliac LN area, 2 in the internal iliac LN area, 2 in the external LN area, 7 in the inguinal LN area and 4 in the presacral area. RT CTV was modified including common iliac region in 1 patient. In addition, in five patients, PET/CT allowed to a dose escalation in the inguinal areas. PET/CT fused images led to change the stage in 5/31 cases (16%): 4 cases from N0 to N1 (inguinal LN) and 1 from M0 to M1 (common iliac LN). In 12 pts the PET/CT had a lower sensitivity in the mesorectal LN detection than MRI.

Conclusions: PET/CT has a potentially relevant impact in staging and target volume delineation in pts affected by AC. Clinical stage variation occurred in 16% of cases. We observed that MRI seems to be more accurate in detecting mesorectal nodes, while PET/CT appears to be more useful in defining LN disease spread in the remaining pelvic and inguinal station.

CO101

MRI DELTA TEXTURE ANALYSIS CAN PREDICT PATHOLOGICAL RESPONSE IN RECTAL CANCER PATIENTS UNDERGOING NEOADJUVANT CHEMO-RADIATION

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Aim: The present study was designed to evaluate MRI delta texture analysis (D-TA) in predicting the outcome in term of complete pathological response, of patients with locally-advanced rectal cancer undergoing neoadjuvant chemoradiotherapy (C-RT) followed by surgery.

Materials and Methods: We performed a retrospective analysis on 70 patients with locally advanced rectal adenocarcinoma undergoing C-RT and radical surgery between January 2013 and December 2019 treated in two centers. The gross tumor volume (GTV) was evaluated at both baseline and after C-RT MRI and contoured on T2, DWI, and ADC sequences. Multiple texture parameters were extracted with LifeX Software and D-TA were calculated as the percentage variations in the two timepoints. By performing univariate analysis and a multivariate analysis (logistic regression), these TA parameters were then correlated with patients' pathological outcome. Complete pathological response (pCR, with no viable cancer cells: TRG 0) were chosen as statistical endpoints. ROC Curves were calculated on the two different datasets.

Results: In the whole cohort 16 patients (23%) showed a pCR. At univariate analysis, different parameters resulted significantly correlated with pCR. Binary logistic analysis showed that the only significant parameter was ADC GLCM-Entropy (p:0,001). AUC for pCR was 0.874 in the Training Cohort and 0.926 in the Validation Cohort.

Conclusions: Our results suggest that D-TA has a significant role in the prediction of pCR. D-TA may

lead to select patients who may achieve a complete pathological response and may, in the next future, potentially avoid surgery.

CO102

RECTAL CANCER RESPONSE PREDICTION: EXTERNAL VALIDATION OF A DELTA RADIOMICS APPROACH ON HYBRID 0.35 T MAGNETIC RESONANCE GUIDED RADIOTHERAPY (MRGRT) IMAGES

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Aims: This study aims to validate the use of two delta radiomics features (variation of length least, ΔLleast; and grey level non-uniformity, Δglnu), previously identified as response predictors in locally advanced rectal cancer (LARC), on an external and independent cohort of patients (pts) undergoing neoadjuvant chemoradiotherapy (nCRT) on hybrid Magnetic Resonance guided radiotherapy (MRgRT) 0.35 T units. The performances of these indicators have been tested for both clinical and pathological complete response (cCR and pCR).

Methods: Pts affected by LARC undergoing nCRT in 3 international institutions and treated according to specific internal protocols (A, B and C) were enrolled for this retrospective study. All the pts enrolled in the study had a 0.35T TrueFastImaging with steady state precession (TRUFI) simulation and daily positioning MR images. The on board images acquired when a BED of 23 Gy (fraction 10 for A and 14 for B and C) was reached were used for delta radiomics calculation purposes, with respect to the original values calculated on the simulation MR. Lleast and glnu features were then extracted from the available images using Moddicom, a R library specifically designed for radiomics analysis. The thresholds identified in the original model were 0.73 for ΔLleast and 0.65 for Δglnu, with pts showing values lower or equal to these thresholds being identified as cCR patients. No pCR prediction was available for the original model. In order to provide a more comprehensive evaluation of the predictive power of these features in the considered dataset, the Receive Operation Characteristic (ROC) Curve was calculated considering cCR and pCR as outcome.

Results: A total of 43 pts were enrolled for this analysis (26A, 9B and 8C). cCR was reached in 8 cases (6 A, 2 B, rate 18.6%) and pCR in 12 cases (10 A, 2 C; rate 27.9%). The values of accuracy, sensitivity, specificity, positive (PPV) and negative (NPV) predictive values calculated at the thresholds proposed in the first model for cCR and pCR prediction are reported in table 1. ΔLleast correctly classified 35/43 (81.4%) (AUC 0.83) pts for cCR prediction and 34/43 (79.1%) for pCR (AUC 0.84). Δglnu performances were lower: 26/43 (60.4%) (AUC 0.67) and 28/43 (65.1%) for cCR and pCR cases respectively (AUC 0.62).

Conclusions: ΔLleast calculated when a BED value of 23 Gy is reached can be considered a promising parameter for both cCR and pCR prediction in LARC pts while Δglnu is a less reliable index.

Table 1.

	cCR		pCR	
	ΔL_{least}	Δglnu	ΔL_{least}	Δglnu
Sensitivity	0.75	0.75	0.58	0.75
Specificity	0.83	0.57	0.84	0.61
PPV	0.50	0.29	0.58	0.43
NPV	0.94	0.91	0.84	0.86
Accuracy	0.81	0.60	0.77	0.65

CO103

FEASIBILITY STUDY OF TANTALUM MARKERS FOR FRACTIONATED CYBERKNIFE TREATMENT FOR UVEAL MELANOMA

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Aims: We aim to describe our experience in the treatment of uveal melanoma (UM) with three different approaches for eye positioning and tracking.

Methods: From April 2014 to May 2019 34 patients (pts) suffering from UM were treated at our Cyberknife (CK) center. All pts were treated with a thermoplastic mask and underwent orbit gadolinium MRI to delineate target volumes. CK can accurately target structures with a rigid relationship to the skull, but does not provide a means to track eye movement. 8 pts were treated using a peribulbar anesthesia performed 20 minutes before the simulation CT and the CT scan prior to each session to evaluate the displacements of the lens/optic nerve insertion. Secondly the immobilization was performed keeping the eye closed with a bandage on it, both during the simulation and the treatment. Also in these case the pts were reimaged prior to every session to estimate eye position. The feasibility of using tantalum markers was investigated to potentially reduce PTV margins. These nonmagnetic markers are sutured to the sclera around the tumor. Preliminary CT and MRI scans were performed placing the markers on anthropomorphic phantoms to assess any metallic artifact and to evaluate their

detectability on the 2D image guidance X-ray images.

Results: Practicing anesthesia proved to be inappropriate, as the eyeball tended to displace from its original position in an unpredictable way. In the second approach the coregistration between the simulation and the pre-treatment CT was performed to check the tumor position and evaluate the goodness of the margins applied. Rotations of the eye were detected in a small number of pts, while translations were always negligible. Starting from the x, y and z displacements of the lens/optic nerve insertion measured on all the coregistered scans and using the Van Herk margin formula, we found that our 2.5 mm in all directions was appropriate. The limit of this technique is that the intrafraction eye movement wasn't monitored during treatment. The first results on tantalum markers seem encouraging: they produce an acceptable level of metallic artifacts and are clearly visible on the X-ray images used for IGRT.

Conclusions: Although not strictly noninvasive, the use of tantalum markers could lead to a margin reduction (estimated to about 1.3 mm), thanks to the capability of performing a real time tracking and is promising for treatment accuracy improvement and potential toxicity reduction.

CO104

THE ROLE OF ADVANCED IMAGING (MPMRI AND 18FCH-PET/TC) IN DETECTION OF BIOLOGICAL TARGET VOLUME (BTV) IN PATIENTS WITH BIOCHEMICAL RELAPSE AFTER RADICAL PROSTATECTOMY TREATED WITH HIGH DOSE SALVAGE RADIOTHERAPY: FEASIBILITY STUDY IN 200 PATIENTS

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Abstract Objectives: After radical prostatectomy from 15 to 40% of patients have a biochemical relapse. Salvage radiotherapy (SRT) is the standard treatment for biochemical relapse with at least 66 Gy delivered to prostatic fossa. Dynamic 18F-Choline PET/TC and multi parametric MRI (mpMRI) could identify site of recurrence, allowing dose escalation to biological target volume (BTV).

Methods: From January 2009 to December 2018, data of over 250 patients with biochemical progression after radical prostatectomy were collected. Of these, 200 patients with biochemical recurrence at diagnosis underwent dynamic 18F-Choline PET/TC and mpMRI, which revealed in all cases a local recurrence without distant metastases. Patients received a total dose of 80 Gy with conventional fractionation of 2 Gy/die directed to the BTV. Acute and late toxicity were collected using the CTCAE scale (vers. 4.3).

Results: The treatment was well tolerated: 173 patients (91%) completed treatment without interruptions. There were no greater than G2 toxicities: 24% of patients experienced acute urinary toxicity (G1 21% and G2 3%) and 39% acute intestinal toxicity (G1 29% and G2 10%). With regard to late toxicity, 28% of patients developed urinary toxicity, of which in one case higher than G3 and 17% intestinal toxicity, of which in only one case higher than G3. With a median follow-up of 69.3 months 53/200 patients (26%) experienced a recurrences.

Conclusions: The new techniques of advanced imaging (dynamic 18F-Choline PET/TC and mpMRI) allow a better definition of target therapy. With a median follow up greater than 5 years, high-dose SRT appears feasible and well tolerated, with low rate of late toxicity.

CO105

STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PRIMARY AND SECUNDARY LUNG CANCER. ANALYSIS OF A MONO-INSTITUTIONAL RETROSPECTIVE SERIES

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Aims: We retrospectively analyzed the outcome of SBRT in the treatment of lung cancer with a mean follow-up >2years.

Materials: Between October 2013 to May 2020, 82 lesions in 74 patients (pts) affected by early stage NSCLC (I-II,according to TNM classification eight edition) or by oligo-metachronous-metastatic lung disease (primary controlled tumor sites were colon in 5cases and breast in 3 cases) were treated in our Institution. Central/peripheral lesion ratio was 14/68.We used the 4DTC acquisition to identify the internal target volume.Treatment plans were studied on Varian Eclipse TPS and performed using VMAT (71 lesions) or dynamic conformal arcs (11 lesions) with IGRT technique. Dose normalization was performed on the minimum PTV value. All points of the PTV must absorb 100% of the prescribed dose. While this normalization offers the best target coverage, it also provides a maximum dose value of approximately 120%. Mean PTV was 22cc (range11.5-27 SD18). Mean ITV was 8.7cc (range3-9.5 SD10.5).Median BED prescribed (α/β=10) was 100Gy (range35-112). Median effective BED was 115Gy (37.5-145). Toxicity was evaluated using CTCAE v4.03, comorbidities using Charlson Index (CI) based on International Classification of Disease and CI age-corrected. We invastigated overall survival (OS),LC, any relapse free status (anyRFS) and lung toxicity. Survivals have been evaluated by Kaplan-Meyer method and the inference by Log-Rank test.

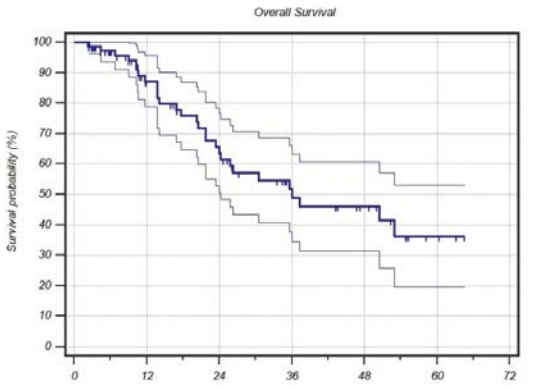

Figure 1.

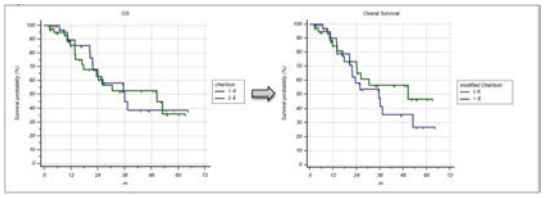

Figure 2.

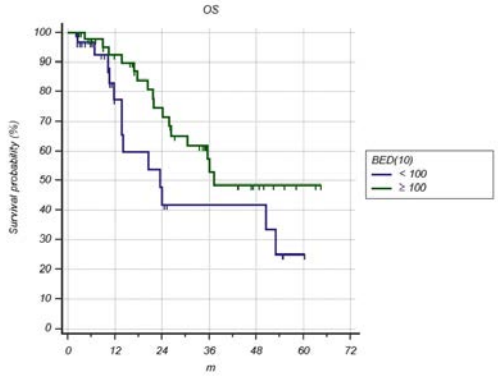

Figure 3.

Results: Median age was 75y (42-88). Male/Female ratio was 52/22. Median follow-up was 24 months (10-36 SD16). Median OS was 36 months; 1,2y were respectively 88% and 62%[Figure 1].LC 1,2 and 3y was respectively 88%,76% and 72%.AnyRFS 1,2 and 3y was respectively 62%,45% and 22%.No pts developed >=G2 chest wall or esophageal toxicity.All pts manifested G1 lung toxicity.Acute toxicity G2 occurred only in 5pts.Late lung toxicity G2 and 3 respectively in 13 and 3pts.These ones had poor pre-SBRT pulmonary function and SBRT hadn't increased lung toxicity >10%.In our experience,chronological age doesn't seem to affect OS significantly,OS according to CI age-corrected versus CI, shows a paradoxical effect[2].

Conclusions: Our experience demonstrated SBRT is a safe and effective treatment.All treatments were characterized by high pts's compliance and completed as planned without interruptions so SBRT can be easily interfaced with systemic therapies as needed. OS reflects the trend described in the literature with better results with BED (α/β=10) >=100[3]. Dedicated clinical registries and prospective trials are required to improve pts selection for SBRT.

CO106

RISK-ADJUSTED PRESCRIPTION DOSE FOR LINAC-BASED SBRT IN ELDERLY PROSTATE CANCER

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Aims: Stereotactic body radiation therapy (SBRT) is replacing prostatectomy mostly in case of low risk setting. However, in selected case of intermediate/high risk, it could be a treatment justified solution. Aim of this study is to evaluate safety and efficacy of Linac-based SBRT in elderly localized PC treated with an approach of risk-adjusted prescription dose.

Methods: Men aged 70 years or older affected by localized PC were treated. The schedule consisted of 35 Gy in 5 fractions. Dose was optimized to isodose 90% and 80% for low/favorable intermediate and unfavorable/high risk cases, respectively. Treatment planning and delivery were performed using the RapidArc® (RA) VMAT technique. Based on PTV and urinary symptoms, the treatment was administrated in 1 or 2 weeks. According to risk group some patients received androgen deprivation therapy (ADT). Toxicity and quality of life (QoL) were assessed at baseline, after treatment and during follow-up (fu) using the Common Terminology Criteria for Adverse Events and International Prostatic Symptoms Score (IPSS). PSA values were recorded before treatment and during fu as biochemical response criteria.

Results: Between 18.07.2019 and 29.05.2020, 33 patients were treated. Median age was 74 years (range 61- 85); 14 were low risk, 14 favorable/unfavorable intermediate risk and 5 high risk group. Median pre-treatment PSA was 5 ng/ml (range 0,61-25). ADT was administrated in 8 patients. In cases in which dose was optimized to isodose 90%, Dmax was 38,9, whereas dose was optimized to isodose 80%, Dmax was 43,8. Median PTV was 109,6 cc (range 75-157,7). Median baseline IPSS was 3 (range 0-6). At the end of treatment no >G1 acute toxicity was observed. At 2-3 weeks after treatment, 2 patients reported G2 acute genitourinary toxicity (urinary frequency, urinary tract pain and urinary retention), while 3 patients referred rectal tenesmus. During the last fu, no late toxicity and no relevant deteriorations of QoL were described. At a median fu of 6 months (range 1-9), excellent biochemical disease control was achieved in all cases with median PSA of

1,7 ng/ml (range 0,01-6,05). No differences were observed between 2 different prescription approaches.

Conclusions: Risk-adjusted prescription dose for Linac-based SBRT in elderly patient affected by localized PC is feasible and well tolerated with excellent biochemical disease control. Longer follow-up is needed to the assess late toxicity profile and long-term clinical outcome.

CO107

ACUTE TOXICITY IN THE STEREOTACTIC BODY RADIOTHERAPY VERSUS MODERATELY HYPOFRACTIONATED RADIOTHERAPY WITH HELICAL TOMOTHERAPY FOR PROSTATE CANCER

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Aims: Low-risk prostate cancer is commonly treated with external-beam radiotherapy. Moderate hypofractionation has been shown to be non-inferior to conventional fractionation. Ultrahypofractionated stereotactic body radiotherapy would allow shorter treatment courses but could increase acute toxicity compared with moderately hypofractionated radiotherapy. In this study we reported the acute toxicity findings from a randomised trial of moderately hypofractionated radiotherapy versus ultra-hypofractionated stereotactic body radiotherapy for low-risk localised prostate cancer, using Helical Tomotherapy (HT).

Methods: From January 2017 to January 2020, 40 consecutive patients with low risk localized prostate cancer (cT1-2, GS=6, PSA<10 ng/ml) were randomized to moderately hypofractionated radiotherapy (30 fractions) to ultra-hypofractionated stereotactic body radiotherapy (5 fractions) using helical Tomotherapy. 20 patients were treated with 30 fractions (Group A) and 20 with 5 fractions (Group B). Patients were monitored before therapy, weekly/daily during therapy, using RTOG GI, GU and hematological toxicity grading scale. Doses were prescribed to planning target volumes (PTVs) as the followings: 72 Gy (2.4 Gy/fx) to PTV-whole prostate in 30 fractions or 36.25 Gy (7.25 Gy/fx) to PTV-whole prostate in 5 fractions. Dose to abdominal cavity, both femoral heads, bladder and rectum were constrained below each tissue tolerance.

Results: Median age of the patients was 72 (range 55-85 years). Median iPSA in the Group A was 5.9 ng/ml (range 2.5-9), while in the Group B was 6.5 ng/ml (range 2.21-10). At the end of the treatments, 8/20 (40%) patients in the Group A vs. 4/20 (20%) patients in the Group B had G1grade of GI toxicity (p=0.09), while only 1/20 (5%) patient in the Group A had G2 grade of GI toxicity. 6/20 (30%) patients in the Group A vs. 7/20 (35%) patients in the Group B had G1 grade of GU toxicity (p=0.7), while only 1 patient (5%) in the Group A and only 1 (5%) in the Group B had G2 grade of GU toxicity. No hematological toxicity was showed. No G3-4 grade of GI and GU toxicity was showed.

Conclusions: Acute toxicity is very low. Our dates suggested that there is no difference in term of toxicity between hypo- and ultra-hypofractionated radiotherapy. Our study confirmed that ultra-hypofractionated scheme offering a shorter overall treatment time and a well-tolerated treatment, so it's represents an excellent option.

CO108

STEREOTACTIC BODY RADIATION THERAPY FOR ULTRA-CENTRAL LUNG OLIGOMETASTASES IN NON-SMALL-CELL LUNG CANCER

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Aims: In recent years, the role of Stereotactic Body Radiation Therapy for the treatment of lung metastases has emerged, thanks to its non-invasive nature, safety and the possibility to achieve radicality. This is particularly relevant in the oligometastatic disease, where the simultaneous ablation of all the metastatic lesions can yield a longer survival benefit or even cure the disease. However, its use in Ultra-Central lung tumors, a subset of tumors whose planning target volume touches or encompasses critical mediastinal structures (proximal bronchial tree, esophagus, pulmonary artery and pulmonary vein) remains controversial, because of the high incidence of severe or even fatal toxicities reported in literature. The aim of our study is to evaluate safety and efficacy of different SBRT regimens for the treatment of ultra-central NSCLC oligometastases and to assess the predictive influence of clinical and treatment-related factors on outcome and incidence of toxicity.

Methods: Clinical and treatment-related parameters have been retrospectively reviewed in a cohort of oligometastatic NSCLC patients, treated with SABR for ultra-central lung metastases. Objective response rate (ORR), local control (LC), distant-metastasis-free survival (DMFS), progression-free survival (PFS), overall survival (OS), incidence and grade of toxicity were evaluated. A Statistical Analysis was carried out to assess the predictive impact of those factors on outcome and toxicity occurrence.

Results: Seventy-two consecutive patients were included, with a median follow-up of 17 months (range 8-24), submitted to SABR (median biologically effective dose (BED10) 105 Gy, range 75-132). At three months from SABR, ORR was 91%. Two-year LC, DMFS, PFS and OS were 83%, 46%, 43%, and 49%, respectively. BED >75 Gy10 was correlated to higher LC ($p = 0.02$), PFS ($p = 0.036$), and OS ($p < 0.001$). Grade ≥3 toxicity rate was 7%, including one G5 esophagitis. No variables were correlated to DMFS or

to the occurrence of overall toxicity.

Conclusions: The aggressive dosimetric approach, used in this study, resulted in satisfactory local control and acceptable toxicity profile. Although limited by its retrospective nature and by the use of several dose-fractionation regimens, this study shows on a large series of patients, that SABR, using dose-intensive schedules, improves outcomes in NSCLC oligometastatic patients with Ultra-central lesions.

CO109

STERETACTIC BODY RADIATION THERAPY FOR NODAL LESIONS IN OLIGOMETASTATIC/OLIGORECURRENT PROSTATE CANCER PATIENTS: A POOLED ANALYSIS OF A PHASE I AND A PHASE II TRIALS.

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[1]Radiotherapy Unit, Gemelli Molise Hospital Campobasso; [2]Medical Physic Unit, Gemelli Molise Hospital, Campobasso, Italy; [3]Radiation Oncology Center, Department of Experimental, Diagnostic and Specialty Medicine DIMES, University of Bologna, S Orsola-Malpighi Hospital, Bologna, Italy; [4]Fondazione Policlinico Universitario AGemelli, IRCCS, UOC di Radioterapia, Dipartimento di Scienze Radiologiche, Radioterapiche ed Ematologiche, Roma, Italy; [5]Università Cattolica del Sacro Cuore, Istituto di Radiologia, Roma, Italy

Aim: Aim of this pooled analysis was to report the toxicity profile and the rate of local control in oligometastatic/oligorecurrent prostate cancer patients treated with stereotactic radiotherapy (SBRT) for nodal metastases.

Methods: We retrospectively collected the clinical data of prostate cancer patients who were enrolled in two institutional prospective studies (DESTROY-1 and DESTROY-2) and treated with SBRT on oligometastatic/oligorecurrent nodal lesions. The first trial was a multi-arm phase I study on SBRT delivered with fixed non-coplanar conformal fields (3D-CRT) or Volumetric Modulated Arc Therapy (VMAT) in patients with primary or metastatic tumours in various extra-cranial body sites. The second one was a radiosurgery trial where radiotherapy was delivered by VMAT technique in patients with primary or metastatic tumours in various extra-cranial body sites. The toxicity profile, the Local control (LC), the Overall survival (OS) and the time elapsed between SBRT and systemic therapy (hormonal or chemotherapy) start/change were analysed.

Results: Data on 46 patients harbouring 64 nodal lesions treated with SBRT at our institution between the 2005 and 2020 were collected. The clinical characteristics of patients and treated lesions are reported in the Table 1. During the treatment only G1 and G2 toxicities were registered as follows: skin toxicity (grade 1: N=2), gastro-intestinal toxicity (grade 1: N=9, grade 2: N=1), genito-urinary toxicity (grade 1: N=4). During follow up one grade 1 late skin toxicity, one grade 1 gastro-intestinal toxicities (slight rectal bleeding) and 1 grade 3 larynx toxicity (oedema) were registered. The median LC was 110 months (IC 95% 94-126 months), while 1-, 3- and 5-year LC was 98%, 88% and 77% respectively. The median OS was 87 months (IC 95%: 66-107 months), while 1-, 3- and 5-year actuarial OS was 93%, 77% and 59% respectively. The median time elapsed between SBRT and systemic therapy (hormonal or chemotherapy) start/change was 67 months (IC 95%: 48-87 months)), while 1-, 3- and 5-year actuarial time free from a new systemic therapy schedule was 80%, 65% and 56%, respectively.

Conclusions. In this scenario SBRT, carrying out a low toxicity profile and an excellent LC rate, can be considered a safe and valuable option. Moreover, this local treatment can delay the start or the changing of an eventual systemic therapy.

Mean age (years)	
73 (62-85)	
ECOG	N°
0	32 (70%)
1	12 (26%)
2	1 (2%)
3	1 (2%)
Comorbidities	N°
Cardiovascular	32 (70%)
Diabetes	10 (21%)
Hepatic comorbidity	2 (4%)
Other tumor	2 (4%)
Pulmonary comorbidity	1 (2%)
Other	4 (8%)
New systemic therapy after SBRT	N°
Hormonal therapy	1 (2%)
Chemotherapy	6 (12%)
Abiraterone	13 (26%)
Enzalutamide	4 (8%)
Radon	1 (2%)
Site	N°
Lung	4 (6%)
Mediastinum	4 (6%)
Superior abdomen	15 (24%)
Pelvis	41 (64%)
Total Dose (Gy) x number of fractions	N°
12x1	6 (9%)
16x1	1 (1.5%)
18x1	1 (1.5%)
20x1	13 (21.5%)
20x5	2 (3%)
22x1	1 (1.5%)
24x2	2 (3%)
24x1	6 (9%)
25x5	1 (1.5%)
30x5	3 (4.5%)
35x5	5 (7.5%)
40x5	5(7.5%)
45x5	13 (21.5%)
50x5	5 (7.5%)
Mean PTV (cc)	
29,15 (1.2-101)	

Figure 1.

CO110

"LONG TERM RESULTS AND PREDICTIVE FACTORS FOR OUTCOME AND TOXICITY OF LOW-RISK AND INTERMEDIATE-RISK PROSTATE CANCER TREATED WITH LINAC-BASED STEREOTACTIC BODY RADIATION THERAPY"

D. Baldaccini[1], C. Franzese[1,2], G.R. D'Agostino[1], M. Badalamenti[1], G. Reggiori[1], P. Mancosu[1], S. Tomatis[1], M. Scorsetti[1,2]

[1]Humanitas Clinical and Research Center – IRCCS, Radiotherapy and Radiosurgery Dept., Rozzano (Mi) – Italy; [2]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele – Milan, Italy

Aims: Stereotactic body radiation therapy (SBRT) is considered an effective treatment in patients with low and intermediate risk prostate cancer (PC). Aim of the present study was to evaluate outcome, early and late toxicity of low and intermediate risk PC treated with Linac-based SBRT.

Methods: We included patients affected by adenocarcinoma PC, classified as low or intermediate risk disease according to NCCN criteria. All patients were treated with Linac-based SBRT with schedule of 35 Gy in 5 fractions delivered on alternate days.

Results: 178 patients were treated from 2012 to 2018. Median follow-up was 58.9 months (range 9.7 – 89.9). Rates of BRFS at 1, 3 and 5 years were 98.3% (95%CI 94.7 – 99.4%), 94.4% (95%CI 89.4 – 97) and 91.6% (95%CI 85.4 – 95.2). BRFS at 5 years was 94.9% (95%CI 86.8 – 98) for ISUP grade group 1, 93.2% (95%CI 80.5 – 97.7) for ISUP group 2 and 74.8% (95%CI 47.1 – 89.5) for ISUP group 3. Rates of mPFS at 1, 3 and 5 years were 98.8% (95%CI 95.5 – 99.7), 96.2% (95%CI 91.9 – 98.3), and 92.9% (95%CI 87.2 – 96.2) and rates of OS at 1, 3 and 5 years were 100%, 97.2% (95%CI 92.9 – 98.9) and 95.1% (95%CI 90 – 97.6). Only one (0.56%) case of grade 3 genitourinary (GU) toxicity and gastrointestinal (GI) acute toxicity was reported in the acute setting. Only one (0.56%) patient with grade 3 late GU toxicity.

Conclusions: At long-term follow-up, SBRT continues to be a valid option for the management localized PC. Biochemical control remains high even 5 years after treatment. Selection of patients is crucial for the prevention of acute and late severe toxicity.

CO111

STEREOTACTIC BODY RADIATION THERAPY WITH CONCURRENT TRABECTEDIN IN METASTATIC SOFT-TISSUE SARCOMA PATIENTS: ASSESSMENT OF EFFICACY AND SAFETY

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Aim: This observational study evaluated the efficacy and safety of Trabectedin (T) in association with stereotactic body radiation therapy (SBRT) in patients with metastatic soft-tissue sarcomas (STS).

Methods: Data from patients treated with SBRT to metastatic lesions and concomitant T were retrospectively collected. T was performed at a dose of 1.5 mg/m^2 in 24-hour infusion, every 21 days. SBRT was considered concomitant when delivered no later than 5 weeks from last cycle of chemotherapy. SBRT with Volumetric Modulated Arc Therapy (VMAT) was adopted. Prescription dose and number of fractions varied according to tumor location and size. Overall response rate was assessed using Response Evaluation Criteria in Solid Tumors version 1.1. Pain response was evaluated according to Numerical Rating Scale (NRS). Adverse events (AEs) were scored according to Common Terminology Criteria for Adverse Events scale version 4.03 and RTOG Common Toxicity Criteria.

Results: Concurrent T and SBRT for distant metastases were performed in 23 metastatic STS patients between March 2009 and December 2019 in Our Institution. Twelve patients had a follow up of at least 3 years. Median age was 47.5 years (range 19-68). The histopathologic subtypes were: leiomyosarcoma (33%), spindle and pleomorphic sarcoma (25%), pleomorphic liposarcoma (8,3%), synovial sarcoma (8,3%), pleomorphic sarcoma (8,3%), spindle cells sarcoma (8,3%) and malignant peripheral nerve sheath tumor (8,3%). Four (33.3%) patients were metastatic at baseline. Sites of metastatic disease treated were: bone (50%), soft tissue (25%), lung (16.7%), lymph nodes (8.3%). Chemotherapy-related Grade 3 or more AEs were mainly hematological: anemia (25%), thrombocytopenia (8,3%) and transaminase elevation (8,3%). SBRT-related AEs were represented by dermatitis of Grade 2 or less in 16.6% of cases and by one case of pathologic bone fracture. After a median follow-up of 39,4 months, 9 (75%) patients had stable disease (SD) and 3 (25%) patients had disease progression (PD). The median time to progression (TTP) was 34 months. According to NRS, median score of pain response 3 months after SBRT was 1.85.

Conclusions: SBRT with concurrent T in metastatic STS patients was safe and resulted in a good local control. The AEs were similar to the toxicity profile of each treatment administered alone. Currently, the combination of T and SBRT is not the standard and prospective trials are needed to confirm our results.

CO112

STEREOTACTIC BODY RADIOTHERAPY FOR LOCAL RECURRENCE IN PROSTATE CANCER PATIENTS PREVIOUSLY TREATED WITH DEFINITIVE EXTERNAL BEAM RADIOTHERAPY

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Aims: In this retrospective study we evaluated efficacy and toxicity of Stereotactic Body Radiotherapy (SBRT) for exclusive local failure after primary External Beam RT (EBRT) for prostate cancer (pCa).

Methods: From September 2012 to December 2015, 28 patients underwent SBRT for local recurrence after definitive EBRT. All patients were treated with a total dose of 30 Gy in 5 fractions PSA was assessed at 2 months, 6 months, and every 3 months following rSBRT. Toxicity was assessed by the Common Terminology Criteria for Adverse Events toxicity scale (CTCAE v.4.03).

Results: All patients had received definitive EBRT for a median total dose of 74 Gy (62- 80 Gy) in 2 (1.8-3.1) Gy/fraction. Patients were stratified in low (5, 17.9%), intermediate (9, 32.1%) and high risk group (14, 50%) at diagnosis. Androgen deprivation (AD) was prescribed for prior biochemical failure in 5 patients. Median time between primary treatment and SBRT was 72.7 months (19.3-149.2). Median PSA at recurrence was 2.6 ng/ml (2.1-14.4). Biochemical response at 2 and 6 months to treatment was detected in 25 patients, with a median PSA decline of 54% (2.2-95%) and 76% (35.9-95%), respectively. After a median follow up of 36 months (9.6-79.3), 14 patients were free from disease, 4 patients had stable disease under AD, while biochemical relapse occurred in 8 patients, of whom 2 had metastatic disease. Two patients died for pCa. Median Biochemical Progression-Free Survival (bPFS) was 33 months (95% CI 23-33). Four patients developed acute rectal toxicity; five cases of acute bladder toxicity were reported. Grade 1-2 late rectal and bladder toxicity occurred in 1 and 8 cases, respectively. One patient experienced both grade 3 acute and chronic bladder toxicity, consisting of acute urinary retention and hematuria respectively. Cox regression analysis showed no correlation between bPFS and the analysed baseline features (PSA at recurrence < 2.6 ng/ml, Concurrent AD, High risk category or time to relapse< 72.7 months).

Conclusions: Focal rSBRT can achieve long-lasting remission and delay initiation of medical treatment, with acceptable incidence of acute and late toxicity, regardless of patients baseline features.

Posters

P001

ABSCOPAL EFFECT AND RADIATION-INDUCED BYSTANDER: TWO CASE REPORTS

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Aims: The effects of radiation on human tissues are not just local as once believed but they can appear even outside of the irradiated field. If the irradiated tumor is forming a physical contact with a not irradiated tumor than the phenomenon of transmission of the radiation damage is called bystander effect, otherwise the phenomenon of communication between irradiated and not irradiated distant tumor is called abscopal effect.

Methods: We describe a case of abscopal effect after radiotherapy (RT) and a case of radiation-induced bystander. No systemic therapies has been registered.

Results: A 54-year-old woman underwent to brain metastasis exeresis in November 2019. Histology was poorly differentiated adenocarcinoma. An RM-WholeBody showed an endometrial tumor of 9x2.8x3cm (CCxAPxLL). CT confirmed the uterine mass and showed pelvic adenopathies and lung metastases (mts). Red blood cells transfusion was necessary for anemia and asthenia due to chronic metrorrhagia. Patient underwent stereotactic RT for primary pelvic lesion. Treatment was performed using a VersaHD platform and 6 MV photons, the prescribed dose was 30 Gy to 80% isodose (total dose to isocenter was 37,5Gy) in 3 fractions. Target was exclusively uterine mass. Two months after the end of the treatment, a CT scan showed a reduction of the irradiated mass (3.5x4x3.5) and, surprisingly, a complete regression of pelvic adenopathies and lung mts. Moreover the patient showed an improvement of the performance status and the resolution of the anemia. A 55-years-old woman affected by adenoid cystic carcinoma of external auditory canal (treated with surgery and adjuvant RT in 2011) and lung mts since 2012 underwent stereotactic RT on larger lesions. We selected 3 mts and the delivered doses were 40 Gy/5fx 60% isodose, 30Gy/3fx 70% isodose and 30Gy/3fx prescribed on isocenter, respectively. Treatment was performed with VersaHD platform using an Active Breathing Control (ABC) device. 40 days after the end of treatment, a CT scan showed reduction >80% of treated mts and a spontaneous reduction of other unirradiated lung lesions.

Conclusions: Localized cancer RT may induce systemic out-of-target tumor response. This effect has been connected to mechanism involving the immune system. Today the growing consensus is that combining RT with immunotherapy provides an opportunity to boost abscopal response rates, extending the use of RT to treatment of both local and metastatic disease.

P002

A FEASIBILITY STUDY: A NEW APPROACH TO IMPROVE EFFICIENCY FOR HIPPOCAMPAL SPARING

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Purpose/Objective: to assess the feasibility of 6 arcs with full collimator opening for an efficient VMAT planning approach for hippocampal-avoidance whole-brain radiation therapy

Material/methods:, 11 patient were considered, prescribed dose was 30 Gy in 10 fractions. Contouring was in accordance to RTOG 0933. VMAT Treatment Planning Techniques was applied using 6 coplanar arcs. Full collimator opening was used with the following parameters: arc1 181°-179° clockwise and 95° collimator, arc2 179°-181° counterclockwise and 265° collimator, arc3 181°-300° clockwise and 350° collimator, arc4 60°-179° clockwise and 350° collimator, arc5 179°-60° counterclockwise and 10° collimator and arc6 300°-181° counterclockwise and 10° collimator. Specific physical objective were used for PTV coverage and hippocampal sparing as RTOG protocol suggested. Conformity and homogeneity index were calculated. Statistical analysis was performed.

Results: The coverage of PTV was warranted D90% = 28.8±0.3 Gy, D2% = 31.6±0.4 Gy and for Hippocampal D100% =8.5±0.6 Gy, max dose = 14.9±0.3 Gy. Conformity and homogeneity index were equal to 1.11±0.01 and 0.86±0.03 respectively. 600±10 segments and a total of 1170±150 MU were used. Total delivery time 516±16 sec.

Conclusion: 6 VMAT arcs full collimator opening for hippocampal sparing was feasible and showed a easy coverage in PTV saving hippocampal in accordance of RTOG 0933 constrains. The specific rotation of collimator in the 6 arcs, warranted a easy calculation and deliverability of the plan, with 1000 MU and 500 sec of delivery time.

P003

RIGID PLAN FUSION COMPARED WITH ALGEBRAIC SUM TO EVALUATE CUMULATIVE ADJUVANT PELVIC RADIOTHERAPY (APR) AND BRACHYTHERAPY (BRT) DOSES IN GYNECOLOGIC CANCER PATIENTS

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Aims: To study reliability of algebraic sum in evaluation of cumulative external beam and brachytherapy doses with respect to rigid plan fusion in gynecologic cancer patients (pts).

Methods: In the year 2019, we treated 26 gynecologic cancer pts with APR and endocavitary high-dose-rate BRT. In this group we retrospectively reviewed a sample of 8 pts treated in supine position in which a rigid fusion was performed between APR and BRT plans. A rigid box assessment on pelvis with MIM-Maestro software v 6.7.7. was adopted. On fused computed tomography (CT) rectum and bladder volumes and doses of the two separate CT plans were transferred. So, organ at risk (OAR) cumulative dose volume histograms (DVH) were calculated. To limit OAR volume variability the mean cumulative doses of each OAR was analysed. Particularly, following dosimetric parameters were examined: Dmax (0.5cc), D20%, D50% for rectum and Dmax (0.5cc), D50% for bladder. Cumulative dosimetric parameters obtained were compared with those resulting from algebraic sum.

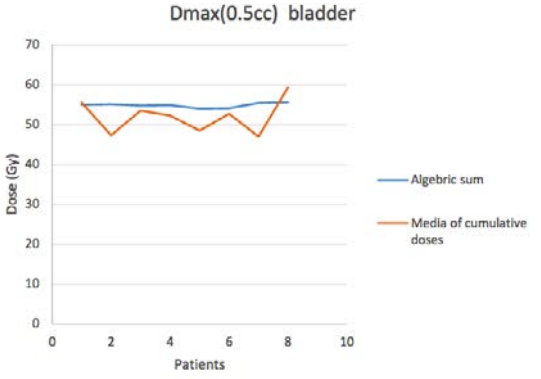

Figure 1. Mean cumulative doses and algebraic sum of doses for Dmax (0.5cc) of the bladder.

Results: Median age was 53 years (range,44-80), median KPS 100% (range, 90-100%), 2 pts had squamous cell cervical cancer and 6 endometrioid cancer, stage IA-IIIB FIGO. All pts have been submitted to surgery and subsequent to APR with volumetric modulated arc therapy (V-MAT), dose of 25x2 Gy. A boost with endocavitary BRT with dose 2x5 Gy was performed in all pts. For rectum, mean differences between mean cumulative doses and algebraic sum were: Dmax (0.5cc) (2.5 +/-7 Gy), D20% (-0.4+/-1.5 Gy), D50% (-1.1 +/-3.3 Gy). For bladder: Dmax(0.5cc) (-2,8 +/- 4 Gy), D50% (-3 +/-6.8 Gy) (Figure 1). Except for rectum Dmax (0.5cc), algebric sum is superior with respect to mean cumulative dose, particularly for bladder dosimetric parameters Dmax (0.5cc) and D50%. All pts completed treatment without significant acute or late toxicities.

Conclusions: Our preliminary analysis shows that algebraic sum of doses slightly overestimates real cumulative OAR doses in gynecologic cancer pts submitted to APR and BRT. Although the small sample size does not allow definitive conclusions, algebraic sum could be generally used in clinical practice reserving

the rigid fusion for critical situations in which it is difficult to respect OAR constrains. Of note, cumulative algebraic sum remains the only available tool when APR and BRT are performed in different centres and DICOM files are not obtainable.

P004

IMPACT OF HYDROGEL PERI-RECTAL SPACER INSERTION ON PROSTATE GLAND INTRA-FRACTION MOTION DURING 1.5T MR-GUIDED STEREOTACTIC BODY RADIOTHERAPY

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Aim: The assessment of organ motion is a crucial feature for prostate stereotactic body radiotherapy (SBRT). Rectal spacer may represent a helpful device in order to outdistance rectal wall from clinical target, but its impact on organ motion is still a matter of debate. MRI-Linac is a new frontier in radiation oncology as it allows a superior visualization of the real-time anatomy of the patient and the current highest level of adaptive radiotherapy.

Methods: We present data regarding a total of 100 fractions in 20 patients who underwent MRI-guided prostate SBRT for low-to-intermediate risk prostate cancer with or without spacer. Translational and rotational shifts were computed on the pre- and post-treatment MRI acquisitions referring to the delivery position for antero-posterior, latero-lateral and cranio-caudal direction, and assessed using the Mann-Whitney U-Test.

Results: All patients were treated with a five sessions schedule (35 Gy/5fx) using MRI-Linac for a median fraction treatment time of 50 minutes (range, 46-65). In the entire study sample, median rotational displacement was 0.1° in cranio-caudal, -0.0022° in latero-lateral and 0.011° in antero-posterior direction; median translational shift was 0.117 mm in cranio-caudal, -0.245 mm in latero-lateral and -0.224 mm in antero-posterior. A significant difference between spacer and no-spacer patients in terms of rotational shifts in the antero-posterior direction (p=0.033) was observed; also for translational shifts a positive trend was detected in antero-posterior direction, although with no statistical significance. (p=0.07)

Conclusions: In our experience, the application of rectal hydrogel spacer for prostate SBRT resulted in a significant impact on rotational antero-posterior shifts contributing to limit prostate intra-fraction motion. Further studies with larger sample size and longer follow-up are required to confirm this ideally favorable effect and to assess any potential impact on clinical outcomes.

P005

IMRT/IGRT HELICAL TOMOTHERAPY: A SUCCESSFUL TREATMENT OF LUNG PARENCHYMA COMPRESSION DUE TO EXTRAMEDULLARY HEMATOPOIESIS IN β-THALASSEMIA. A CASE REPORT

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Aim: Thalassemia is a chronic Hemolytic Anemia, endemic in Mediterranean basin. Extramedullary hematopoiesis (EMH) is a natural compensatory reaction involving several organs or tissues. This case reports a dyspnoea due to bilateral dorsal paravertebral EMH treated successfully with IMRT/IGRT Helical Tomotherapy (HT).

Methods: A.I. , a 53 years old Woman, diagnosed with β-Thalassemia intermedia from age of 2 years, treated with blood transfusion till 2009. In 2009, Hydroxyurea was started due to occurring allogenic immunization and self-immunization. On September 2019, it is the first time that A.I. is examined at the Radiotherapy Department of CIVICO Hospital of Palermo, for Anemia (Hb 6,3gr/dl) and Dyspnoea suggestive of compression of the lung parenchyma. Chest scan revealed several bilateral dorsal paravertebral masses due to EMH. That's why, it is decided to treat A.I., with IMRT\IGRT Helical Tomotherapy (HT) with a total dose of 20 Gy in 10 fractions (2 Gy/fx) over two weeks.

Results: In two weeks, A.I. got encouraging results: a. Increasing in Hb value (Hb 7,8 gr/dl) b. Remarkable reduction of dyspnoea already by the end of the first week of treatment At one month, no more dyspnoea and stable Hemoglobin values: new Chest scan showed a reduction in size of EMH masses with resolution of compressive atelectasis in Right Lower Lobe (RLL). After six months: complete resolution of subjective symptoms and CHEST scans comparison pre-IMRT\IGRT and post-IMRT\IGRT revealed a further reduction in size of EMH masses.

Conclusions: Nowadays, therapeutic approach to EMH still remains controversial, with no pre-established protocols, including serial blood transfusions, Hydroxyurea, Radiation Therapy and surgical decompression. This clinical case description reports as IMRT\IGRT HT should be used as a valid and effective treatment to compressive atelectasis due to EMH cause it gains rapid and remarkable results, in the meaning of improvement of Patient Subjectivity (no more dyspnoea and increasing of Hb values) toghether with gain in Chest scan Objectivity (reduction in size of EMH masses).

P006

A FEASIBILITY STUDY: CAN A V/DOSE MODEL AND AP IN HNC STANDARDIZE PLANS AND OPTIMIZE PLANNING TIME?

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Purpose/Objective: To assess the feasibility of an automatic planning (AP) strategy, based on python script implemented in our treatment planning system (TPS), that minimize planning time reducing parotid glands toxicity on Head Neck Cancer (HNC) radiotherapy treatment planning.

Material/methods: 15 patient underwent VMAT treatment planning techniques using simultaneous integrated boost (SIB) in head neck cancer (HNC), were retrospectively analyzed. The mean dose of parotid glands were correlated with fraction of volume outside PTV. Plots described two areas, green and red as in figures. In the green area were represented plans with total mean dose of parotid glands that respect the constrains and in red area plans that were unable to respect the constrains (Merlotti *et al.* Radiation Oncology 2014). Considering the middle area between the green and the red one, were possible to fit data linearly. The linear model was implemented in a python script integrated in our TPS as priority settings for new treatment plans: with Volume% of parotids outside PTV and with eq.1 we calculated the mean dose limit for parotid gland outside PTV. 6 arcs were implemented in order to avoid shoulders (from arc angle 186° to 235°, 270° to 90°, 125° to 174°, clockwise and counterclockwise), help structure as spine expanded of 5 cm subtracted with PTV low dose expanded of 0.6 cm was defined to minimize low dose distribution outside PTV and around the spine. Planning time was measured and compared with manual planning time.

Results: The linear dose/volume models obtained for parotid glands, was eq.1 y=4103.2*x - 1666.6 R2=0.7519. Equation warranted to plot% volume outside PTV vs. dose, indentifying as showed in fig 1, if glands were preserved or not. The plans obtained using AP end eq. 1 were able to minimize the median dose of entire glands reducing risks of toxicity in accordance with guide lines (Merlotti et al. Radiation Oncology 2014); the median dose of entire glands was reduced using AP of 12%±2% and planning time was of 21±8 min vs. 68±19 min planning manually.

Conclusions: AP based on linear model for parotid glands resulted a feasible strategy in SIB HNC. Linear model offered the possibility to foresee the expected toxicity in glands before to plan. AP saved planning time offering more time for planner in favour of minor tweaking steps at the end of plans. AP warranted the standardization of high quality plans and treatment outcome in SIB HNC.

P007

THE IMPACT ON LOCAL CONTROL OF STEREOTACTIC RADIOSURGERY FOR MULTIPLE BRAIN METASTASIS: OUR EXPERIENCE

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Aims: To evaluate local control and intracranial failure among patients with multiple brain metastasis (MBM) from solid tumors treated with stereotactic radiosurgery.

Methods: From 1 November 2018 to 15 June 2020 we enrolled patients affected by MBM with controlled or controllable extracranial tumor burden and candidated them to stereotactic radiosurgery with a monoisocentric technique, prescribing a peripheral dose to each PTV (obtained by an isometric expansion of GTV of 1 mm) equal to 18-22 Gy. We evaluated local control by means of RECIST criteria for each lesion and intracranial progression, to be understand as appearance of new brain metastasis, by brain contrast-enhanced magnetic resonance (MR) imaging scheduled for follow-up. We also registered, if any, treatment-related toxicity according to Common Toxicity Criteria for Adverse Events.

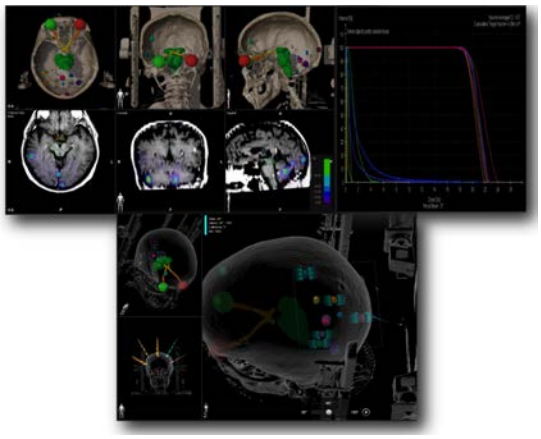

Figure 1. Patient with 9brain metastasis treated with monoisocentric technique and 7 non-coplanar dynamic conformal arcs.

Results: We treated 10 patients of median age of 69.5 years (range 49-95) with the aforementioned characteristics for a median study follow-up of 15.5 months (range 1-19). Primitive histologies were non small cell lung cancer (8), melanoma (1), rectal cancer (1). Median number of lesions was 12 (range 3-17), corresponding to a medium total treatment volume (PTV sum) of 4.38 cc (range 1.09-6.37). At the last follow-up (15 June 2020) 3 patients were dead for unknown cause (at 3, 6, 7 months after treatment end, respectively) and can be considered censored because of lack of appropriate neurological imaging. Another patient died after 6 months for extracranial disease progression (likely for

hepatic failure) and controlled intracranial disease. 6 patients are still alive after a median follow-up of 16 months (range 1-19), of which 1 patient was not yet submitted to MR imaging; the other ones were treated on cumulative 52 lesions (on average 10.4 lesions/patient), judged as stable and/or in regression until at least 12 months after treatment (with the exception of 1/52 lesion, slightly larger, 1 former lesion previously treated with Gamma Knife in another institution and 1 patient with a follow-up of only 4 months) and with a median time to intracranial failure of 9 months (range 2-11). No treatment-related toxicity was registered.

Conclusions: Stereotactic radiosurgery with monoisocentric technique for patients with MBM and controlled or controllable extracranial disease is feasible with excellent tolerability and offers an optimal local control, deferring whole brain radiotherapy at the intracranial progression time.

P008

MACHINE LEARNING FOR HEAD AND NECK CANCER IN RADIATION ONCOLOGY: A CLINICALLY-ORIENTED SYSTEMATIC REVIEW AND METHODOLOGICAL ASSESSMENT

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Aim: Radiotherapy (RT) for head and neck cancers (HNC) is taking advantage from "big data" based approaches, including artificial-intelligence methods. Among these, machine learning (ML) could provide Radiation Oncologists with accurate models to optimize patients' care paths. The aim of the present study is to review available evidence on ML applications in the RT workflow for HNC.

Methods: Original manuscripts on ML applications in HNCs were considered eligible for the analysis. Interventions included investigations on (auto)segmentation, treatment planning and outcome prediction (either oncological or toxicity). Only works written in English were included, electronic databases were screened up to March 2020 without date restrictions. Included works were reviewed and evaluated by an adapted version of the 55-points quantitative scoring system for ML in biomedical research proposed by Luo et al, which rated the following sub-sections: Title, Abstract, Introduction, Methods, Results and Discussion.

Results: Forty works published between 1998 and 2019 met the inclusion criteria. Of these, 21 (53%) focused on ML algorithms for autosegmentation either for target volumes (9/21) or organs at risk (12/21). Eleven (27%) studies aimed at predicting oncological outcomes, 7 (18%) RT-related toxicities and 1 (2%) the determinants for post-operative RT delays. The most common imaging modality was computed tomography (45%); while radiomics and dosimetric parameters were used as inputs in 8 (20%) and 4 (10%) of cases, respectively. Considering a maximum achievable score of 58 in the Luo rating system, median score was 40 (IQR: 36-45, minimum and maximum values: 33 and 53, respectively). When analyzing the Methods scores only (maximum theorical score of 33), median rank was 23 (IQR: 20-25, minimum and maximum values: 18 and 32, respectively). Supporting vector machines and neural networks resulted the most frequent algorithms. The Area Under the Curve was the most common parameter for reporting model performance, which was satisfactory in the majority of cases, with acceptable computational times.

Conclusions: ML-based predictive modeling is an expanding field in the Radiation Oncology setting, holding the promise contribute to the development of tailored treatment strategies and to the optimization of clinical workflow towards the era of personalized medicine.

P009

ROTATIONAL CONTRIBUTION IN PATIENT POSITIONING FOR OCULAR PROTON THERAPY

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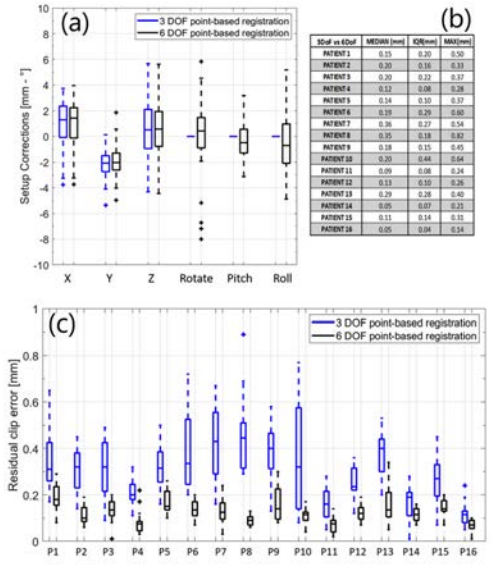
Aims: Ocular melanoma proton therapy (OPT) treatments started at our facility in 2016. Patient positioning verification is performed through in room stereoscopic radiographic imaging acquisitions, where radiopaque tantalum clips surgically sutured to outline the tumor volume, are manually identified. Setup is refined by comparing the daily clip displacement to the corresponding reference configuration as defined by our treatment planning system (Eclipse, Varian). The correction vector (CV) is computed through a point-based rigid registration algorithm by a dedicated software (Verisuite PT, Medcom, Germany). Patient setup is consequently updated relying on the high mechanical accuracy (0.3 mm; 0.3°) of a treatment chair specifically designed for this purpose. In this study we retrospectively compared patient set-up accuracy benchmarking two different CV calculations: setting a translational setup compensation only (3 DoF) or with rotational errors included in the optimization of setup (6 DoF).

Methods: Data of 16 consecutive patients who received OPT were evaluated, corresponding to a total of 64 pairs of x-ray images acquired for setup optimization. For each pair of images, the CVs were off-line calculated imposing both 3DoF and 6DoF registration. The residual errors have been evaluated in terms of 3D

clip to clip distances in respect to the reference positions.

Results: Results are presented as the difference between the 3D residuals calculated with the two different approaches. Although very high rotational contributions has been observed (max rotation = 7.99°, Patient 3 - Fraction 2 - around craniocaudal axis, Figure panel a), 3DoF registration contributed for fractions of mm (Figure 1, panel c. Median = 0.18 mm, iqr = 0.18 mm). A maximum deviation of 0.82 mm was observed for Patient 10 in the third fraction (Figure 1 - panel b).

Conclusions: The analysis exposed in this study confirmed that the application of 3DoF correction vectors was sufficient to guarantee precise and repeatable patient positioning, with median values of residual errors comparable to the positioning system accuracy.



3DoF vs 6DoF	MEDIAN [mm]	IQR[mm]	MAX[mm]
PATIENT 1	0.15	0.20	0.50
PATIENT 2	0.20	0.16	0.33
PATIENT 3	0.20	0.22	0.37
PATIENT 4	0.12	0.08	0.28
PATIENT 5	0.14	0.10	0.37
PATIENT 6	0.19	0.29	0.80
PATIENT 7	0.36	0.27	0.54
PATIENT 8	0.35	0.18	0.82
PATIENT 9	0.18	0.15	0.45
PATIENT 10	0.20	0.44	0.64
PATIENT 11	0.09	0.08	0.24
PATIENT 12	0.13	0.10	0.26
PATIENT 13	0.29	0.28	0.40
PATIENT 14	0.05	0.07	0.21
PATIENT 15	0.11	0.14	0.31
PATIENT 16	0.05	0.04	0.14

(a) Distribution of the first setup 3DoF and 6 DoF correction vectors. X = latero-lateral Y = antero-posterior and Z = cranio-caudal direction. (b) Discrepancies between 3 and 6 DoF registration for 16 Patients. (c) Clip-to-clip 3D residuals after the computation of 3 and 6 DoF point-based registration for each patient.

Figure 1.

P010

LINAC BASED STEREOTACTIC ARRHYTHMIA RADIOABLATION (STAR) OF VENTRICULAR TACHYCARDIA: A CASE REPORT

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Aim: The STereotactic Arrhythmia Radioablation (STAR) was recently introduced for ventricular tachycardia(VT). With precise high-dose of radiation targeting arrhythmogenic substrates in the heart that cause cardiac arrhythmia, STAR could become more than an option in the next future. Few data are present in literature about this therapeutic option. Here, the first clinical patients in Italy treated with Lin-ear Accelerator (Linac)-based STAR was reported.

Methods: In July 2019, a 67-year-old man with a VT, ischemic cardiomyopathy, low ejection fraction (25%) and frequent ventricular ectopies (VE, more than 20000/day), who developed electrical storm (44 ICD interventions in 2 months), came to our Cardiac Unit. Catheter ablation was hampered due to left ventricular apical aneurism with thrombosis. The cardiac surgeon considered the intervention not feasible due to excessive risk. Thus, he underwent to STAR. In order to determine the target myocardial tissue, a merge study including premature ventricular contractions (PVC) morphology, cardiac-gated computed tomography (CT) and cardiac PET-CT was performed before the treatment. A 4-D CT scan was obtained with patient in the supine position using a personalized immobilization device. The diagnostic images were exported to the treatment planning system and fused with the treatment planning CT. A dose of 25 Gy in one fraction, optimized to have a prescription isodose line of 75%, was prescribed to the planning target volume (PTV). Treatment plan was generated with volumetric modulated arc therapy. IGRT (image guided radiotherapy) and SGRT (surface-guided radiotherapy) were used to reduce set-up error and to monitoring patients during fraction. The treatment plan was delivered in 6 minutes.

Results: Patient was treated on 6 September 2019. No acute side effects were documented. At 1 month followup, the intracardiac defibrillator did not record VTs. The VEs decreased from 24000/24h to 123/24h. The patient had 2 shocks at second month from procedure and 1 ICD intervention at third month from procedure. After fourth month, the patients did not have ICD interventions. PET-CT and SPECT performed after six months from procedure, revealed an improvement in ejection fraction (35%) and a significant necrosis of myocardial region treated by STAR.

Conclusions: For patients who suffer of VT and for whom no standard treatment approach could be proposed, LINAC based stereotactic radiotherapy was a safe and effective treatment. Further study with longer follow-up are necessary to evaluate results and side effects.

P011

EFFECTS OF RADIATION THERAPY ON CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIED)

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Aims: Pacemakers (PM) and implantable cardioverter defibrillators (ICD) may develop malfunction during external beam radiotherapy (EBRT). We described our clinical practice in PM/ICD patients (pts) underwent to RT.

Methods: We reviewed medical records of all PM/ICD patients who received RT in our center. A multidisciplinary team (MDT) involving physicists and cardiac electrophysiologists was implemented from 2012 and a close communication between Cardiologists and Radiation Oncologists was warranted. All pts were evaluated by the cardiac electrophysiologist of our MDT before, at start and during RT. After radiotherapy the pts were followed by their own cardiologist

Results: From January 2008 to June 2020 more than 5000 patients received radiotherapy for cancer in our department using megavoltage linear accelerator. Among them 23 patients were with CIED, 21 with PM and 2 with ICD. Mean age was 71,6 (range 37-93), 16 male and 7 female, location of treated tumor was below the diaphragm in 13pts and above the diaphragm in 10 pts. 6 pts were PM dependent. 22 pts were treated with 6-MV and 1 with 10 MV photons. The mean radiation doses to CIED was 0.83 Gy (range 0.1-2.1) and mean Dmax was 2.8 Gy (range 0.4-9.1). The mean annual number of RT courses in PM/ICD patients was 2.4 (range 1-7). Safety measures included reprogramming (2 pts), and application of a magnet to the CIED during RT (6 pts), 50% required daily control and one pt required deactivation and daily ECG and audio-visual monitoring. Relocation of the device has not been necessary. During RT one 83 years old pt receiving IMRT for head and neck cancer experienced a non-sustained ventricular tachycardia. At device evaluations after the RT we observed a premature battery depletion in 1 74-year-old man treated with 6 MV IMRT to the prostate. No electrical resets nor life-threatening events or PM/ICD removal were registered.

Conclusions: Although the rate of RT in PM/ICD patients is increasing, the damaging effects of RT on the devices seem to be rare but possible. The multidisciplinary work and frequent monitoring permitted a safe treatment of our patients. Based on suggestions of a national consensus document the MTD will soon implement a local guideline, considering practical and local aspects for a safe management of these patients.

P012

DELTA RADIOMICS INCREASES MULTICENTRE REPRODUCIBILITY: A PHANTOM STUDY

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Aims: Texture analysis (TA) can provide quantitative features from medical imaging that can be correlated to clinical endpoints. The challenges relevant to robustness of radiomics features has been analyzed by many researchers, as it seems to be influenced by acquisition and reconstruction protocols. Delta texture analysis (D-TA), conversely, consist in the analysis of TA feature variations in different acquisition times, usually before and after a therapy. Aim of this study was to investigate the influence of different CT-scanners and acquisition parameters in the robustness of TA and D-TA.

Methods: We scanned a commercial phantom (CIRS model 467, Gammex, Middleton, WI, USA) that is used for the calibration of electron density in two times varying the disposition of the plugs, using three different scanners. After the segmentation, we extracted TA features with LifeX and calculated TA features and D-TA features, defined as the variation of each TA parameters extracted from the same position varying the plugs, with the formula (Y-X)/X. The robustness of TA and D-TA features were then tested with intraclass coefficient correlation (ICC) analysis.

Results: The reliability of TA parameters across different scans, with different acquisition parameters and ROI positions has shown poor reliability in 12/37, and moderate reliability in the remaining 25/37, with no parameters showing good reliability. The reliability of D-TA, conversely, showed poor reliability in 10/37 parameters, moderate reliability in 10/37 parameters and good reliability in 17/37 parameters. The comparison between TA and D-TA ICCs showed a significant difference for the whole group of parameters (p:0,004) and for the subclasses of GLCM parameters (p:0,033), whereas for the other subclasses of matrices (GLRLM, NGLDM, GLZLM, Histogram) the difference was not significant.

Conclusions: D-TA features seem to be more robust than TA features. These findings reinforce the potentiality for using D-TA features for early assessment of treatment response and for developing tailored therapies. More work is needed in a clinical setting to confirm the results of the present study.

P013

AUTOMATED TREATMENT PLANNING AS A DOSE ESCALATION STRATEGY FOR STEREOTACTIC RADIATION THERAPY IN PANCREATIC CANCER

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Aims: To assess the feasibility of automated SBRT-VMAT planning using a SIB approach as a dose escalation strategy for SBRT in pancreatic cancer.

Methods: Twelve patients with pancreatic cancer were retrospectively replanned. Dose prescription was 30 Gy to the planning target volume (PTV) and was

escalated up to 50 Gy to the boost target volume (BTV) using a SIB technique in 5 fractions. All plans were generated by Pinnacle3 Autoplanning using 6MV dual-arc VMAT technique for flattened (FF) and flattening filter-free beams (FFF). An overlap volume (OLV) between the PRV duodenum and the PTV was defined to correlate with the ability to boost the BTV. Dosimetric metrics for BTV and PTV coverage, maximal doses for serial OARs, integral dose, conformation numbers and dose contrast indexes were used to analyze the dosimetric results. Dose accuracy was validated using the PTW Octavius-4D phantom together with the 1500 2D-array. Differences between FF and FFF plans were quantified using the Wilcoxon matched-pair signed rank.

Results: Full prescription doses to the 95% of PTV and BTV can be delivered to patients with no OLV. BTV mean dose was >90% of the prescribed doses for all patients at all dose levels. Compared to FF plans, FFF plans showed significant reduced integral doses, larger number of MUs and reduced beam-on-times up to 51% for the highest dose level. Despite plan complexity, pre-treatment verification reported a gamma pass-rate greater than the acceptance threshold of 95% for all FF and FFF plans for 3%-2 mm criteria.

Conclusions: The SIB-SBRT strategy with Autoplanning was dosimetrically feasible. Ablative doses up to 50 Gy in 5 fractions can be delivered to the BTV for almost all patients respecting all the normal tissue constraints. A prospective clinical trial based on SBRT strategy using SIB-VMAT technique with FFF beams seems to be justified.

P014

AUTOMATION OF TREATMENT PLANNING IN HEAD-NECK CANCER: A GAME-CHANGER FOR QUALITY IN RADIATION THERAPY?

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Aims: The applications of artificial intelligence in radiation oncology are translating in technological advancements for treatment plan automation, with the potential to improve overall plan quality. We aimed to perform a comprehensive dosimetric and clinical evaluation of the new algorithms implemented in Pinnacle3 for full planning automation, comparing automatically generated plans (AP) with the historically clinically accepted manually-generated ones (MP) by experienced medical physicists.

Materials/methods: Fifteen consecutive delivered head-neck treatment plans were re-optimized using the Pinnacle Personalized full automated engine. Radiotherapy was prescribed using VMAT technique and simultaneous integrated boost strategy. Comparison between MP and AP plans were performed using dose-volume histogram metrics and a blinded clinical evaluation by two senior radiation oncologists. Planning time between MP and AP approaches was compared.

Results: For similar targets coverage, AP plans reported less irradiation of healthy tissue, with significant dose reduction for spinal cord, brainstem and parotids. On average, the mean dose to parotids and maximal doses to spinal cord and brainstem were reduced by 13-15% ($p<0.001$), 9% ($p<0.001$) and 16% ($p<0.001$), respectively. The integral dose was reduced by 16% ($p<0.001$). The dose conformity for the three PTVs was significantly higher with AP plans ($p<0.001$). The two oncologists chose AP plans in more than 80% of cases. Overall planning times were dramatically reduced to less than 30 minutes for automated optimization.

Conclusion: Complex head-neck plans created using full automated template-based models provided an overall increase of plan quality, in terms of dose conformity and sparing of normal tissues. The "a priori" DVH prediction module provided treatment plans that allow OARs dose sparing well beyond the clinical objectives.

P015

PROTON AND CARBON ION RADIATION-INDUCED TOXICITY IN CANCER PATIENTS WITH AUTOIMMUNE DISEASES

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Aims: The rate of severe radiation related toxicity (Grade ≥ 3 (G≥3) according to Common Terminology Criteria for Adverse Events, CTCAE in cancer patients affected by autoimmune diseases (ADs) is reported to be 10-15%. No data are available for particle therapy. This study aims at evaluating whether proton (PT) or carbon ion (CIRT) therapies cause unusual side effects in cancer patients with ADs.

Methods: We retrospectively collected data of 45 consecutive patients treated from 2013 to 2019, 28 (62%) with PT and 17 with CIRT (38%). We assessed the incidence of G≥3 toxicities based on CTCAE). Toxicity is categorized as occurring within two possible phases: acute (within 6 months of treatment) and late (more than 6 months after treatment). Contingency tables were analysed with Fisher's exact test.

Results: Among 45 patients with ADs treated, 38 were female and 7 male. Median age was 57 years (range 20-79). Median dose was 60GyRBE (range 45-75) and 65.6GyRBE (range 54-73,6) for PT and CIRT, respectively. The most common AD was psoriasis. After a median follow-up of 21 months, data about acute toxicity were available for all 45 patients while late toxicity data were available for 41 patients (26 PT

and 15 CIRT). The majority of patients (80%) developed G1-2 acute toxicity. Late G1-2 toxicity was reported in 58% of patients. In PT group, 3 patients (10%) developed G≥3 acute toxicity while 2 (7%) patients developed G≥3 late toxicity. In CIRT group, acute and late high grade toxicity was reported in 3 (17%) and 4 (26%) patients respectively. Most of severe acute and late toxicity affected mucosal and soft tissues. We found no relationship between type of particle, total dose, sex, age and toxicity (both acute and late).

Conclusions: ADs patients do not appear to have an elevated risk of acute and late severe toxicity with PT. CIRT seems to be associated with a not statistically significant increase of G≥3 radiation-related late effects. This result could be related to pro-inflammatory and pro-immunogenic proprieties of CIRT. A longer follow-up is needed in order to define toxicity burden in ADs patients.

P016

STEREOTACTIC RADIOTHERAPY ABLATION FOR ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW

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Aims: Atrial fibrillation (AF) is one of the most common forms of cardiac arrhythmia. Its main trigger resides in the pulmonary veins, making this site the main target of ablation. The purpose of this study is to collect available evidence on the feasibility and efficacy of external beam radiotherapy (RT) in AF, and to provide Radiation Oncologists with a practical overview on this topic.

Methods: The following keywords were chosen for literature search: cardiac radioablation; cardiac radiosurgery; cyberheart; radiosurgery atrial fibrillation; noninvasive cardiac radiotherapy; radiosurgical ablation atrial fibrillation. Overall, 530 articles were retrieved. Only reviews and full articles on both preclinical and clinical studies were included; no data restrictions or language limitations were applied. Studies dealing exclusively with ventricular or nodal arrhythmia or particle beam RT were omitted. Selected works were analysed for comparing target selection, treatment plan details and the accelerator employed. Furthermore, an overview on pre- and post-procedure exams and on the efficacy and side-effects of the treatments was performed.

Results: Following duplicates elimination, 17 works published from 2010 to 2020 were included. Six studies analysed a total of 59 animals, with delivered doses ranging from 15 to 80 Gy. Six studies focused on humans (either in silico or delivered plans: 4 and 2 studies), with doses from 16 to 50 Gy. All but two studies used single-fractionated schedules. The average follow-up was 6 months for animals and 4 years for humans, respectively. Efficacy was defined as either the presence of a myocardial scar (animals) or the absence of AF recurrence (humans). 25 Gy was the minimum prescription dose for efficacy; the evaluation of respiratory and cardiac target motions were the most critical issues; efficacy was reached in all cases but one human, who experienced AF recurrence 6 months following the procedure. No acute or late RT-induced toxicity were recorded. Details for all studies are provided in Table 1.

Conclusions: Target motion and doses to the organs at risk are the most important issues to be considered when irradiating AF foci. Cardioablation appears to be particularly suitable for older patients with multiple comorbidities, for whom the classical procedures of ablation can be contraindicated. In conclusion, more studies are warranted to define the best method to perform an efficient stereotactic RT ablation treatment.

Table 1. Main characteristics of the studies included in the analysis.

Author	N°	Species	Total Dose (Gy)	N° of Fraction s	Targe t	Fiducials	Accelerato r	Respiratory motion control	Cardiac motion control	Delivere d plan	Follow-up (months)	Efficacy	Toxicity
Sharma A., Heart Rhythm 2010	16	Mini-Pigs	38 - 80	1	LPV	Yes	CK	Yes	Yes	Yes	1-6	Yes	No
Maguire P., Cureus 2012	2	Mini-Pigs	25 - 35	1	PVA	Yes	CK	Yes	Yes	Yes	6	Yes	Trace MVR
Gardner E.A., J Appl Clin Med Phys 2012	4	Canines, Mini-Pigs	20 - 35	1	PVA	Yes	CK	Yes	Yes	Yes	5	N/A	No
Blanck O., Int J Radiat Oncol Biol Ph 2014	10	Mini-Pigs	15 - 35	1	RPV	N/A	CLA	Yes	Yes	Yes	6	Dose ≥ 32.5 Gy	No
Bode F., Europace 2015	8	Mini-Pigs	23 - 40	1	RPV	No	CLA	Yes	Yes	Yes	6	Dose ≥ 30 Gy	Dose ≥ 37.5 Gy
Zei P. C., Heart Rhythm 2018	19	Canines, Mini-Pigs	15- 35	1	PVA	Yes	CK	Yes	Yes	Yes	3-6	Dose ≥ 25 Gy	No
Blanck O., Cureus 2016	24	Treatmen t Plans	25	1	PVA	Yes	CK	Yes	Yes	No	N/A	N/A	N/A
Gardner E.A., Cureus 2016	4	Treatmen t Plans	16 - 25	1	PVA ± LPW	No	CK	N/A	N/A	No	N/A	N/A	N/A
Xia P., Cureus 2016	20	Treatmen t Plans	50	5	PVA	No	CLA	No	No	No	N/A	N/A	N/A
Lydiard S., Phys Med Biol 2018	15	Treatmen t Plans	50	5	PVA	No	CLA	Partially	Partially	Dynamic Phantom	N/A	N/A	N/A
Monroy E., Cureus 2016	1	Human	25	1	PVA	N/A	CK	Yes	N/A	Yes	12	No	No
Qian P., J Arrhythm 2020	2	Humans	25 - 35	1	N/A	Yes	CK	Yes	Yes	Yes	48	50%	No

Abbreviations: LPV = Left Pulmonary Veins, PVA = Pulmonary Veins Antra, MVR = Mitral Valve Regurgitation, RPV = Right Pulmonary Veins, LPW = Left Posterior atrial Wall, N/A = Not Available, CLA = Common Linear Accelerator, CK = CyberKnife

P017

COMPARISON BETWEEN TWO DIFFERENT RADIOTHERAPY TECHNIQUES BY MEANS OF LOW DOSES EVALUATION IN STEREOTACTIC RADIOTHERAPY FOR LUNG LESIONS

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Aims: As several studies have shown that also in stereotactic setting lung low doses are related to pulmonary toxicity, we investigate the dosimetric difference between two stereotactic methods that use different techniques in the radiotherapy treatment for patients with lung lesions. Two radiotherapy equipments, Accuray Tomotherapy HI-ART and Varian Novalis-TrueBeam STx linear accelerator (linac), were used to compare lung plans for same patients in order to evalu-

ate differences in dose distributions and in predictive dose parameters typically associated with radiation pneumonitis.

Methods: 8 lung patients previously undergoing stereotactic body radiotherapy with lesions located in different positions within the lung were retrospectively analyzed. The treatment plans were recalculated by physicists from two centers that use different techniques and algorithms: linac-based radiotherapy with AAA and tomotherapy with CCCS. Dose prescriptions ranged from 40 Gy/5 fractions to 45-48 Gy/3 fractions, based on target position in the lung. For the comparison we considered: the volume of both lungs minus the gross tumor volume (GTV) receiving from 2.5 to 50 Gy (V2.5, V10, V20, V30, V40, V50) and the mean lung dose (MLD). Moreover, we carefully evaluated the differences in dose distributions and dose to main organs at risk (heart, esophagus, chest wall, spinal cord) between the two planning techniques.

Results: Although V2.5 to V50 values are always lower for the stereotactic linac-based technique with respect to tomotherapy, the differences between the two compared methods are not statistically significant ($p > 0.05$). Greater differences were recorded for V10, however this factor is always below the cutoff value corresponding to the incidence of radiation pneumonitis (19%). On the other hand, we found a statistically significant difference ($p = 0.036$) in the MLD in favor of the linac plans, probably due to the use of non-coplanar arc technique. Moreover, for the two patients with lung lesions near the esophagus and bronchi, respectively, we obtained with linac a halving of the low lung doses (V2.5, V5 and V10) compared to tomotherapy, at the expense of a slight decrease in the GTV coverage for linac plans.

Conclusions: No significant differences were found between the planning methods, except for MLD. Regarding dose constraints, in general linac-based stereotactic technique offers greater dose saving to organs at risk compared to tomotherapy.

P018

COULD STEREOTACTIC RADIOSURGERY BE A BETTER ALTERNATIVE TO WHOLE BRAIN RADIOTHERAPY AMONG PATIENTS WITH GREATER THAN OR EQUAL TO FIVE BRAIN METASTASIS? A QUESTION TO BE ADDRESSED BY A FOCUSED TRIAL

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Aims: To evaluate neurocognitive performance, daily activity and quality of life and local control among patients with brain metastasis (MBM) ≥ 5 due to solid tumors treated with Stereotactic RadioSurgery (SRS) or Whole Brain RadioTherapy (WBRT).

Methods: This multicentric randomised controlled trial will be conducted at the Fondazione IOM (Viagrande), Policlinico Universitario G. Martino (Messina) and Ospedale Civico ARNAS (Palermo). It will involve, within 5 years starting from 1 August 2020, the enrollment of 100 patients (50 for each arm) with MBM ≥ 5, age ≥ 18 years, Karnofsky Performance Status (KPS) ≥ 70, life expectancy > 3 months, histological confirmation of primary tumor, with controlled or controllable extracranial disease, baseline Montreal Cognitive Assessment (MoCA) of 20/30, Barthel Activities of Daily Living score 90/100, to be subjected to stereotactic radiotherapy on each brain lesion by LINAC with monoisocentric technique and non-coplanar arcs (sperimental arm) or to WBRT (control arm). The primary endpoints are neurocognitive performance, quality of life and autonomy in daily-life activities variations, the first one assessed by Moca Score and Hopkins Verbal Learning Test - Revised, the second one through the EORTC QLQ-PAL-15 and BN-20 questionnaires, the third one through the Barthel Index, respectively. The secondary endpoints are time to intracranial failure, overall survival, retreatments frequency, acute and late toxicities, KPS decrease. It will be considered significant a statistical difference of at least 29% between the two arms (statistical power of 80% with a significance level of 95%).

Results: This trial has been approved by the local ethics committee on July 7th(record 70).

Discussion: Several studies debate what is the predominant factor accountable for the development of neurocognitive decay among patients undergoing brain irradiation for MBM: radiotherapy, especially if extended to the entire brain, or intracranial disease progression? Answer to this question may come from current opportunity, thanks to recent technological advancement, to treat, with significant time savings, improved patient comfort and at the same time minimizing the dose to healthy brain tissue, Multiple Brain Metastasis simultaneously, otherwise attackable only by panencephalic irradiation. The pursuit of a local control rate comparable to that obtainable with WBRT remains the fundamental prerequisite for the aforementioned related assessments.

P019

INNOVATIVE ROBOTIC-ARMS POSITIONING SYSTEM FOR A GANTRYLESS SOLUTION IN PROTONTHERAPY

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Mains: Proton therapy has provided many evi-

dences on quality and accuracy in planning a treatment. Pencil-beam scanning technology with protons enables clinicians to precisely manipulate and steer the beam to conform dose to the tumor. The actual main issue concerning proton therapy has been technology behind it and the huge expenses compared to conventional radiotherapy. To take full advantage of this relatively new treatment technique, we propose a gantryless solution alternative to the standard systems, which are proved to be very expensive in costs, installations, daily QA and long term maintenance.

Methods: Two robotic arms are used as positioning system. Each arm has six degrees of freedom. The first one is handling the couch while the second one is endowed with an imaging system that uses a Cone Beam CT installed on a C-arc ring. The positioning system is controlled and interfaced with a dedicated software which translates complex motions into their equivalent (the equivalent ones) in conventional treatments.

Results: Full Monte Carlo investigations have been performed for all configurations. We see then advantages of combining such solutions in offering new smart way of fully exploiting the hardware in our disposal nowadays. This solution is well integrated within the whole treatment workflow from the accelerator control to the planning system.

Conclusions: This work has explored the feasibility and the advantages in the use of a gantryless configuration combined with a robotic positioning system focusing on outcomes in treatment planning. According to the results obtained, costs and benefits are reported together with additional non-standard field setups that propose planning improvements.

P020

STAGING MRI RADIOMICS BASED RESPONSE PREDICTION IN RECTAL CANCER: AN INTERCONTINENTAL EXTERNAL VALIDATION ON REAL WORLD DATA

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Aims: Predict pathological complete response (pCR) in patients affected by locally advanced rectal cancer (LARC) who underwent neoadjuvant chemoradiotherapy (nCRT) is a challenging field of investigation, but many of the published models are burdened by a lack of reliable external validations. Aim of this study was to evaluate the replicability of an already published pCR predictive model in LARC, using an extra-European validation cohort.

Methods: The original model was based on both clinical and radiomics features, extracted from staging magnetic resonance images (MRI) of patients affected by LARC. Area under the curve (AUC) of the receiving operator characteristic (ROC) values of the original model were 0.73 and 0.75 for internal and external validation, respectively. A Chinese validation cohort was enrolled for further extra-european external validation.

Results: A Chinese cohort of 60 patients who underwent neoadjuvant short course neoadjuvant radiotherapy or nCRT and with a pCR occurrence of 16% (10 patients) was used for the external validation of the original model. A ROC AUC of 0.83 was achieved on the whole Chinese validation dataset.

Conclusions: Despite the introduction of significant different variables (*i.e.* ethnic origin, MRI field strength, different radiotherapy) the proposed model appeared to be replicable and stable on a real-world data extra-European patients' cohort.

P021

HYPOFRACTIONATED HIGH DOSE PALLIATIVE RADIOTHERAPY IN PATIENTS WITH POOR PERFORMANTS STATUS UNFIT OF STANDARD RT TREATMENT; SURVIVAL, ACUTE AND LATE TOXICITY ANALYSES

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Purpose: The aim of this study was to evaluate survival rates as well as acute and late toxicity after hypofractionated high dose palliative radiotherapy (RT) in patients (pts) with low performance status unfit of standard RT treatment

Methods: Between November 2013 and June 2020, 170 pts underwent hypofractionated high dose palliative RT. The prescribed dose was 36,75 – 42 Gy in 7-8 fractions given one fraction a week of 5,25 Gy. Of them 90 pts (53%) were male and 80 (47%) female. Mean age was 78 years old (range 42-100 years old). Majority of pts were elderly (80%) with 2 or more comorbidity. Primary cancers treated were head and neck cancer (36%), lung (13%), breast (5%), gynecological (12%), sarcomas (2%), prostate (8%), gastrointestinal (8%) and other metastatic disease (20%). Nighty-four pts (55%) received 3DCRT and 76 patients (45%) VMAT or IMRT technique. Concomitant systemic CT was administered in only 40 patients (23%). At the moment of RT start the median KPS was 60 (range 40-80).

Results: After a mean follow-up of 10 months the

OS was 9 months. Overall, 77% of patients completed RT at the prescribed dose and 23% interrupt it due to PD, clinical worsening or lose motivation. A clinical or radiological examination response was observed in 75% of pts (CR 33%, PR 42%), SD in 5% and a PD 19% of patients. Patients that completed RT treatment at the prescribed dose had a higher survival rate compared to patients which interrupt it (p-value 0,0001). Moreover, KPS > 70, PTV < 300 cc, CTV/GTV < 100cc, clinical or radiological response were prognostic factors regarding OS (p- value < 0,05). RT technique did not influence survival rate or local control, however pts treated with 3DCRT had higher rates of G3-G4 late toxicity (p-value < 0,048). Age, systemic treatment and temporary RT interruption did not influence survival rates. A G3 or higher acute toxicity was observed in only 1,8% of patients. Reading late toxicity G3 or high late toxicity was observed in 8 pts (4,7%).

Conclusion: This hypofractionated radiotherapy schedule appears acceptable in pts with poor performants status unfit of standard RT treatment, with a response rate of 75%. Radiotherapy total doses delivered, KPS > 70, PTV < 300 cc, CTV/GTV < 100cc resulted prognostic factors regarding overall survival. IMRT technique is recommended to be used for this schedule of hypofractionated palliative treatment due to reduce G3 or higher late toxicity.

P022

HIPPOCAMPAL-SPARING RADIOTHERAPY IN PATIENTS WITH BREAST SPHENOID METASTASIS AND AN INITIAL GARCIN SYNDROME

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Aims: The purpose of this study was to report a rare case of Garcin Syndrome treated with an Hippocampal-Sparing approach.

Methods: We report a case of a 49 y.o. woman who underwent radiation therapy (RT) for treating a skull base and cranial bone metastases, with an initial leptomeningeal involvement from breast cancer. Clinical presentation was suggestive for an initial Garcin Syndrome, caused by a lytic lesions in the left sphenoid wing. According to the good performance status(PS) and the young age, she was candidate to receive an advanced RT approach. She showed left increasingly worsening left otalgia with initial hearing loss, moreover she complained left facial numbness and omolateral decreased facial sensitivity, left increased lacrimation, and tingling tongue. We performed a Hyppocampal sparing whole brain (WB) VMAT plus a sequential boost on skull base lesion. A brain RMN imaging was used to delineate the PTV and the OARs. The planning CT scan images were fused with T1 weighted MRI axial sequences. Bilateral hippocampal contours were generated on the fused planning MRI/CT image set according to RTOG 0933 contouring atlas. After that a hippocampal avoidance region was created by expanding the hippocampal contours by 5 mm in all directions according to Brown *et al*. The planning target volume (PTV-HA) was defined as the WB parenchyma, meninges and skull, excluding the HA-region, dose prescription 30Gy/10fx; the PTV-Boost was defined as the sphenoidal metastases, dose prescription of sequential boost was 12Gy/4fx. VMAT was used to deliver the conformal RT plan. Planning priorities that should be followed were: Hippocampus, OpticChiasm, OpticNerve L or OpticNerve_R, Lens_L or Lens_R.

Results: These are our results of plan sum: for PTV-HA D2%=43.43 Gy, D98%=26.36 Gy, V30=94.96%; for Hippocampus D100%=8.78 Gy, Dmax=17.24 Gy; for Left OpticNerve Dmax=33.51%; for Right OpticNerve Dmax=29.25%; for OpticChiasm Dmax=35.93%. The neurological symptoms improved after the end of RT with a complete resolution two months later, at first follow-up visit.

Conclusions: Several studies demonstrated that sparing dose to the hippocampus during WB-RT can help preserve a patient's neurocognitive function. Sequential boost demonstrated to be feasible and effectiveness. For patients with a good PS, young age, long life expectancy, advanced RT techniques may be used to customize treatment that allow to preserve cognitive impairment with a good clinical results.

P023

THE IMPACT OF METAL ARTIFACT REDUCTION (MAR) CT-ALGORITHM IN THE FEASIBILITY OF A PROSTATE CANCER RADIATION TREATMENT FOR A PATIENT WITH BILATERAL FEMORAL HEADS PROSTHESIS

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Aims: The radiotherapy treatment may result very difficult (even impossible) in patients with bilateral femoral heads prosthesis. Artifacts caused by metallic implants severely degrade the image quality and decrease the diagnostic power of the examination, appearing as dark and bright streaks at computed tomography (CT). The aim of the work is studying the impact of a projection-based metal artifact reduction (MAR) algorithm, applied after CT image acquisition, in the feasibility of a prostate cancer radiation treatment

for a patient with bilateral femoral heads prosthesis.

Methods: A VMAT plan was calculated, with a 6 MV photon beam provided by a TrueBeam (Varian Medical System) with HD 120 MLC, on both CT images with and without MAR application. The plan was calculated with the configured algorithm Acuros XB (AXB) version 15.06.06. The same MUs number obtained from plan calculated with MAR correction was used for plan without MAR. Evaluation in terms of Dose Volume Histogram (DVH), target coverage, isodose difference distribution and inhomogeneity has been performed on both plans. The 95% dose distribution regarding the part of PTV extending inside rectum was evaluated for both plans with and without MAR and the QUANTEC dose constraints for rectum (V43.9Gy, V52.6Gy, V57Gy, V61.4Gy) were quantified.

Results: Table 1 reports the detail about QUANTEC rectum constraints, D98% and 3D Dmax for PTV respectively for plan calculated on CT without and with MAR. For plan without MAR the 95% isodose curve extended for a distance of 0,71 cm inside rectum, while it was reduced to 0,33 cm in the case of MAR application.

Conclusions: The use of MAR algorithm has shown to be the only possible solution to plan a VMAT radiation treatment on CT images of patients with bilateral femoral prosthesis.

Table 1.

	CT-NO MAR PROCESSED	CT-MAR PROCESSED
RECTUM	V43,9Gy = 34,6 %	V43,9Gy = 26,8 %
	V52,6Gy = 25,7 %	V52,6Gy = 17,9 %
	V57Gy = 22,2 %	V57Gy = 14,4 %
	V61,4Gy = 18,5 %	V61,4Gy = 11 %
PTV	D98%= 92%	D98%= 95%
	DMax= 107,5%	DMax= 108,4 %

P024

PRE-CLINICAL VALIDATION OF MOBIUS3D AS SECOND- CHECK DOSIMETRY SYSTEM IN CLINICAL ROUTINE

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Aims: Mobius3D system was validated with the purpose to use it as a modern second – check dosimetry system in our clinical practice. Using treatment parameters exported from primary treatment planning system (TPS) and log files produced by the treatment machine, Mobius3D and MobiusFX allow for a full recalculation of dose on the patient CT-dataset and for quality assurance of treatment plan through a "delivered dose" calculation.

Methods: A pre-clinical analysis was performed and ten selected VMAT (Volumetric Modulated Arc Therapy) treatment plans were exported from our TPS Eclipse to Mobius. Plans, concerning head&neck, brain, lung and pelvis districts, were performed with a TrueBeam accelerator using 6MV and 10MV photon beam energy. For each plan, isocenter dose was measured using Mobius Verification Phantom (MVP) and ionization chamber and these values were compared with the calculated ones by Eclipse. For all 10 plans, the dose distributions calculated on the patient's CT-dataset by Mobius and our algorithms were compared using the following metrics: target mean dose percent difference, target D90% percent difference, global 3D gamma passing rate over the entire dataset and gamma passing rate over the target. The same metrics were used for comparison between TPS calculated dose and delivered one (reconstructed by the system through treatment log files). According to the ten normo-fractionated studied treatment plans, the gamma criteria used were 3%-3mm.

Results: The average point dose difference on MVP between our algorithms and measurements with ionization chamber was 2.36% (from 2.28% to 2.47%). Concerning comparison on the CT-dataset between TPS and Mobius3D we found an average target mean dose percent difference of 1.57% (from -0.215% for pelvis to 2.94% for H&N). The average D90% difference was 1.42% (from 1.105% to 2.05%); 3D global gamma passing rate ranged from 94.1% for H&N district to 99.6% for lung. Gamma passing rate for target was >95% for all studied treatments. Results regarding the comparison between TPS and delivered dose were in agreement to the TPS/M3D differences listed above.

Conclusions: A pre-clinical validation of Mobius second check system was performed demonstrating that all studied VMAT plans can be safely verified using Mobius system. A more substantial amount of data is being studied with the purpose to implement the use of Mobius for all treatment plans in our hospital.

P025

INTERREGIONAL NETWORK MODEL FOR THE FIRST EVALUATION IN PATIENTS THAT CAN BE ADDRESSED TO PROTON AND CARBON IONS THERAPY

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Objective: To report about an organizational solution designed and implemented between two radiotherapy centers, one of these being a proton and carbon ions therapy (PCIT) facility, to facilitate access and reduce unnecessary health migration to high tech RT centers like PCIT, resulting in an interregional network collaboration.

Methods: Two radiation oncologists and one medical physicist working in a non- PCIT center spent a training period at a PCIT facility in order to learn technical skills and particle therapy–based management strategies, including follow-up. After this, at their institution, they established a dedicated patients' visit room for potential candidates to particle therapy. Then, a weekly telematic tumor board discussion among the teams of the two centers took place to confirm the indication according to clinical and radiological data. Thus, patient was evaluated at the PICT facility to preliminarily plan the treatment. Rival plans with particle therapy and photons were eventually assessed for dosimetric and TCP/NTCP comparison. After approval by region administration, the patient was therefore sent to PICT center. FUP programs were shared among the two Centers for patients unable to refer to the PICT facility.

Results: From June 1st 2019 to Jun 30th, 2020 41 patients were evaluated at not-PICT center in 87 visits: 8 (20%) received indication to PICT, 7 (17%) were FUP addressed from PICT center, 14 (34%) photon radiotherapy treatment either for not having received the region approve to PICT treatment or for lack of indication to PICT itself, 12 (29%) didn't have indication to any type of radiation treatment. The most frequent diagnosis was the chordoma (8 pts, 15%), two of whom as new diagnoses and treatment.

Conclusions: This implementation of an organized framework for an interregional collaboration allowed for effective case screening, resulting in a significant reduction of potential self-referral of patients coming from central-southern Italian regions. In addition, this framework could allow a reduction of waiting time to start particle therapy after the regional approval.

P026

HYPOFRACTIONATED RADIATION THERAPY FOR PROSTATE CANCER: TECHNOLOGIES IN COMPARISON

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Aims. IGRT is mandatory to accurately deliver high doses. The purpose of this study is to compare acute toxicity from hypofractionated radiation therapy for prostate cancer using different options of image guidance (IG): kV CBCT guidance of CT-LINAC system (True Beam, Varian) vs MRgRT (MR Guided Radiation Therapy) of MR-hybrid LINAC system (MRIdian, Viewray).

Methods: Radiation treatment was prescribed to a dose of 62 Gy in 20 daily fractions of 3.1 Gy. An anisotropic 7mm-margin (5mm posterior) was created around the prostate for the planning target volume. Treatment was delivered using different IG strategies: CBCT pre-treatment imaging used in the first 5 days and than 2 days/week vs. daily pre-treatment MR scan and cine-MR (organ motion in real time) during on-line adapted delivery. Common Terminology Criteria for Adverse Events, version 5.0, was used to score gastrointestinal and genitourinary toxicity during treatment.

Results: Between May 2015 and June 2020 acute toxicity was analyzed in 171 patients (pts) with prostate cancer treated with moderate hypofractionated RT, retrospectively. Pre-treatment CBCT was performed in 144 treatments, real-time adaptive MRgRT strategy was used for 27 pts. Using CBCT-IG, grade 2 and 3 acute rectal toxicity occurred in 18 and 3 pts respectively, whereas 21 pts with Grade 2 and no grade 3 of urinary toxicity were observed. No grade 2 and 3 toxicity was recorded during treatments performed using real-time MRgRT.

Conclusions: Advanced IGRT strategies can reduce acute toxicity from moderate hypofractionated radiation therapy for prostate cancer. Further studies to evaluate the optimal balance between advantages of modern IG technologies and additional cost in terms of time and complexity are needed.

P027

HADRONTHERAPY AND CARDIOTOXICITY: WHICH ROLE FOR MULTIPARAMETRIC CARDIAC MONITORING?

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Aims: Previous studies showed a linear dose-response relationship between hearth-Dmean (Dm) and risk of cardiac disease. Due to the lack of data about hadrontherapy-induced heart disease, we designed a prospective study aimed to investigate side acute effect

on cardiac structure and function during curative hadrontherapy for para-cardiac or intra-cardiac tumors.

Methods: 8 consecutive patients (pts) (64 ± 12 yrs, 5 males) were enrolled so far, including 2 cases of primary intra-cardiac tumors and 6 cases of sarcoma metastases in the mediastinum (n=4) or the sternum (n=2). Most (n=6) were treated with carbon ions radiotherapy (mean total dose 55.8 GyE, from 3 to 4.3 GyE fraction/day). A solid thermoplastic mask provided thoraco-abdominal compression. Robust treatment plan optimization aimed at sparing hearth and cardiac substructures while preserving optimal dose corverage for the moving target. Plans were delivered with respiratory gating and rescanning. 4 pts underwent previous cardiotoxic chemotherapy and showed a baseline mean left ventricular ejection fraction (LVEF) of 56±5%. 6 pts had cardiovascular risk factors, 2 pre-existing cardiac condition (severe mitral regurgitation and post-operatory pericarditis, respectively). Cardiac (Troponin I, TnI,brain natriuretic peptides) and inflammatory biomarkers, electrocardiogram (ECG), echocardiogram and 24-hours 12-leads Holter ECG (including heart rate variability measurements) are obtained at fixed time intervals before, during and immediately after handrontherapy. High precordial ECG leads are used in case of lesions nearby the right ventricle (RV), in order to detect potential for Brugada-like ECG pattern due to RV direct or indirect compression/damage.

Results: The heart-Dm was <5 GyE with RV-Dm <4 GyE in all the analyzed cases. In the treatment of heart sarcoma, heart-Dm was 7.7 GyE. The sinus node Dm ranged form 0 to 19.4 GyE with the highest dose recorded when GTV was stuck to it. 7 patients completed the treatment: no acute changes in cardiac and inflammatory biomarkers, heart rate and right as well as LVEF were observed. No type 1 Brugada like patterns were detected. Additional analysis on ECG, Holter ECG and advanced echocardiographic index of contractility are ongoing.

Conclusions: Hadrontherapy to para/intra-cardiac tumors allowed to maintain low hearth-Dm and did not show any sign of acute cardiac toxicity. Long-term data will be collected as well to evaluate late toxicity.

P028

STEREOTACTIC MR-GUIDED ADAPTIVE RADIATION THERAPY (SMART) FOR LOCALIZED URETER CARCINOMA

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Aims: The standard treatment of upper tract urothelial carcinoma (UTUC) is surgery. The role of Radiotherapy (RT) is generally adjuvant to reduce local failure risk and there are rare reports of curative RT alone. SBRT, with an online adaptive approach guided by MR images, can assure an efficient high dose for curative radiotherapy to reach a good patient outcome without acute or late toxicities. The aim of this single case report of SBRT with modern hybrid MR-Linac on a patient with surgery-rejected localized UTCC is to propose an alternative therapeutic strategy for this setting of patients.

Methods: An 88 years old male patient was diagnosed with ureter cancer T2N0M0 and refused surgery. After a laser ablation of ureteral tumor with placement of a JJ stent, a CT scan showed a tumor regrowth and an obstruction in left ureter despite stent, with dilation of upper ureter few months later. The patient underwent SBRT on ureteral lesion on March 2020. Treatment prescription for the lesion of left ureter was 35Gy (7Gy/fr) delivered on 5 days (3fr/week). The planning target volume (PTV) included GTV plus a 3-mm isotropic margin. Prior to each fraction, a daily 128 second TRUFI magnetic resonance images was used to online adapt the treatment plan of the day. Original plan was accepted for 2 fractions, new plans were calculated online and delivered for 3 fractions because of bowel motion. An intrafraction motion management strategy was applied, consisting of a gating approach based on the real-time acquisition of a sagittal cine MRI during the whole fraction time (temporal resolution: 4 frames/s). The GTV was defined as gating target structure: the beam was turned off every time GTV movements exceeded the chosen 3-mm isotropic boundary.

Results: No acute radiation-related adverse events were observed during the treatment. A contrast enhanced CT scan 2 months after the treatment showed signs of inflammation.

Conclusions: SBRT with modern hybrid MR-LINAC allows to improve target volume coverage while meeting OAR constraints that is necessitated by daily gastrointestinal organ motion and deformation, using daily adapted treatment plans. It also enable to control intrafraction target movement, using real-time tumor tracking and automated gated delivery. No acute adverse events were observed in the case presented herein. However, a longer follow up is needed to more accurately estimate late toxicity. Stereotactic MR-guided adaptive radiation therapy (SMART) may become one of the treatment options for localized UTCC patients.

P029

THE CONE BEAM CT ANGIOGRAPHY IN RADIOTHERAPY PLANNING: A PHANTOM-BASED DOSIMETRIC EVALUATION

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Aims: Radiotherapy (RT) represents a therapeutic option for patients bearing arteriovenous malformations

(AVM) in critical areas of the brain. The standard RT planning procedure include the planning CT that has to be coregistered with RM and or angiographic images in order to perform the contouring and calculate RT doses. Dose calculation from CBCT is challenging owing to the inconsistency of the Hounsfield units . The aim of the present proof of concept study was to explore the feasibility of the implementation of a cone beam CT angiography (CBCTan) in radiotherapy planning.

Methods: RTsafe Reference PseudoPatientTM 3D printed head phantom (HP) of realistic anatomy, including bone inhomogeneities, was used. HP images were acquired in standard supine position by using both a conventional CT scanner and the CBCT embedded on the Siemens Artis Zee equipment. A set of contours, including targets (GTV and PTV) and OARs, that simulate a clinical setting of a patient affected by AVM who underwent to stereotactic radiosurgery (SRS) was generated on CT images. The two studies were rigidly coregistered and then the contours were transferred from CT to CBCTan. For the 3D data set CT images, a 3DCRT plan was generated by Philips Pinnacle3 Treatment Planning System (TPS) v. 9.10 using Collapsed Cone Convolution Superposition algorithm with a prescription dose of 13 Gy in single fraction. The plan was optimized for a Varian TrueBeam STx Linac (Varian Medical System, Palo Alto, CA) equipped with a High Definition 120 multileaf collimator (HD120MLC). 3DCRT technique consists of multiple static fields: 4 coplanar and 2 non coplanar (couch angle 90° and 315°) 6 MV photon beams. For plan evaluation, dose-volume-histograms (DVHs) of PTVs and OARs were evaluated, producing clinically acceptable plan. The same plan was calculated on CBCTan.

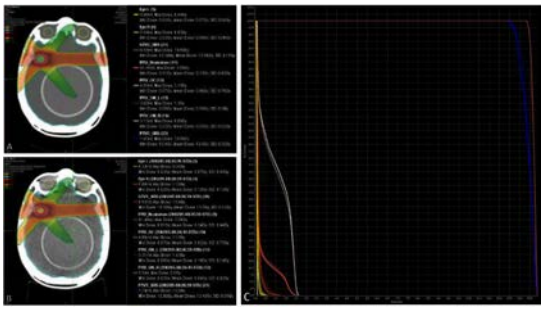

Figure 1. Comparison between CT (A) and CB-CT (B) dose distributions in color-wash and dosimetric data of GTV, PTV and organs at risk. The dose-volume histogram of GTV, PTV, PRV_optic chiasm, PRV_optic nerve L, PRV_optic nerve R, PRV_brainstem, Eye L and Eye R in two plans (C). The same color lines representthe same regions of interest.

Results: Concerningly OARs, no significant dosimetric differences were observed between the CT plan and CBCTan plan. With regard to PTV coverage, V95 and V98 for CT-plan were 100% and 96.8% while for CBCTan-plan were 99.7% and 96.3%, respectively. The homogeneity index of PTV was 0.11 for CT plan and 0.13 for CBCTan plan, respectively. In Figure 1 are reported the dose distributions, the DVHs and the dosimetric summaries for each plan.

Conclusions: The present proof of concept study suggests that the use of a cone beam CT angiography in radiotherapy planning is feasible. Further measures are needed in order to better clarify the potential use of CBCT in RT planning with particular reference to the Hounsfield unit concerns.

P030

COMPARATIVE DOSIMETRIC ANALYSIS OF TREATMENT PLANS DEVELOPED WITH 3D-CONFORMAL TECHNIQUE VERSUS VMAT IN LOCOREGIONAL RADIOTHERAPY IN PATIENTS AFFECTED BY BREAST CANCER WITH METASTATIC LYMPHADENOPATHY: PRELIMINARY ASSESSMENT

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Aims: To compare beforehand dose coverage at treatment volumes and organ-at-risk dose (OAR) between single-isocentre 3D treatment plans and VMAT technique in patients undergoing locoregional Radiation therapy for stage III breast cancer.

Methods: 12 women with breast cancer (6 right, 6 left) and axillary metastatic lymphadenopathies were selected, subjected to radical or conservative surgery, and subsequently to locoregional Radiotherapy at Radiation Oncology and Radiobiology Unit of "De Lellis" Hospital in Catanzaro; the dose prescription was 50 Gy/25 fx. at both volumes; in the case of conservative surgery, any boost dose prescription was not considered in the assessment. All patients, except 2, were treated with 3D-conformal technique. The same operator performed the re-contouring of treatment volumes CTV and PTV of chest wall/mammary gland and supra-infraclavicular ipsilateral nodes) and OAR (contralateral breast, lungs, whole heart, left ventricle, left descending artery (LAD), thyroid, oesophagus, spinal cord, ipsilateral scapular humeral joint, ipsilateral brachial plexus), and it was verified by another operator, both dedicated to the mammary disease; then, a treatment plan with 3D conformal technique at single isocentre and half fields by Oncentra Masterplan TPS v. 4.5.3 (calculation algorithm Collapsed Cone) and a treatment plan VMAT by Monaco TPS v. 5.11.02 (calculation algorithm Monte Carlo) have been developed for each patient. Optimisation of the plans was achieved by seeking PTV coverage of 95% of the prescribed dose. For PTV of chest walls the best possible coverage was accepted after optimization. OARs constraints were those routinely in use at our Institution. The obtained data were entered in a worksheet and the average of each parameter was calculated, filtering, as regards cardiac parameters, only the patients treated on the left. No statistical analysis has been carried out due to the small

number of the test sample.

Results: The average PTV coverages obtained with VMAT planes were more favorable than the 3D technique (about 96.5% vs. <94% on chest wall/mammary gland, >98% vs. 94% on LFN). Otherwise, the values on the contralateral breast were slightly better with the 3D technique, especially in terms of Dmean and V5 (<0,5 Gy and 0% vs. about 2 Gy and 1,41%, V10 0% with both techniques). Similar feedback was obtained for lung volumes, with a clear advantage in terms of average dose, V5 and V10 on the ipsilateral lung and the average doses of the contralateral lung and total lung capacity for 3D treatment plans: V5 data were significantly higher and out of constraints in VMAT plans (about 65% vs. 33% of the average 3D). About whole heart, although most of the dose constraints were within limits, except for the Dmean, slightly exceeded in both techniques, at low doses was calculated a slight advantage for 3D plans; an important data clearly against the VMAT has been recorded for the left ventricle, in which the V5 has turned out to be of 52,46% vs. 13.23%; in contrast, it was a clear benefit in the VMAT plans for all constraints related to LAD (Dmean about 6 Gy vs. 10.5, V30 and V40 0% vs. 20 and 18% respectively). With regard to the oesophagus, thyroid, spinal cord, brachial plexus and humeral scapular joint, the tendency to a better profile of dose constraints has been confirmed by 3D plans, although with both techniques the values have been largely within limits.

Conclusions: The results of our study, although conducted on a limited number of patients, confirm the data of literature, which show that the coverage of target volumes seems to be more favorable in the VMAT treatment plans. However, the worst low dose profile for major OAR is confirmed: the lung and heart muscle data are highlighted: the mean values obtained are affected by constraints for two patients in particular, where probably the artifacts due to metal valve of expanders heavily affected the dose distribution. In contrast, the LAD constraints profile was much more favorable in the VMAT plans, so that the only 2 patients treated with VMAT technique did not fall into the constraints with the 3D plan. For the other organs at risk, the averages values showed that with both techniques it is possible to respect the dose constraints, although with a slight prevalence for 3D plans. Our preliminary assessment, seems to suggest that the use of VMAT technique may be a valid surrogate for breath-hold techniques in patients with coronary artery disease or with unfavourable anatomy, suffering from left breast cancer. However, any further consideration requires an adequate number of patients and a statistical analysis, which will be achieved with the continuation of the study.

P031

WAITING TIME EVALUATION FOR BREAST ADJUVANT RADIOTHERAPY, USING ARTIFICIAL INTELLIGENCE

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Aims: The benefit of the radiotherapy (RT) for breast cancer in the adjuvant setting is proven and there is a large literature about the timing within it should be completed. In the real-world life, there is a lack of a guardian system to detect this interval online. This study is a proof of concept that artificial intelligence systems can extract data by hospital system for evaluate waiting time for adjuvant radiotherapy.

Methods: We set a multidisciplinary team with engineers and bioinformatics to identify pathway for data extraction and elaboration. ICD9 codes for diagnosis and surgery were selected for identifying pts with breast cancer who underwent surgery. We evaluated 10 main variables in order to extract by the text-mining technology the time lapses in which the RT was performed: 7 were structured variable, such as the date of birth or the kind of surgery, and 3 were unstructured variables (multidisciplinary board indication to chemotherapy, radiotherapy or both). Text mining selected patients with multidisciplinary indication to adjuvant chemotherapy and radiotherapy. Waiting time interval was calculated as interval between surgery and first day of treatment.

Figure 1. Output of time intervals between surgery and first day of radiotherapy, with stratification on age and residency.

Results: From January 2017 till December 2019, a cohort of 2074 patients who underwent surgery for breast cancer. Between them, 655 pts were addressed to adjuvant RT alone, 113 to adjuvant chemotherapy

alone, 153 to both. Of this cohort, 1023 underwent RT in our center. Mean waiting time was 119 days (31-345). They were divided into three groups based on waiting time interval: 154 patients underwent to RT within 60days from the surgery; 407 patients starting from 60days after the index breast surgery and up to 90days; and 462 patients who were treated after 90 days from surgery (Figure 1). Patients who came from other regions, and so, far from our center experienced a wider delay in the beginning of RT.

Conclusions: This study showed that it is feasible to extract data from different data sources inside hospital system. Output of this evaluations needs to be implemented and integrated inside system hospital to have alert for managing patients waiting time delay. Prospective studies are needed to highlight predictive factors that can influence the timing of RT.

P032

ARTIFICIAL INTELLIGENCE FOR KEY PERFORMANCE INDICATORS (KPIS) IN BREAST CANCER PATIENTS CARE: A PROOF OF CONCEPT

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Aims: In the Italian National Health System background, the increase in the oncology expenditure has led to an increasing attention on the efficiency of the way the healthcare resources are allocated. It becomes therefore essential to measure the performance of the various activities, but data are often distributed on different source. We projected an artificial intelligence (AI) data extraction system for populating breast cancer (BC) DataMart and facilitate data elaboration. This study aims to be a proof of concept to determine the feasibility of a set of Key Performance Indicators (KPIs) to confirm feasibility of automated data extraction.

Methods: We set a multidisciplinary team with engineers and bioinformatics to identify pathway for data extraction and elaboration. ICD9 codes for diagnosis and surgery were chosen for selecting pts with breast cancer who underwent surgery. According with the aim of the study we selected 9 KPIs to be extracted (Table 1). For each KPI, variables for its definition were selected and divided in structured and not structured. The last one were extracted by text mining.

Results: From January 2017, Artificial Intelligence automated pathway of extraction identified 2144 patients. Five different data sources were used for data extraction. Nine structured (age, ICD9 diagnosis, ICD9 surgery, ICD9 diagnostic exams, data of beginning chemotherapy and/or radiotherapy, data of recovery and dismissal, data of pathology exam) and 4 not structured variables by text mining elaboration (subtypes, staging, multidisciplinary board therapeutic indications) for KPIs calculation were identified. Extraction populated all KPIs and mean rate of data extraction in text mining elaboration were 78% and 88.3% respectively for staging and subtypes' characterization. KPIs their performance was respectively: 1) 20.91%; 2) 17.88%; 3) 26.9%; 4) 0.25%; 5) 1.72%; 6) 44.6%; 7) 92.2%; 8) 95%; 9) 67.3%.

Conclusions: This study confirms that it is feasible to extract data inside hospital system. KPIs extraction was feasible, even if further validation are necessary to implement data extraction and optimize quality of data, to create online simultaneous outputs, integrated inside hospital system.

Table 1. KPIs description.

KPI name	KPI description
KPI pre-surgery	Percentage of stage I and II breast cancer patients who underwent at least one radiological exam in the 60days prior to the breast surgery
KPI post-surgery	Percentage of stage I and II breast cancer patients who underwent at least one radiological exam within the 60days after the surgery
KPI follow-up	Percentage of stage I and II breast cancer patients who underwent at least one radiological exam from 60days after the index breast surgery and up to 365 days after this surgery
KPI Subsequent Breast Reconstruction/Axillary dissection	Percentage of patients with BC who underwent subsequent surgery
KPI subsequent breast surgery	Percentage of patients with BC who underwent subsequent surgery following a partial resection
KPI chemotherapy timing	Percentage of patients with BC who, as candidates for chemotherapy, initiated adjuvant treatment within 60 days of the index breast surgery
KPI radiotherapy timing	Percentage of patients who initiated radiotherapy within 180 days of the last surgery
KPI time of recovery	Percentage of patients who presented a recovery time in less than 7 days
KPI pathology exam	Percentage of patients who received a pathology exam in less than 15 days

P033

DIET AND NUTRITIONAL STATUS IN CANCER PATIENTS RECEIVING RADIOTHERAPY

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Aims: Clinical evidences indicate that a proper feeding and maintenance of adequate nutritional status

since diagnosis can help to reduce complications and to improve the outcomes of treatments in cancer patients. Aim of this study has been to evaluate knowledge and perceptions about the role of diet habits and nutritional status in a sample of cancer patients, requiring nutritional information at Radiotherapy Center of Casa di Cura San Rossore in Pisa.

Methods: 36 patients (40-76 yrs.) receiving radiotherapy (21% of patients admitted to the Center during 3 months) have been studied monitoring personal and anthropometric data, the request of nutritional advice, site of the tumor, therapies, possible comorbidity, main dietary/nutritional issues, recall 24h, eating modifications after diagnosis, physical activity. Nutritional status of each patient has been evaluated through an energy and protein intake analysis and body weight changes from diagnosis.

Results: Sample is represented by 12 patients with breast cancer (average BMI 24,7 Kg/m^2), 15 patients with urogenital cancers (average BMI 24,2 Kg/m^2), 3 patients with pancreatic cancer (average BMI 17,5 Kg/m^2), 6 patients with glioblastoma (average BMI 28 Kg/m^2). Most patients have normal BMI, but in the whole sample we found a poor protein intake (1 g/Kg/day). The 50% of the sample follow an unbalanced and selective diet in an attempt to avoid symptoms from anti-cancer therapies. Three patients were severely malnourished (average BMI 17,5 Kg/m^2 with weight loss of 30% from diagnosis), 18 patients with risk of malnutrition (average BMI 22,3 Kg/m^2, daily energy intake 21,7 Kcal/Kg/day and protein intake 0,9 g/Kg/day), three were with overweight and six with obesity (average BMI 30,7 Kg/m^2, daily energy intake 31,7 Kcal/Kg/day and protein intake 1,2 g/Kg/day). Only three patients had been given specific dietary indications, and all patients show lack of knowledge about adequate nutrition and poor awareness of negative impact of malnutrition.

Conclusions: The study shows the importance that each cancer patient gets information from oncologists and radiotherapists about the relevance of nutritional monitoring and support, as well as integrating anti-cancer therapy with nutritional specialized counseling.

P034

KETOGENIC DIET FOR PATIENTS UNDERGOING RT FOR HIGH GRADE GLIOMA

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Prognosis of high grade gliomas, even after surgery and chemo-radiotherapy, remains poor. Glial neoplastic cells, as other transformed cells, preferentially use the glycolytic pathway even in well oxygenated environments. This phenomenon is known as Warburg effect and may be exploited in the attempt to contrast disease evolution. Ketogenic diet (KD), that includes meals mainly with fat and proteins and very low carbohydrates, lowers the glucose level increasing ketones in the blood. It has been hypothesized that KD may reduce VEGFR2 expression with consequent reduction of cancer driven neo angiogenesis, and metalloproteases (MMP) and vimentin that are markers of tumor aggressiveness and may increase radiosensitivity reducing antioxidant production. We designed a study to test if a KD can ameliorate progression free survival (PFS) in patients with histologically proven high grade glioma treated with postoperative radiotherapy and temozolomide. The level of ketosis reached by patients in 10 days of KD alternated with a 5 days pause will be assessed during the treatment. As secondary outcomes the study will evaluate the tolerance of the patients to the proposed dietary regime, and overall survival (OS). Twenty patients will be enrolled in twenty four months according to predefined inclusion and exclusion criteria. Patients will undergo a normo-caloric ketogenic diet for ten days, alternating with their usual nutrition regime for five days. A dose of 60 Gy using 30 fractions given five days a week will be administered to patients. Patients will be measured in terms of height, weight, BMI and body composition (fat and muscle body percentage) at the beginning, during and one week after conclusion of the RT treatment. Serum glucose will be assessed on a daily base. Insulin levels, beta-hydroxybutyrate and IGF-1 dose and toxicity of patients will be recorded as well during the RT treatment. Brain MRI every three months will be used to assess PFS.

P035

ACUTE GASTROINTESTINAL AND GENITOURINARY TOXICITY AFTER WHOLE-PELVIS IRRADIATION: IS DIETARY SUPPLEMENT WITH "CIS 400" OF CLINICAL BENEFIT? PRELIMINARY RESULTS OF A MONOISTITUTIONAL CLINICAL TRIAL

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Aims: Whole pelvic RT (WPRT) is used for irradiation in prostate, rectal and gynecological cancer. The aim of our prospective study was to evaluate gastrointestinal (GI) and genitourinary (GU) toxicity in patients (pts) underwent WPRT and receiving dietary supplement with Cis 400.

Methods: From November 2019 to June 2020, 9 pts (4 male and 5 female) received WPRT with or without concomitant chemotherapy (CT) were analyzed. Of them, 4 patients were affected by prostate cancer (44%), 2 pts by rectal cancer (22%), 2 pts by uterine cancer (22%) and 1 by cancer of vagina (12%). WPRT was delivered using an Elekta LINAC and a VMAT

technique. The total doses prescribed to the pelvis was 45-50 Gy given in 25-28 daily fractions, 5 fractions at week. In pts receiving adjuvant CT, RT treatment was performed three weeks after CT. All pts were evaluated at the the beginning of RT treatment by a radiation oncologist and (if not contraindications) dietary supplement with Cis 400 daily was prescribe for whole duration of RT. According to CTACE vs 5 acute GI and GU toxicity was evaluated by radiation oncologist at baseline (star of RT treatment) and weekly during the RT treatment.

Results: At the data analyses the median age was 63 years old with a range wide from 28-75 years old. Overall three patients (33%) received concomitant chemotherapy. According to CTACE vs 5, four patients reported G1 GU or GI toxicity at the moment of radiotherapy beginning (4 patients reported cystitis and two patients abdominal swelling). A benefit of dietary supplement with Cis 400 one week after the treatment was observed in all cases of cystitis (100%) and in 1 patient with abdominal swelling (50%). At the doses of 45 Gy only 2 patients (22%) had G1 acute GI/GU toxicity that consisted in dysuria, nocturia, anal pain, proctitis, diarrhea and abdominal swelling. All patients completed radiotherapy treatment without temporary of definitive RT treatment interrupt. Finally, at the end of radiotherapy treatment there were not observed G2 or higher acute GI or GU toxicity

Conclusions: These results appear to suggest that supplement dietary with Cis 400 is of a clinical benefit in terms of GI and GU acute toxicity, to delay arise of acute toxicity, decrease G2 or G3 acute toxicity during RT treatment, even in those patients with initial GI or GU disorders. We will increase the number of patients of this trial and follow them due to evaluate the efficacy of CIS 400 in preventing of GI and GU acute and late toxicity in patients receiving WPRT.

Conflict of interest: We are grateful to Leonardo Medical srl who provided free medical samples of Cis 400 to patients enrolled in this study.

P036

LOW FODMAP DIET IN RADIOTHERAPY FOR PROSTATE CANCER

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External beam Radiotherapy (RT) is an option of the standard of care for the definitive treatment of localized Prostate Cancer, achieving results in terms of overall survival comparable to Radical Prostatectomy. Modern techniques of treatment delivery such as intensity modulated RT (IMRT) or volumetric modulated arc therapy (VMAT), greatly improved dose distribution, while Image guided RT with on board cone-beam computed tomography (CB-CT), allows to achieve a more precise treatment with a better sparing of organs at risk (OARs), particularly the rectum . Since the prostate is a mobile organ, there may be significant differences in the internal target volume situation in the initially developed plan and that at the time of the procedure. Therefore, one of the main problem of external beam radiation in prostate cancer patients, is to obtain a reproducible positioning of the prostate and rectum by proper gastrointestinal preparation, which should reduce the rectal volume, stabilize the prostate and increase the distance between the rectum and the target volume. Several studies have focused their attention on the physiopathologic impact of FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monisaccharides and Polyols) on the gastrointestinal tract. FODMAPs are a type of carbohydrates poorly digested in the small bowel that, once fermented by the colonic flora, produce significant amount of rectal gas. FODMAPs have also shown osmotic properties for which they recall liquids within the gastrointestinal lumen. The combination of these effects leads to an increase in rectal volume. Our intention is to enroll prostate cancer patients in a particular diet protocol characterized by a Low – FODMAP daily intake. The main aim of our study is to evaluate the impact of a Low-FODMAP diet on the degree of rectal filling, as well as to compare rectal volumes differences between the study group and the control group. Furthermore, we are going to study the acute and late gastrointestinal toxicity manifested in the two groups. As a secondary outcome the study will also evaluate the compliance of the enrolled patients to the proposed dietary regime. Fifty patients will be enrolled in a twenty-four months period according to predefined inclusion and exclusion criteria. Twenty-five patients will be included in the study group and the remaining in the control group. The study group patients will undergo a predefined low-FODMAP diet for six weeks. The control group patients will maintain their usual nutrition regime. A dose of 67.5Gy using 25 fractions given five days a week will be administered to patients. A CB-CT scan will be performed daily for the first three RT sessions and then every three days. The CT scans obtained during the RT treatment together with the planning CT will be evaluated in order to record differences in rectal volumes. Patients will be measured in terms of height, weight and BMI at the first meeting and weekly during RT treatment. Patients will be asked weekly to report their adherence to the proposed diet regime as well as the development of gastrointestinal or urinary symptoms.

P037

THE ADDITION OF SILIBININ TO THE STANDARD ADJUVANT THERAPY IN MALIGNANT GLIOMAS

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Aims: Glioblastoma (WHO grade IV) is the most common primary brain tumor and has poor therapeutic outcomes despite aggressive multimodal therapy. Silibinin, a natural polyphenolic flavonoid isolated mainly from milk thistle (Silybum maria num), has been shown to inhibit in vitro cell growth in several cancer models, including malignant gliomas. We hypothesized that silibinin would potentiate the efficacy of current treatment of glioblastoma.

Methods: We proposed treatment with silibinin to all patients with newly diagnosed glioblastoma undergoing surgery after 1st March 2020 and candidates for standard adjuvant therapy. The current standard of care involves maximal safe surgical resection followed by radiation therapy (60 Gy in 30 fractions or ipofractionated radiotherapy) with concurrent low dose daily temozolomide followed by adjuvant chemotherapy (temozolomide 1 week on/3 weeks off). We administered silibinin in the form of 650 mg capsules also containing vitamin B1 (Sillbrain) at the following dosage: two capsules a day for the first two weeks of radiotherapy, then one a day continuously. Histological data, and molecular predictive and prognostic factors such as IDH1 and IDH2 mutations and MGMT amplifications were recorded for all patients. Standard follow-up included clinical examination, blood tests and brain MRI with contrast every 3 months for the duration of adjuvant chemotherapy and beyond, up to progression of disease. Any toxicity was recorded according to the CTC AE v4.0 classification. Second-line treatment was eventually chosen by the oncologist.

Results: In this moment we have 3 patients in treatment; 1 patient ipofractionated radiotherapy with silibinin; 2 patients conventional radiotherapy with concurrent Temozolomide. Other 2 patient will begin radiotherapy with concurrent Temozolomide and Silibinin in the next week.

Conclusions: The addition of silibinin to the standard treatment is well tolerated by patients. The small number of patients and the short follow-up do not allow at the moment to draw any conclusions on late toxicity, responses, progression-free and overall survival.

P038

A RADIOTHERAPY CAN INCREASE OVERALL SURVIVAL IN PATIENTS TREATED WITH IMMUNE-CHECKPOINT INHIBITORS? A META-ANALYSIS OF PUBLISHED STUDIES

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Background: Immune-checkpoint inhibitors are emerging as a new treatment in a variety of solid tumors. Clinically, little is known about the integration of a radiation treatment with their effectiveness, despite biological results are extremely promising.

Objective: To assess the effects of combination of radiotherapy with an Immune-checkpoint inhibitors treatment on the increase of overall.

Data Sources: Computerized bibliographic searches of MEDLINE and CANCERLIT (1970–2019) were supplemented with hand searches of reference lists.

Study selection: Studies were included if they were comparative studies between combination ICI-RT and radiotherapy (RT) alone. Overall survival (OS) was analyzed according to treatment strategy. In 8 studies, 1260 were treated with association of ICI-RT and were compared to 2510 patients treated with radiotherapy alone.

Data extraction: Data on population, intervention, and outcomes were extracted from each srudy, in accordance with the intention to treat method, by two independent observers, and combined using the DerSimonian method and Laird method.

Results: Association ICI-RT compared to RT alone significantly increases the 1-year (OR 0.63; 95%CI 0.53-0.74, $p<0.00001$) and 3-year overall survival (OR 0.65; 95% CI 0.54-0.79, $p<0.0001$).

Conclusions: In patients with solid cancer, integrating RT to ICI increases 1- and 3 yrs overall survival compared to RT alone.

P039

PALLIATIVE RADIOTHERAPY IN A CLEAR CELL RENAL CANCER PATIENT TREATED WITH NIVOLUMAB: AN ABSCOPAL RESPONSE AND A REVERSION OF RESISTANCE

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In radiation oncology, an abscopal response is a well-defined phenomenon: an action at a distance from the irradiated volume but within the same organism. Despite, biological studies have suggested a radiation-induced model; in clinical practice abscopal effects are not so frequent.

The introduction of Immune-checkpoint inhibitors in cancer treatment is opening up new scenarios, especially for exploring potential therapeutic combinations.

We report on a 67-year-old male who was diagnosed with clear cell renal cell carcinoma (RCC) in clinical stage IV with lung metastasis. In January 2018 he underwent laparoscopic nephrectomy and CT guided biopsy of a pulmonary nodule, confirming pT3a pNx M1. In April 2019, after two lines of treatments with Sunitinib and Cabozantinib, revaluation CT imaging showed progression of disease with multiple metastases in all lung segments, the largest of which, with a diameter of 5 cm, is located at the left upper lobe. Other lesions were in mediastinal and abdominal lymph nodes, in both adrenal gland and in several dorsal and lumbar vertebrae. As third-line regimen, the patient was treated with anti-programmed death 1 (PD-1) monoclonal antibody Nivolumab at a dose of 3 mg/kg intravenously every 14 days. In October 2019, after 12 cycles of nivolumab the patient experienced severe

lumbar spine pain, poorly controlled by drugs, and revaluation CT imaging showed a progression especially in lumbar vertebrae, with invasion of the spinal canal at the level of L2. Because of his symptoms, an antalgic radiotherapy regimen was delivered with a total dose of 20 Gy in 5 daily fractions. A second radiation treatment, with total dose of 24 Gy in 3 daily fractions was administrated to new lung metastasis in lower left lobe. The patient continued treatment with nivolumab during radiotherapy and thereafter. A CT scan 2 months after radiotherapy (16 nivolumab applications in total) showed a significant numerical and volumetric reduction of all lesions. The patient today is still receiving maintenance nivolumab treatment (26 nivolumab applications) without significant adverse events and with a stable disease. This case report suggests that Immune-checkpoint inhibitors and radiotherapy have a potential therapeutic synergy with the goal of improving patient outcomes in metastatic RCC. Other clinical studies should further investigate this combination to translate preclinical models into clinical practice.

P040

RADIOFREQUENCY THERMOABLATION (RFA) AND RADIOTHERAPY (RT) COMBINED TREATMENT FOR BONEMETASTASES IN OLIGOMETASTATIC SETTING. A SYSTEMATIC MINI REVIEW OF THE LITERATURE

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Context Approximately 50% of cancer patients are diagnosed with bone metastases in their natural disease history. The management of metastatic bone disease requires a multidisciplinary approach. Both Radiofrequency thermoablation (RFA) and Radiation therapy (RT) showed to be safe and effective in the management of painful metastases, even if they rely on totally different action mechanisms. It is hypothesized that the combination of RT and RFA may synergistically function to achieve better pain control Objectives We performed a systematic review to describe the feasibility and effectiveness of combining RFA and RT for pain treatment of bone metastases in oligo-metastatic patients evaluating its role in alleviating bone pain, reducing the risk of fractures and consequently ensuring a better quality of life.

Methods: This systematic review included studies that reported populations meeting the following inclusion criteria: (I) confirmed bone metastases in adult patients; (II) active bone metastases pain; (III) patients treated with combined RFA-RT; (IV) Original studies.

Results: We selected 3 articles that evaluated the combined treatment with doses ranging from stereotactic body radiation therapy (SBRT) and moderately hypofractionated 3D conformal RT (3D CRT) schedules.

Conclusion: The RFA-RT combined strategy resulted to be promising in terms of efficiency and safety with good pain control and quality of life improvement, with a positive effect also on time to LF and OS increase. Further prospective studies are needed to better delineate RFA-RT treatment benefits.

P041

RADIOCHEMOIMMUNOTHERAPY INTEGRATION IN THE TREATMENT OF LOCALLY ADVANCED NON SMALL CELL LUNG CANCER: A SINGLE INSTITUTIONAL EXPERIENCE

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Aims: Assessment of the impact in terms of efficacy and toxicity of integrated radiochemotherapy (RT-CT) and sequential immunotherapy (durvalumab) in patients (pts) with unresectable non-small-cell-lung cancer (NSCLC) and PDL1 receptor positivity.

Methods: From February 2019 to April 2020 our radiotherapy department enrolled 20 pts with unresectable NSCLC treated with RT-CT. 8 pts were excluded from the analysis due to PDL1 receptor negativity (PDL1<1%) (5), use of immunotherapy drug pembrolizumab (2) and unexpected death from Sars-Cov-19 viral infection (1). 12 pts, at the end of RT-CT, showed no disease progression on CT scan and started immunotherapy with durvalumab (anti PDL1 receptor). Of all pts involved in the analysis (12), 8 pts underwent sequential radiation therapy after chemotherapy mainly for high volume of thoracic disease, while 4 pts were treated with concurrent RT-CT. In accordance to current guidelines all pts were treated with planning target volume prescriptions of 60 Gy, with the exception of one (54 Gy), and conventional fractionation (1.8-2 Gy/fr).

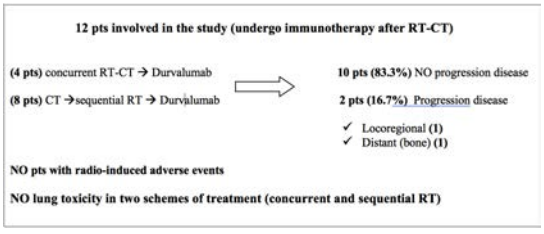

Figure 1. Data analysis of patients (pts) involved in the study.

Results: To date, the follow-up (f.u.) analysis indicates that 10 pts (83.3%) undergo durvalumab immunotherapy (median f.u. of 5 months), one of which stopped treatment after one cycle due to suspected immunorelated toxicity (muscle and joint pain), and nobody shows disease progression. 2 pts (16.7%), on the other hand, stopped taking durvalumab due to distant (bone) and local disease progression after 4 and 3 months of drug therapy respectively. No pts developed radio-induced adverse events and there was no significant difference between the two treatment schemes (sequential radiotherapy versus concomitant RT-CT) in terms of lung toxicity.

Conclusion: The addition of durvalumab to standard RT-CT treatment is confirmed effective in pts with unresectable NSCLC compared to a low toxicity profile.

P042

VMAT-SBRT FOR SPINAL METASTASES FROM RENAL CELL CARCINOMA. A CASE REPORT

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Aims: We evaluated the feasibility and pain resolution after VMAT-SBRTtreatment (Volumetric Modulated Arc Therapy-Stereotactic Body Radiation Therapy) for spinal metastases

Methods: A 65 year-old man was diagnosed with clear cell renal carcinoma G2 (pT1c) stage I and underwent a nephron-sparing surgery without adjuvant therapy in February 2018. One year later the bone scan subsequently confirmed with a spine Magnetic Resonance Imaging (MRI), revealed bone metastasis on the left side of the vertebral body, pedicle, lamina and articular processes of T10 spine. At presentation, he complained of pain with VAS score of 5, without neurologic symptoms and an ECOG performance status of 1. Thepatient started first-line therapy in March 2019 with tyrosin-kinasy inhibitors (Pazopanib) 800 mg orally once a day, Denosumab 120 mg s.c. q 28 days and also he was treated by VMAT-SBRT with a total dose of 24 Gy in 3 fractions. MRI image was fused with CT simulation for target and OAR (Organ at Risk) contouringin accordance with parameters in the International Spine Radiosurgery Consortium Consensus Guidelines for Target Volume Definition in Spinal Stereotactic Radiosurgery and the recommendations of RTOG 0631. Treatment were performed by Elekta Versa HD linear accelerator. Planning was performed with Monaco Planning System (v.5.11.03) using one double arc. The plan was evaluated according to ICRU 91 indices (D95%, D98%, D2%, D50%, Homogeneity index HI, Conformity Index CI). OAR was evaluated by comparing doses to the spinal cord (Dmax, D0.35, and D1.2 cc), esophagus (Dmax and D5 cc), heart (Dmax, D15 cc), and lung (V5 and V10).

Results: At 24 months after treatment the MRI detects stable lesion and the patient's pain improved with VAS score of 2. Currently the patient continues the treatment with Pazopanib 800 mg die and Denosumab 120 mg s.c. q 28 days. The last MRI examination has an area of altered signal unchanged compared to the previous checks, with phenomena of osteochondrosic suffering. A total body CT placed the suspicion on a further lesion to the left sacral wing undergoing diagnostic definition.

Conclusions: VMAT-SBRT is an attractive therapeutic modality for the treatment of spinal metastases, feasible, safe and effective, especially in radio-resistant tumors such as renal clear cell carcinoma and also the treatment with tyrosin-kinasy inhibitors has produce a good result by improving the pain symptoms and stabilizing the progression of the disease.

P043

BRAIN RADIATION THERAPY AND INTEGRATION OF AN ORAL NUTRACEUTICAL PRODUCT CONTAINING SILIBININ IN PATIENTS WITH LUNG CAN-CER AND HIGH-GRADE GLIOMAS: THE CLINICAL EXPERIENCE OF PIACENZA HOSPITAL

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Introduction: It is estimated that 20% of all patients with CA develops BM over time, with higher frequency in pts with lung, breast, colorectal, melanoma, and kidney CA. Development of BM contributes to global mortality from CA in pts with advanced stage, in fact the prognosis remains poor, with median survival from the onset of BM of months. Among primary brain tumors, gliomas are the most frequent. The most malignant glioma is Glioblastoma Multiforme (GBM), with a median survival of less than 1 yr. The purpose of our study is to evaluate the activity of a nutraceutical product containing silibinin (a flavonoid) on the clinical and radiological progress of BM in patients with lung CA and radiological response in patients with GBM, undergoing brain RT.

Material and Methods: From September 2019 to May 2020, 10 pts were treated with RT for GBM or BM in association and / or sequential to systemic therapy, in addition to anti-edema treatment. The pts were treated with an oral supplement containing Silibinin, which has a high antioxidant and hepatoprotective activity, and Vit B1 with a supporting role in both central and peripheral neuronal function. The supplement was taken by the pts once a day both during and after RT. Patients and treatment characteristics are reported in Tables 1,2,3

Results: All the pts completed RT. 80% one month after RT maintained their ECOG-PS 1, continuing with subsequent treatments; only 2 (20%) affected by SCLC (Stage IV) and ECOG-PS 2 at the beginning of RT, had clinical worsening within 1 month from the end of RT for PD (ECOG-PS 3) and undertook palliative care. In

our case study the administration of Silibinin was well tolerated and the clinical conditions of the pts remained stable. The evaluation of the response in terms of local regression of the tumor requires a longer follow-up and a comparison with our historical series.

Conclusions: Pts with BM or with GBM need new therapeutic strategies to improve a poor prognosis. The integration with Silibinin and RT, the effectiveness of which on the control of some mechanisms of cellular proliferation is demonstrated (inhibition of STAT3) with an excellent tolerability, suggests continuing to explore its role in this setting.

Table 1. Caratteristiche dei pazienti (Radioterapia Ospedale di Piacenza).

	N 10
Sex	
Male	8 (80%)
Female	2 (20%)
Age	
< 70	2 (20%)
> 70	8 (80%)
Mediana (Range)	65
Karnofscky PS	
≤70%	2 (20%)
> 70%	8 (80%)
ECOG -PS	
2	2 (20%)
1	8 (80%)

Table 2. Caratteristiche dei pazienti (Radioterapia Ospedale di Piacenza).

Metastasi extracraniche	
Presenti	4(40%)
Assenti	3(30%)
Istologia del Tumore Primitivo	
Smallcell (SCLC)	2(20%)
Adnocarcinoma (NSCLC)	5(50%)
Altri (Gliomi)	3(30%)
BM status	6 (60%)
Nuova Diagnosi	4 (40%)
PD (Progressive Diseasese)	2 (20%)
Non BM	1 (10%); (SCLC in RC Torace)●
GPA prognostic class	6 (60%) pz BM; 1 (10%) pz●
3.5-4.0	0
2,5-3,0	0
1,5-2,0	1 (10%)
0,0-1,0	5 (50%)
Gene status	
EGFR pos.	2(20%)
ALK pos	2(20%)
Numero di BM	
Dimensioni delle BM:	max 30 mm
Mediana (Range)	8 mm-30 mm

Table 3 Programma Radioterapico nei pazienti trattati anche con Silibinina (Settembre 2019 – Maggio 2020).

N° 10	Tumore Primario (Polmone)	Tipo Istologico	Trattamento Radioterapico
		CA non a piccole cellule (NSCLC)	
2			RT pall-sint. WBRT); Dose30 Gy.
1			SRT su 3 lesioni encefaliche; 21 Gy in 3fr.
1			RT(WBRT) pall-sin; Dose30 Gy, dopo RT sequenziale alla CT per PD. SRT frazionata su 2 lesioni encefaliche; 30 Gy in 6 fr; dopo RT (WBRT) eseguita in 10/2018.
1			
		CA a piccole cellule (SCLC)	
			RT (WBRT) profilattica; 25 Gy dopo RT di consolidamento su Mediastino sequenziale alla CT in pz con RC Torace.
1			
1			RT pall-sint. (WBRT); Dose 30 Gy.
	Tumore Primitivo Encefalo		
		Glioblastoma Multiforme	
2			RT-CT concomitante adiuvante alla CHIR su; letto operatorio 60 Gy.
1			RT-CT esclusiva su lesione encefalica; 54 Gy.

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P044

THERMO-CHEMO-RADIOTHERAPY: PRELIMINARY ASSESMENT OF FEASIBILITY

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Aims: Hyperthermia has been demonstrated to enhance the effect of radiation, chemotherapeutic agents, and immunotherapy, to trigger changes in perfusion and oxygenation of cancer, as well as to inhibit the DNA repair mechanisms. There is also evidence for immune stimulation and the induction of systemic immune responses. The aim of this study was to assess the feasibility of hyperthermia as a combined treatment.

Methods: From December 2019 to May 2020, patients with different histotypes were selected for combined therapy (radiotherapy, chemotherapy, radiochemotherapy), including hyperthermia. We administered heat via radiative heating systems: BSD-500 for superficial treatments and BSD-2000 for deep regional treatments (Pyrexar Medical, Salt Lake City, USA) up to a temperature of 41-45°C. All patients treated with deep regional hyperthermia underwent a CT simulation to plan a personalized treatment using Sigma

Hyperplan® TPS. During the treatment, the local temperature was controlled through thermometric probes applied close to the neoplasm. Furthermore, the patients' vitals were monitored every ten minutes. Adverse events were analyzed according to National Common Terminology Criteria for Adverse Events (CTCAE), version 4.03.

Results: We treated 22 patients (mean age 69 years, range 44-87 years) with neoadjuvant or radical intent. Among them, hyperthermia was combined with radiochemotherapy in 6 cases, with radiotherapy in 11 cases and with chemotherapy in 5 patients. The patients were affected by primary locally advanced or recurrences of abdomen, pelvis or extremities. Most patients (95%) received treatment without relevant toxicity with a very high acceptance. Only one patient developed localized or diffuse power-dependent discomfort during the regional hyperthermia in the pelvic region. No other toxicity has been reported. Notably, there were no interruptions in any patients during radiotherapy and/or systemic treatment, due to hyperthermia. At the time of analysis, clinical and radiological re-evaluation was performed in nine patients after the combined therapy: four patients had a complete response, two patients a partial response, two a stable disease and one patient a disease progression.

Conclusions: The integration of radiative hyperthermia to radiotherapy and chemotherapy is feasible and tolerable. These preliminary findings encourage us to continue this integrated strategy.

P045

CRANIAL AND EXTRACRANIAL STEREOTACTIC RADIATION THERAPY WITH CONCURRENT IMMUNOTHERAPY IN OLIGOMETASTIC-OLIGOPROGRESSIVE PATIENTS: TOXICITY ANALYSIS AND IMPLICATIONS FOR THE SYSTEMIC TREATMENT CHANGE

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Aims: Cranial and extracranial stereotactic radiation therapy (SRT) is used in oligometastatic patients receiving concurrent immune checkpoint inhibition (ICI). This retrospective single institution study was aimed to evaluate the safety of SRT with concurrent ICI for the cranial and extracranial disease and to assess the rate of patients who need to change the ongoing systemic treatment.

Methods: Records from a single academic institution were reviewed to identify oligometastatic-oligoprogressive patients treated with SBRT and concurrent ICI. Checkpoint inhibitor (anti-cytotoxic T-lymphocyte-Associated protein 4 (CTLA4) and antiprogrammed death-1 (PD1) was used. Cranial and extracranial lesions were included in this analysis. Treatment-related adverse effects of SBRT were assessed. The primary endpoint was the rate of SBRT adverse events and the secondary endpoints included the rate of in-field response rates assessed as the overall response rate (complete, partial response or stable disease) and the need to change the ongoing systemic treatment. In-field-response was scored using the Response Evaluation Criteria in Solid Tumors V.1.1 criteria 3 months after completion of SBRT.

Results: Our cohort included 22 patients with 30 irradiated target lesions. SBRT was delivered to the lungs (n=11), bones (n=3), lymph nodes (n=7), liver (n=3) and brain (n=6). SBRT dosing varied by site and ranged from 15 to 50 Gy in one to eight fractions and was delivered by VMAT-IGRT. All subjects received the prescribed course of SRT. With a median follow-up of 6,3 months (95% CI 4,5 to 8,2), the cumulative rate of SBRT related toxicity (G1) was 13.3% (n=2), consisting of cough and esophagitis. No grade 2 or higher toxicity was detected. Radiographic response of in-field-lesions lesion was reported in 10 patients (45.5%), with complete response in 7 (32%) patients and partial response in 4 (18%). No abscopal effect was observed in these patients. In-field-lesions remained stable in 13 patients (60%). With a median follow-up of 6,3 months (95% CI 4,5 to 8,2), the in-field overall response was 100%. During follow-up five patients (22,7%) progressed in out-field lesions and three changed ICI treatment. The rate of patients who do not change the ongoing ICI treatment was of 86.3%

Conclusions: Cranial and extracranial SRT in patients treated with ICI is well tolerated and could delay the need to change the ongoing ICI treatment.

P046

FIRST EXPERIENCE USING HYPERARC TECHNOLOGY

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Aims: Multiple brain metastases stereotactic radiosurgery (SRS) treatments with single isocenter approach are increasingly used in many radiotherapy

departiments. The complexity of this kind of treatment requires that the typical Quality Assurance (QA) process is accompanied by pre-treatment verification (patient specific QA), to verify the agreement between both the calculated and measured dose distribution and point dose values. In this work we report the first patient specific QA experience for a multi target case study treated with HyperArcTM technology, using a 3D-printed anthropomorphic head phantom.

Methods: One patient with 4 brain metastases (diameters <3 cm) and prescription dose of 24 Gy in three-fractions was planned using HyperArcTM technique. The treatment plan was calculated using AcurosXB 15.6.06 algorithm on TPS Eclipse Varian Medical Systems (15.6), 6 MV Flattening Filter Free (FFF) mode, maximum dose-rate of 1400 UM/min, mono-isocenter technique and 4 non-coplanar arcs on a TrueBeam machine (Varian Medical System) with HD 120 MLC (Figure 1). For patient specific QA procedures, the verification plan was created using a 3D-printed anthropomorphic head phantom; point dose measurements were performed using a CC04 ion chamber (IBA dosimetry) in two different points: inside each target (high doses) and in low dose regions. Dose distribution differences were evaluated with Electronic Portal Imaging Device (EPID) and EPIQA software in terms of ɣ index analysis.

Results: Mean point dose differences of 1.5% [min 1.3% – max 1.7%] and 1.2% [min 1.0% – max 1.3%] were found respectively for high and low dose regions. Results obtained in terms of ɣ index passing rate show an agreement > 99% with 2%2mm criteria.

Conclusions: Our patient specific QA approach confirms the agreement between measured and calculated dose distribution, such as the point-to-point dose differences, for the evaluated HyperArc treatment. Further investigations will regard gel dosimetry measurements to verify 3D-dose distribution with 3D-printed anthropomorphic head phantom.

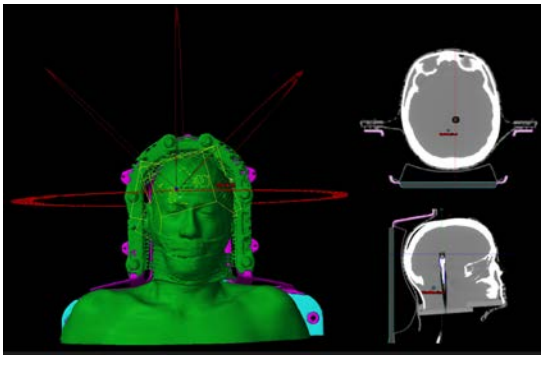

Figure 1.

P047

RADIOLOGICAL FINDINGS OF PNEUMONITIS AFTER LUNG STEREOTACTIC RADIOTHERAPY WITH CONCURRENT IMMUNE CHECKPOINT INHIBITORS (ICI): A MONO-INSTITUTIONAL EXPERIENCE

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Aims: To evaluate the development of pneumonitis within radiotherapy (RT) field in patients (pts) treated with stereotactic body radiotherapy (SBRT) and concurrent immune checkpoint inhibitors (ICI) for melanoma lung metastases.

Materials and Methods: From April 2018 to May 2020 13 pts (16 lesions total) with melanoma lung metastases were treated with SBRT using Cyberknife (CK) system and concurrent ICI at our Institution. Median total dose was 50Gy (range 32.5-54) delivered in 3-5 fractions, according to the institutional protocols. Median prescribed isodose line was 80% (range 75-81). All pts received ICI for primary tumor and were regularly evaluated by clinical examination, CT scan and FDG PET after completion of SBRT. Pneumonitis grading was assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.3.

Results: Among the 13 pts, 3 (23%) developed radiological finding suspicious for pneumonitis within radiation field during ICI treatment. Median time from the end of SBRT to radiological finding of pneumonitis was 2 months (2-4). 2 pts out of 3 were asymptomatic (G1 according to CTCAE v4.03) while 1 pts had cough and temperature so medical intervention with steroids plus antibiotic was performed (G2 according to CTCAE v4.03).This patient was under Pembrolizumab at the time of radiological finding while the other 2 pts were under Nivolumab and Ipilimumab.

Conclusions: The optimal integration, as well as the correct timing of SBRT and ICI has to be determined yet. Clearly the risk of pneumonitis should be carefully evaluated when offering pts ICI concurrent to ablative RT. Our data, in line with the current evidence, seem to confirm the feasibility and safety of lung SBRT as well as the acceptable toxicity profile when administered concurrent to ICI. Further studies are needed.

P048

IS RADIOTHERAPY NECESSARY TO CONSOLIDATE AND FULLY EXPLOIT THE POTENTIAL OF IMMUNOTHERAPY? RESULTS FROM A MULTICENTRIC RETROSPECTIVE ANALYSIS

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Aims: Radiation is a one of the mainstays of curative and palliative cancer therapy and is very effective in locally controlling disease. Immunotherapy has dramatically improved systemic disease control but nevertheless a large number of patients progresses at some point. No information as to the use of radiotherapy to "consolidate" the results of immunotherapy in progressive patients has been available. This analysis provides, for the first time, an estimate of the percentage of patients treated with immunotherapy that undergo radiotherapy at some time of their disease course, particularly simultaneously or after the initiation of immunotherapy.

Methods: A retrospective multicentric analysis was conducted in 6 neighbouring radiotherapy and oncology departments. The study included all patients treated with palliative or radical/adjuvant RT and at least one line of systemic therapy with immunotherapy for lung cancer/melanoma/renal carcinoma/head and neck carcinoma. Treatments were defined as concomitant when administered during IT; prior or sequential when RT was administered, respectively, three months before or after the administration of IT.

Results: Preliminary results were extracted from the database: from January 2015 to December 2019, 651 patients were treated withdifferent immunotherapeutic agents (Table 1). In 46% of patients were one or multiple radiation treatments were performed mostly with palliative intent (Table 1). In patients treated with Durvalumab, all patients were treated with radical intent with the PACIFIC regimen. Globally, patients were treated for multiple progression disease or oligometastic progression, respectively in 59% and 14% of cases.

Conclusion: The preliminary data collected in our study, represents a"real-life" panorama across several neighbouring oncology referral centers of the role of RT as an integral element to improve overall control of active immunotherapy treatments.Radiotherapy seems to be necessary to consolidate the excellent results with immunotherapy in a large fraction of patients across a variety of histologies.

Table 1.

	Period of accrual	Patients	Patients submitted to RT	Concomitant RT and IT	Intent of RT	RT ≤ 3 months before or after the administration of IT	Intent of RT	RT > 3 months before or after the administration of IT
IPILIMUMAB	2013-2019	47	46%	14%	Palliative 100%	36%	Other 75% Palliative 15%	50%
NIVOLUMAB	2015-2019	373	48%	24%	Other 11% Palliative 88%	38%	Other 13% Palliative 87%	38%
PEMBROLIZUMAB	2015-2019	195	42%	52%	Other 12% Palliative 88%	31%	Other 16% Palliative 84%	17%
DURVALUMAB	2018-2019	11	46%	0		37%	Other 100%	63%
ATEZOLIZUMAB	2018-2020	25	44%	18%	Palliative 100%	16%	Palliative 100%	66%

P049

FRACTIONATED STEREOTACTIC RADIATION THERAPY (FSRT) FOR RESECTED BRAIN METASTASES

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Aims: Cavity radiosurgery (SRS) or FSRT are emerging treatment options after surgical resection of BM. Randomized trials, have confirmed the association of neuro-cognitive decline to whole brain irradiation (WBRT). The phase 3 NCCTG study comparing SRS and WBRT for resected BM showed comparable overall survival and superior preservation of cognitive function after SRS. We report our experience on surgical cavity FSRT.

Methods: Between May 2011 and May 2020, 39 patients (pts) with surgical resected BM were irradiated with FSRT in 5 fractions. Median age was 59.5 years (range, 46-74); primary tumor was non-small cell lung cancer, breast cancer, gastrointestinal cancer, others in 14, 9, 9 and 7 pts, respectively. All pts were evaluated according to Karnofsky performance status (KPS). FSRT target was obtained using fusion of computed tomography (CT) and magnetic resonance imagings (MRI) of the brain. Gross tumor volume (GTV) was defined as radiologically visible surgery cavity in contrast-enhancing T1-weighted MRI sequences, clinical target volume (CTV) was coincident with GTV and planning target volume (PTV) was GTV/CTV plus an additional 2-3 mm in all directions (PTV average 28.6 cc). Pts were treated with a 6-MV linear accelerator fitted with a dynamic micro-multileaf collimator. 15 pts received 5x6 Gy and 24 5x7 Gy. All pts were followed by MRI and clinical examination 3 months after FSRT and at 3 months intervals thereafter. Local control (LC) was defined as a lack of relapse of the irradiated surgi-

cal cavity, and brain control (BC) as LC in absence of other documented BM. A brain failure at the site of FSRT was defined "in-field relapse", whereas appearance of new BM "out-field relapse".

Results: After a median follow-up of 14,7 months (range 2-89), 35 of 39 pts were evaluable because two were lost to follow up and two too early. 20 pts (57,14%) had LC and BC, 12 (34,28%) reached LC without BC, three (8,57%) had in- and out-field relapse. So 32 (91,4%) pts, reached a LC of whom more than one-half had BC. 12 pts with out-field relapse were re-irradiated, 8 with SRS, 2 with WBRT and 2 with WBRT followed by SRS. No acute toxicity was registered, 1 case of symptomatic radionecrosis was observed.

Conclusion: Our results showed that surgical cavity FSRT for resected BM achieves an excellent LC and a satisfactory BC with a good neuro-cognitive outcome. WBRT and/or SRS can be reserved to pts with further brain progression of disease.

P050

DOSES TO ORGANS AT RISK (OAR), TOXICITY AND OUTCOME IN PATIENTS RECEIVING RE-IRRADIATION (RERT) FOR RECURRENT GLIOBLASTOMA (RGBM): A SINGLE INSTITUTION EXPERIENCE

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Aim: To retrospectively evaluate doses to OAR, clinical tolerance and outcome in patients submitted to reRT for rGBM.

Methods: Between December 2017 and October 2019, twelve patients with rGBM were re-irradiated at recurrence. Patients' data, 4 males and 8 females (median age at time of re-irradiation 59 years, range 37-72), were analysed. Six had reRT after second surgery, the remaining underwent re-irradiation alone. GTV was defined by MRI T1-weighted contrast-enhancing lesion. PTV was defined by GTV plus a 1-cm margin. Maximum cumulative dose for optic chiasm, optic nerves and brain stem was extracted from DVHs. CTCAE v4.0 was used to define toxicity.

Results: Primary treatment doses were 60 Gy in 30 fractions in 11 patients and 40.05 Gy in 15 fractions in 1. The mean interval between first and second treatment was 12 months (range 5.6-20 months). All patients underwent concomitant Temozolomide (TMZ). ReRT doses were 54 Gy, 46 Gy, 40 Gy, 36 Gy in 27, 23, 20, 18 fractions in 3, 1, 1, and 6 patients, respectively. One patient underwent a hypo-fractionated reRT (30 Gy in 6 fractions). The cumulative BED between the two treatments had a median of 118.5 Gy (range 115.2–136.8). VMAT was used in 10 patients and Tomotherapy in 2. Eight patients had an in-field relapse, 2 a marginal relapse and 2 an out-field relapse. Mean GTV and PTV at retreatment were 36.3 cm^3 (range 3.9-98.1 cm^3) and 150.4 cm^3 (range 15.8-286 cm^3), respectively. The mean cumulative dose to chiasm was 47.5 Gy (range 16.1-76.4), to right optic nerve 31.1 Gy (range 10.6-66.7), to left optic nerve 33.6 Gy (range 5.9-61), and to brain stem 66 Gy (range 24.7-99.6). No treatment related grade 3 or 4 toxicities were experienced. One patient had a disease progression immediately at the end of reRT, with dramatic worsening of clinical conditions. Fotemustine, as second-line chemotherapy after reRT, was administered in 7 patients and TMZ in 3, while 2 patients received no second-line chemotherapy. Mean follow-up from the end of reRT was 6.8 months (range 2-11.7). Median overall survival from the end of reRT was 6.4 months (range 2-11.7). Currently, two patients are still alive after 7.7 and 11.7 months from the end of reRT, respectively.

Conclusions: ReRT was feasible and well tolerated in our series, with manageable toxicity. Further studies are needed to define dose constraints.

P051

RE-IRRADIATION FOR RECURRENT GLIOBLASTOMAS

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Aims: Several authors in literature described the feasibility and safety of a second RT course (re-RT) for recurrent GBM with a median PFS and OS time of approximately 5–7 months and 8–10 months, respectively, along with acceptable toxicity. Recently a meta-analysis, including all studies about re-irradiated recurrent GBMs from 1998 to 2008, showed that re-RT provides encouraging outcomes in disease control and survival rates with overall low toxicity rates. In this report, we describe our experience in dealing with recurrent GBMs in terms of efficacy and toxicity of re-RT with 3DCTR or VMAT protocols. We carefully reviewed our patient's outcomes and additionally performed a comprehensive and more updated meta-analysis of recent recurrent re-RT GBMs literature to compare our results with the ongoing outcomes of the recent studies.

Methods: We retrospectively collected data regarding recurrent glioma patients who underwent re-RT between 2017 and 2020 at our Institution. Also, we used the random-effects model to pool outcomes across studies about re-RT GBMs from the recent literature to have a more homogenous cohort in terms of treatment modalities, thus reducing the selection bias.

Results: Re-irradiation was performed at a median interval time of 13.5 (range 4 - 192 months) months from the first RT. Surgical resection before re-RT was performed in 92.3% of patients; the majority underwent GTR (61.5%), followed by partial or subtotal resection (23%) and stereotactic biopsy (11.5%). The median re-RT dose was 18 Gy (range 12–36 Gy), and the median fraction size was 3,45 Gy (range 1,8–6 Gy). The total median equivalent dose (EQD2) was 84 Gy (range 65.7 – 110 Gy). Our cohort median PFS is 12.5 months

(range 4 – 192 months), while the median OS was 26 months (range 6 – 213 months). Our results show that the OS-6 and OS-12, from time of re-irradiation, to be 69.2% and 30.7% respectively and the PFS-6 and PFS-12 to be 76.9% and 23.0%, respectively. None of our patients experienced cases of acute radio-toxicity. In our literature research, we e found 22 eligible studies, including 1065 patients. The results of the pooled outcomes were : OS-12 rate 35% (95% CI: 30–40%), PFS-12 rate 16% (95% CI 13–19%), and Grade 3 + AE rate 5% (95% CI 0–22%).

Conclusions: Our data are in line with what already reported in the literature and again confirm how re-RT as a safe and feasible treatment with a limited rate of toxicity for salvage treatment in recurrent GBMs.

P052

ANALYSIS OF OUTCOME DATA AND PATTERNS OF RECURRENCE IN PATIENTS WITH GLIOBLASTOMA. THE EXPERIENCE OF THE RADIOTHERAPY DEPARTMENT OF AOUI OF VERONA

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Aims: To evaluate outcome, PFS, OS and toxicity in patients treated for Glioblastoma (GBM).

Methods: From January 2017 to March 2020, clinical and imaging data of 94 consecutive patients with GBM treated at the Verona Radiotherapy Department, were analyzed. The majority of patients had undergone surgical resection followed by concurrent Temozolomide (TMZ) and localized Radiation Therapy (RT). Disease progression was assessed according to the RANO-HGG criteria. Magnetic Resonance (MR) images acquired prior, post radiotherapy and during follow-up, were analyzed and used to define three categories of recurrence: in-field if >80% of the recurrent tumor was located within the 95% isodose surface; marginal if 20-80% of the recurrent lesion was within the 95% isodose surface; distant if <20% of the recurrent lesion was within the 95% isodose surface. Overall survival (OS) and progression-free survival (PFS) from the first diagnosis and recurrence were measured using the Kaplan-Meier method.

Results: 94 consecutive patients were evaluated; of these 55 were male and 39 female. Median age was 63 years (range 35-88). Mean Karnofsky Performance Status was ≥80. 7 patients underwent biopsy, 9 partial resection and 78 gross total resection. 70 patients entered the Stupp protocol (RT 60Gy/30F + concomitant TMZ) while 24 received a hypofractionated RT schedule (40.05Gy/15F) plus concomitant TMZ. 41 of the 94 patients relapsed: 83% in field, 7% marginal and 10% out-field. 6 out of the 41 patients underwent second surgery followed by re-irradiation, 7 re-irradiation alone and 28 second line chemotherapy. Re-irradiation doses ranged from 36 to 54 Gy in 18-27 fractions. No G2-G4 toxicities were observed. Median OS from first diagnosis was 82.5%, 55.8% and 40.6% at 12, 24 and 36 months respectively. Median OS from re-irradiation was 50% at 7 months. PFS from primary treatment to re-irradiation was 57.7% and 39.2% at 12 and 24 months respectively.

Conclusions: Our experience demonstrated that rates and patterns of recurrence of GBM after primary treatments and re-irradiation were similar to literature. Current knowledge confirms that GBM remains a disease with a poor prognosis. But new technologies and experience allow us to carry out targeted treatments with a good tolerance. It is necessary for the future to implement new re-irradiation protocols.

P053

ATYPICAL PNEUMONIA IN PATIENT WITH GLIOBLASTOMA AND MYELOPROLIFERATIVE SYNDROME TREATED WITH RADIOCHEMOTHERAPY

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Aims: Temozolomide (TMZ), concurrent with radiotherapy and sequentially as monotherapy in patients affected by glioblastoma (GBM), is an oral alkylant agent that can be associated with T-cell dysfunction and several opportunistic infections. Patients receiving TMZ should be carefully monitored and special attention should be paid in case of elderly patients, comorbidities or corticosteroid therapy. We describe the case of an elderly patient developing severe bacterial and fungal pneumonia after chemoradiation with TMZ for GBM.

Methods: A 78 year-old man presented to emergency department for persistent asthenia, back pain, right lower limb pain and ipsilateral hypoesthesia. Five months earlier he was diagnosed a right temporal GBM treated with surgery and chemoradiation (30 fractions of 2Gy with concurrent daily TMZ 75 mg/m2) without relevant treatment related toxicities. Patient had a history of insulin dependent diabetes and presented neutrophils leukocytosis correlated to a mieloproliferative disorder treated with Oncocarbide. Dexamethasone and Bactrim as antibiotic prophylaxis were administered during RT-TMZ course. At emergency department a thorax CT scan showed acute pulmonary embolism, a small left pleural effusion, bilateral areas of cavitation (the biggest 11x12.5x10 cm in the upper right lobe), and ground-glass opacities in the lower lobes. The vital signs were normal, leukocytes were 41720/uL, neutrophils 37700/uL, lymphocytes 1840/uL, hemoglobin 11 g/dl, platelets 271000/uL. Sputum culture and BAL were positive for Pseudomonas aeruginosa and Candida parapsilosis. Pneumonia was treated with Ceftriaxone, and a stenting of iliac and right femoral artery was per-

formed. The lymphocytes count at discharge was 3860/uL (Table 1).

Results: After 1 month CT scan reported a moderate dimensional decrease of the areas of cavitation and the ground glass opacities, with partial resolution of pulmonary embolism and no signs of pleural effusion. Patient did not receive the first sequential TMZ cycle due his poor conditions.

Conclusions: The case suggests that close monitoring of patients receiving TMZ for opportunistic infections should be carried out. In old ill patients aspecific and common symptoms like asthenia should not be underestimated because infections could affect outcomes and treatment options. In 1/3 of the cases multiagents pneumonia could be a rare and lethal event: therefore, a prophylaxis against infective agents should always be recommended.

Table 1. Shematic sequence of main events (Timeline).

DATE	*EVENT*	
28/10/2019-11/12/2019	**Radiotherapy** **Treatment**	RT Dose: 60 Gy (2 Gy/die) Temozolomide (75 mg/mq/die) + Bactrim 80+400 mg on alternate days.
05/1/2020	**Emergency department access**	Hospitalization due to persistent asthenia, back pain, right lower limb pain and ipsilateral hypoesthesia.
08/1/2020	**Thorax RX**	In the upper right lobe lobulated nodule of 11 cm. A CT scan is suggested.
11/1/2020	**Thorax CT**	Acute pulmonary embolism, a small left pleural effusion, bilateral areas of cavitation (the biggest 11x12.5x10 cm in the upper right lobe), and ground-glass opacities in the lower lobes.
11/1/2020	**Lower limbs angio-CT**	Right external iliac artery and bilateral femoral artery stenosis.
12/1/2020	**Infective evaluation**	Sputum culture and BAL performed after prescribing Ceftriaxone 2g/die
13/1/2020	**Surgical evaluation**	Contraindication of surgery for arterial stenosis due to patient's poor conditions.
	Sputum culture and bronchoalveolar lavage	Positive for *Pseudomonas aeruginosa* and *Candida parapsilosis*.
23/1/2020	**Surgical evaluation**	Stenting for the iliac artery and right femoral artery endarterectomy.
26/1/2020	**Hospital discharge**	Medications continued at home.
-	**Adjuvant Temozolomide**	Not administered for poor clinical conditions.
10/2/2020	**Thorax CT**	Moderate dimensional decrease of the areas of cavitation and the ground glass opacities, with partial resolution of pulmonary embolism and no signs of pleural effusion.
-	**The patient did not repeat further exams due to COVID pandemic**	

P054

HYPOFRACTIONATED (HYPORT) VERSUS CONVENTIONAL RADIOTHERAPY (NORMORT) PLUS TEMOZOLOMIDE (TMZ) IN PATIENTS WITH GLIOBLASTOMA (GBM): EFFICACY EVALUATION AND PROPENSITY SCORE (PS) MATCHED ANALYSIS. A RETROSPECTIVE, SINGLE-INSTITUTION EXPERIENCE

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Aims: HypoRT with TMZ is considered the standard treatment for old patients with GBM. The comparison of HypoRT and NormoRT plus TMZ in terms of overall survival, both in older and younger, poor prognosis patients, is the main aim of this retrospective propensity score matched analysis.

Methods: Between 2015 and 2019, 139 patients were treated for GBM and evaluated for this study: 73 patients were treated with NormoRT (60 Gy/30 fr) and 66 with HypoRT regimen (40.05 Gy/15 fr) plus TMZ. Data about clinical and therapeutics variables were collected: age, performance status, MGMT promoter methylation status, type of surgery, RT technique - 3DCRT, IMRT, VMAT, helical IMRT- and chemotherapy (CT) timing -concurrent (cCT) and/or sequential (sCT). Considering the treatment, the patients were divided in three arms: Group 0 (NormoRT with cCT and sCT); Group 1 (HypoRT with cCT and sCT); Group 2 (other treatments: NormoRT or HypoRT with cCT or sCT or without CT). Prognostic factors were analyzed using univariate Kaplan–Meier survival and Log Rank test and multivariate Cox models. A propensity score matched analysis, considering age, Karnofsky performance status and surgery extension was performed, to assess patients in a balanced manner while reducing selection biases (70 patients).

Results: Patients in the Group 1 were mostly aged >65y (p=0.003) and not submitted to radical surgery (p=<0.0001). At univariate analysis on the entire series better OS was evident for younger patients (p=0.065) with better KPS (p=0.0003), undergone radical surgery (p=0.0001) and CT (p=0.0001), with MGMT methylation (p=0.01) and for patients treated in the Group 0. At multivariate analysis, the variables maintaining statistical significance were surgery (better partial and radical) and treatment group (better Group 1). At multivariate analysis, only for patients <65y, benefit in survival was attested for those submitted to partial or radical surgery and treated in the Group 0 or 1. After the PS match, the multivariate analysis showed equivalent OS for patients in Group 0/1. Also MGMT promoter methylation obtained better survival at multivariate analysis.

Conclusions: HypoRT with TMZ is the better treatment for older patients and may be a reasonable and feasible option for poor prognosis younger patients. TMZ plus RT is confirmed as a fundamental part of therapeutic approach of GBM, regardless of fractionation.

P055

PLEOMORPHIC XANTHOASTROCYTOMA: A SINGLE INSTITUTION RETROSPECTIVE ANALYSIS AND A REVIEW OF LITERATURE

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Aims: Pleomorphic xanthoastrocytoma (PXA) is a rare low grade brain tumor with good prognosis.

Anaplastic xanthoastrocytoma (aPXA) is a distinct entity with stimulation mitotic activity (>5 mitoses/10 hpf). Several mutations as BRAF V600E, TERT promoter mutation and CDKN2A homozygous deletion, could be related to anaplastic progression with worse prognosis. Standard management after surgical resection is debated. Adiuvant radiotherapy (RT) is usually added when surgery wasn't complete or in case of anaplastic features, with or without temozolomide (TMZ). The aim of the study is clarify the natural history and prognosis of PXA and analyse the impact of treatments on survival endpoints.

Methods: We retrospective analysed a cohort of 16 patients with PXA, afferred after primary neurosurgical management to our Radiation Oncology Unit from 1997 to 2019. Anatomopathological features were confirmed after independent revision. All patients underwent an early post-operative MRI. Treatment response was evaluated by periodic MRI according to RANO criteria. RT and chemotherapy doses, number of cycles and treatments tolerance were collected. PFS was defined as the time from primary neurosurgical treatment until progression or death or the last follow up. OS was calculated from primary neurosurgical treatment to the most recent follow up or death. Survival endpoints were estimated using Kaplan- Meier method and 95% CIs and log rank test was applied. χ^2 test was applied to analyze statistical significant differences between defined class frequencies.

Results: From January 1997 to January 2019 we treated 16 PXA patients. Median follow up was 60 months (4-218). Median age at presentation was 31.3 years. At the beginning patients mostly have focal neurological disorders (56.3%)and headache (31.3%). After surgery 6 patients had residual disease. 10 patients received adjuvant RT with median DTF 60 Gy. 8 of them received concurrent adjuvant TMZ 75 mg/mq daily. 6 patients underwent only radiological follow up and 5 of them relapsed after a median time of 16.55 month. Median PFS was 32.5 months and median OS 52.8 months. No statistically significative differences emerged in terms of OS neither PFS for some variables as sex, age, neuroanatomical localization, histological grade, adjuvant chemotherapy and RT, MGMT methylation status, IDH mutation, BRAF mutation and mib1 value. OS showed an association with recurrent disease (p=0.002) and chemotherapy adjuvant treatment (p=0.049). A borderline statistical significant association was recognized with BRAF mutation (p=0.058).

Conclusion: Despite our analysis didn't evidence a strong prognostic or predictive factor able to address PXA management, after neurosurgical primary resection addition of adjuvant RT and chemotherapy treatment has to be considered in selected patients. Target therapies are the new perspectives towards which studies are directed.

P056

HEALTHY BRAIN SPARING FOR CENTRAL NERVOUS SYSTEM RADIATION THERAPY: DRIVE TEST OF NEW IMMOBILIZATION SOLUTION

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Aim: Aim of this prospective study was to test interfraction reproducibility, intrafraction stability, technician aspects and patient/physician's comfort of new dedicate immobilization solution (Solstice TMCIV-CO®).

Method: Patients affected by CNS disease suitable of RT according to international guidelines were enrolled. Single/fractionated stereotactic RT(SRS/SFRT) or conventional RT(cRT) were permitted. Two technicians carried out mask during simulation (sim) procedures, collecting data regarding ease of use and stability of pll/mask clips, therm shrinkage, reporting score in 4 levels(poor/fair/good/excellent) and sim setup time(SST). For each treatment session, 3-1 CBCT in SRS/SFRT-cRT were performed, respectively, to evaluate inter and intra-fraction variation, considering that for SRS/SFRT and cRT a margin of 1 and 5 mm was used for PTV, respectively. Brief survey was completed by patient and physician to assess comfort.

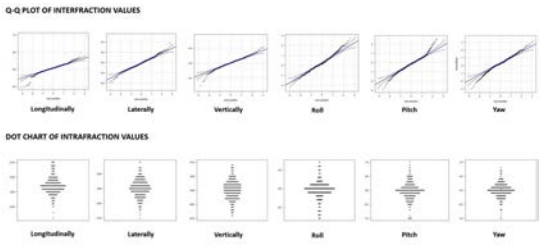

Figure 1.

Result: Between 10/2019-04/2020, 69 patients(21 female/48 male) were treated for a total of 556treatment session and 865CBCT. SRS/SFRT were 45 with a median dose of 27Gy(range12-30), median fraction of 3 (range 1-5) and median target volume of 6.15cc (range 0.7-104); cRT were 24, including 10 whole brain (WB), with a median dose of 40Gy (range20-60), median fraction of 15 (range5-30) and median target volume, excluding WB, of 178.6cc (range 98.8-470.3). Between sim-treatment a median of 8 days (range 2-15) occurred. Median SST was 15 minutes (range 10-20 minutes), reporting excellent score for ease of use/stability of pll/mask clips/therm shrinkage. Interfraction median values, for entire study population, were: longitudinally 0.04cm (IQR-0.03/0.1), laterally -0.02cm (IQR-0.08/0.05), vertically 0.005cm (IQR-0.09/0.1), roll 0.15° (IQR-0.2/0.7), pitch -0.1°(IQR-0.6/0.3), yaw 0.2°(IQR-0.2/0.8). Intrafraction median values, for SRS/SFRT subgroup, were: longitudinally 0.02cm

(IQR0/0.04), laterally 0cm(IQR-0.02/0.02), vertically 0cm(IQR-0.02/0.02), roll 0°(IQR-0.1/0.1), pitch 0°(IQR-0.2/0.1), yaw 0°(IQR-0.1/0.1). A median of 4 coach rotations were used (range0-4). Patient and physician comfort were assessed, respectively, with good and excellent score in all cases.

Conclusion: The analysis showed this immobilization solution is reproducible and stable, reporting excellent characteristics in terms of ease of procedures and patient/physician's comfort. Future evaluations combined with surface-guided radiotherapy are needed to assess conclusive data.

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SURFACE GUIDED RADIATION THERAPY: LOOKING AT INTRAFRACTION MOVEMENTS FOR BRAIN LINAC-BASED RADIOSURGERY

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Aim: To evaluate intrafraction accuracy, reproducibility, stability, using Surface Guided Radiation Therapy (SGRT) to monitor movements for Brain Linac-based Radiosurgery (SRS).

Method Patients with brain disease suitable of SRS according to international guidelines were enrolled. In all cases, open-face masks were used and 3CBCT were performed(2before-1after SRS): first to revise setup treatment, second to confirm shifts and third to verify position at the end of SRS. For each treatment session, SGRT was applied to evaluate intrafraction variations, acquiring data in 3 different time points: initial(i)-final(f)-monitoring(m) (before, end and during SRS, respectively). PTV was defined by 1mm isotropic margin. FFF VMAT plans with 2-more coplanar/non-coplanar arcs were generated for each lesion. Prescription dose(Dp), normalization, optimization were according to ICRU91.

Result: Between 10/2019-04/2020, 45patients(11 female/34 male) underwent to SRS for a total of 145treatment session and 435CBCT. Median age was 68years(range32-87). 25 were brain metastases, 10 recurrence glioblastoma and 10 benignant lesions. 3 were localized in mesencephalic area, 6 were cerebellar, 12temporal/occipital and 24parietal/frontal. Median Dp was 27Gy(range12-30), median isodose optimization was 80%(range75-90), median fractions were 3(range1-5) and median PTV was 6.15cc(range0.7-104). In 7 cases were used 2 coplanar arcs, in 5and33 cases were used 3and4 non-coplanar arcs, respectively. Median monitor units were 2121.7(range1037.9-6151.2) with a mean overall treatment time of 2minutes. Intrafraction CBCT median values were: longitudinally 0.02cm (IQR0/0.04), laterally 0cm (IQR-0.02/0.02), vertically 0cm (IQR-0.02/0.02), roll 0° (IQR-0.1/0.1), pitch 0° (IQR-0.2/0.1), yaw 0°(IQR-0.1/0.1). Intrafraction SGRT median values were: i_longitudinally 0cm(IQR0/0), f_longitudinally 0cm(IQR-0.03/0.02), m_longitudinally 0cm(IQR-0.03/0.04); i_laterally 0cm(IQR0/0), f_laterally -0.01cm(IQR-0.02/0.01), m_laterally 0cm(IQR-0.03/0.02); i_vertically 0cm(IQR0/0), f_vertically 0.01cm(IQR0/0.03), m_vertically 0cm(IQR-0.02/0.02); i_roll 0°(IQR0/0), f_roll 0°(IQR-0.1/0.1), m_roll 0°(IQR-0.1/0.2); i_pitch 0°(IQR0/0), f_pitch 0°(IQR-0.2/0.1); i_pitch 0°(IQR-0.2/0.2); i_yaw 0°(IQR0/0), f_yaw 0°(IQR-0.1/0.2), m_yaw 0°(IQR-0.2/0.2).

Conclusion: Analysis, combining CBCT-SGRTdata, showed accuracy, reproducibility, stability for Brain Linac-based SRS. UsingSGRT,CBCT for confirmation and verification could be omitted.

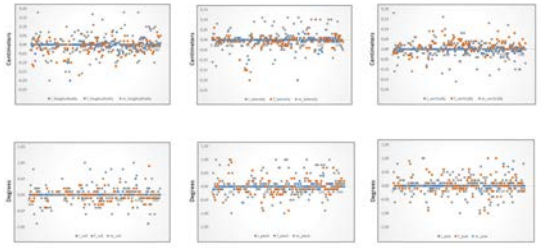

Figure 1.

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BRAIN METASTASES VOLUME AND NON-BRAIN METASTASES CONTROL AS OUTCOME PREDICTORS IN BRAIN RADIOSURGERY FOR BREAST CANCER METASTASES

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Aims: to explore prognostic factors associated with local control (LC) and overall survival (OS) in a mono-institutional experience in stereotactic radiosurgery (SRS) for brain metastases from breast cancer.

Methods: We retrospectively reviewed the data of 95 patients (190 lesions) who underwent SRS with CyberKnife (Accuray, USA) for brain metastases from January 2012 to December 2017. Primary clinical outcomes were OS, LC of the single lesion treated and distant brain control (DBC) and they were determined using Kaplan-Meier analysis. Univariate and multivariate Cox proportional hazard regression models were

used to assess the association between demographic and disease characteristics and outcomes. This study was part of the research notified to our Ethic Committee

Results: After a median follow-up of 18 months (range 1-82), at least one radiological evaluation was available for 79 patients (156 lesions). LC was reported in 136/156 treated lesions (87%). Overall, 3-years OS was 31.5%. 1- and 3-year LC were 93% and 79.5%, respectively, but LC was higher in case of lesions with a volume < 0.80 cm^3. In multivariate analysis, age (< 60 years), the status of systemic disease (absence or controlled) and number of brain metastases (single lesion) were independent predictive factors for survival while single-lesion volume (< 0.80 cm^3) and treatment fractionation (single fraction with high BED) influenced LC.

Conclusions: The present results confirm that age, the status of systemic disease and number of brain metastases were predictive factors for survival in brain metastases from breast cancer treated with SRS. OS and LC rates were in line with reported literature with high local control for smaller lesions.

P059

RECOMMENDATION FOR THE CONTOURING OF LIMBIC SYSTEM IN PATIENTS RECEIVING RADIATION TREATMENT: A PRACTICAL MR-BASED ATLAS FOR THE EVERYDAY PRACTICE AND EDUCATION

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Aim: The limbic circuit is a group of interconnected subcortical and cortical regions devoted to linking emotion to behavior and cognition. Sparing this circuit, has proven its effect on the preservation of cognitive function after radiotherapy. The aim of this study is to create the first proposal of radiation oncologist's practical MR-based contouring guide for the delineation of the limbic system for the everyday clinical practice and education.

Methods: Atlas development information was sought from (i) textbooks, (ii) IMAIOS e-anatomy, (iii) key articles describing the structures of limbic anatomy and sulci. During a multi-disciplinary session, two radiation oncologists discussed the delineation of the limbic system structures in collaboration with an expert neuroradiologist and came to consensus on a first draft atlas. The approved first draft atlas was shared with the other all coauthors for assessment, input, and final approval. A diagnostic 3-Tesla MRI T1-weighted BRAVO sequence of a male subject without pathological findings was anonymized and used to delineate the limbic circuit. MR was obtained in the supine position with the head in a neutral position.

Results: a step-by-step MR-based atlas of limbic system structures was created. the hippocampal-amygdala-uncus formation and mammillary bodies were contoured on an axial plane. Fornix, septal region and thalamus were contoured on a coronal plane. Cingulate gyrus was contoured on a sagittal plane. For each structure key anatomical information with detailed description of the anatomical boundaries is reported.

Conclusions: This atlas provides step-by-step recommendations for the contouring of the limbic system in the setting of patients receiving radiation treatment and education. A complex relationship exists between the individual structures of the limbic system and radiation dose. Therefore, incorporation of all anatomical contributors to cognitive dysfunction within radiotherapy plans can be of clinical importance in reducing inappropriate dose to normal tissues.

P060

IMPACT OF FIRST, SECOND AND THIRD MRI FOLLOWING RADIOCHEMOTHERAPY IN CLINICAL DECISION MAKING IN PATIENTS WITH GLIOBLASTOMA

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Purpose: Despite the current approach (radiochemotherapy, RTCT) has been adopted more than 15 years ago, some aspects of gliobastomàs therapy still remain unknown. There is not a consensus about the best timing to perform the first and the second Magnetic Resonance (MR) after the RTCT; a transient increase in tumor enhancement called pseudoprogression (PSD), with the same radiological features of tumor progression, occurs in almost 30% of patients. PSD is difficult to differentiate from true tumor progression making the first MRI untrustworthy. Our aims was to assess the impact of first, second and third MRIs performed after

RTCT in clinical decision making of glioblastoma patients.

Methods: We evalutated the MRI of 140 patients with gliobastoma treated in Pisa University Hospital between 2012 and 2019, undergoing surgery and CRT. Surgery was performed as gross tumor resection or stereotassic serial biopsy. GBM was diagnosed according to WHO criteria and the tissue used both for histological and molecular diagnosis. All patients were treated with adiuvant CRT. Radiotherapy treatments were performed using DHX platform or Varian TrueBeam, using 6 MV photon (3D and VMAT techniques, CTV = surgical area +/- tumor remains after surgery puls 2 cm margin, 60 Gy (30 fractions 200 cGy). Concomitant and sequential chemotherapy consisted in temozolomide (75 mg/m^2 daily) followed by 12 cycles of maintenance (150 -200 mg/m^2/28 days). First MRI and clinical control was planned after 45 days from the end of CRT, than every 3 months.

Results: In March 2020, at data analysis, we evaluate the impact of clinic and progression disease in MRI. Progression disease (INfield and OUTfield) in first MRI was not significatively associated to change in therapeutic algorytm ($p < 0,001$ for both INfield and OUTfield). On the contrary, progression notice on second and third MRI is linked with new therapeutic decision ($p < 0.001$). Abnormal clinic is associated with changes in decision making, as suggested in all the guidelines.

Conclusions: We demonstrate how the impact of the first MRI in decision making is limited. MRIs performed shortly after the end of CRT (2 – 6 weeks) are not usefull in the decisional algorytm; MRI progression disease is often ignored if not correlated by clinical progression signs. On the contrary, we found that progression showed in second MRI are strongly associated to changes in decision making either the first MRI was pathologic or in the case it was normal.

P061

CLINICAL CHARACTERIZATION OF GLIOBLASTOMA PATIENTS LIVING LONGER THAN 2 YEARS

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Purpose: Despite the advances in surgery and radiochemotherapy the prognosis of glioblastoma (GBM) remains poor with about 13% of patients alive at 24 months.

Methods and Materials: 75 GBM patients, defined long-term survivors (LTS) since alive at least 24 months from diagnosis, were retrospectively analyzed. Overall survival (OS) and recurrence-free-survival (RFS) were calculated and related to patient characteristics and treatment received.

Results: Median age and Karnofsky performance status (KPS) were 56 years and 100%, respectively. After surgery (gross tumor resection-GTR in 62, 83% patients), all LTS received concomitant temozolomide (TMZ) with radiotherapy (RT) and 70 (93%) also adjuvant TMZ. Of the latter, 10 (13%) discontinued TMZ prior the completion of 6 cycles, 37 (49%) received 6 cycles and 23 (31%) >6 cycles. 69 (92%) patients experienced a first tumor recurrence at a median time of 21 months. Of these, 32 (46%) were submitted to a second surgery, 34 (49%) to other no-surgical treatments, and 3 (5%) to only supportive care. At multivariate analysis, OS was significantly improved by second surgery after first recurrence (p=0.0032) and by the number of cycles of adjuvant TMZ (i.e., >6 vs ≤6; p=0.05). More than 6 cycles of TMZ significantly conditioned also first RFS (p=0.011) and second RFS (p=0.033).

Conclusions: The large majority of LTS had <65 years, had a high KPS and received GTR. OS and RFS resulted significantly related to an extended administration of adjuvant TMZ (>6 cycles) and a second surgery in case of recurrence.

P062

BEVACIZUMAB IN RECURRENT HIGH GRADE GLIOMA: A SINGLE INSTITUTION RETROSPECTIVE ANALYSIS ON 92 PATIENTS.

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Background: High-grade gliomas are the most aggressive central nervous system primary tumors and they are characterized by a high risk of recurrence and a poor prognosis despite treatments. Re-operation, re-irradiation, chemotherapy, alone or in combination, are options in this setting, although the best therapy has not been established and prognosis remains poor. Bevacizumab was approved on the basis of two Phase 2 trials that evaluated his efficacy in monotherapy or in combination in patients with recurrent glioblastoma.

Aims: In a poor prognosis disease despite treatments, with low therapeutic choices after primary management, we aim to study bevacizumab impact on survival outcomes, confirm safety profile and recognize factors related to response to treatment.

Materials and methods: We have retrospectively review data of patients with high-grade glioma treated at our institution, that undergone radiological or histological progression after at least one systemic treatment for recurrent disease. Bevacizumab was administered 10 mg/kg every two weeks alone or in combination with chemotherapy until disease progression or unac-

ceptable toxicity, according to standard practice. Bevacizumab mono or poly-chemotherapy regimen were analyzed to assess PFS and OS. Histological, molecular and clinical features of the entire cohort were collected. Median overall survival (OS) and median progression-free survival (PFS) was calculated by Kaplan-Meier method. The Cox regression model hazards was used to assess the effect of factors identified as significant on survival analysis by Kaplan-Meier.

Results: We reviewed data from 92 patients, treated from April 2009 to November 2019, with histologically confirmed diagnosis of high-grade gliomas and recurrent disease. A PFS of 55.2%, 22.9% and 9.6% was observed at 6, 12 and 24 months, respectively. At Kaplan Meier analysis, performance status, age at diagnosis (<65 or >65 ys) and use of corticosteroids during bevacizumab therapy were strongly associated with PFS. The OS was 74.9% at 6 months, 31.7% at 12 months, 10.1% at 24 months. In our cohort 51,1% were long-term responders (PFS> 6 months). Globally, bevacizumab treatment was well tolerated.

Conclusion: Our analysis confirms the efficacy of bevacizumab in recurrent high-grade glioma patients with an acceptable toxicity profile, in keeping with its known safety in literature.

P063

ACUTE TOXICITY IN GLIOBLASTOMA PATIENTS TREATED WITH INTENSITY MODULATED RADIATION THERAPY VERSUS 3D CONFORMAL RADIATION THERAPY

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Aims: To evaluate acute toxicity problems in patients treated for Glioblastoma with IMRT vs 3D-CRT techniques.

Methods: We consulted clinical records of 60 Glioblastoma patients treated with radiotherapy (RT) and Temozolamide (TMZ) from January 2017 to June 2020 in our Centre. The toxicity was evaluated with RTOG scoring.

Results: All patients were under 70 years of age and were treated with concurrent use of Temozolomide and RT to 6,000 cGy in daily fractions of 200 cGy over 30 days, followed by adjuvant TMZ treatment for 6 months. Patients received TMZ 75 mg/m² , seven days a week for the duration of radiotherapy and TMZ from 150-200 mg/m², for 5 days a week every 28 days (six cycles) as adjuvant treatment. 37 patients were treated with IMRT and 23 with 3D-CRT. At the time of the simulation visit about 1 week before the start of the RT, the patients had cortisone therapy. The most frequent side effects were asthenia and nausea, observed in almost all patients and about half of the patients developed thrombocytopenia. Upper limb coordination deficits and visus reduction in a patient undergoing IMRT, hemianopsies in a patient treated with 3D-Conformational radiotherapy and walking deficit in a patient treated, instead, with IMRT were observed.

Conclusions: There are not differences about acute toxicities between the two groups of patients treated with IMRT or 3D-CRT.

P064

SURVIVAL OUTCOMES AND PROGNOSTIC FACTORS IN HIGH GRADE GLIOMAS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Aim: The aim of our study was to analyze survival outcomes in patients affected by high grade gliomas treated with radiotherapy +/- Chemotherapy with Temolozomide (TMZ).

Methods: From July 2014 to May 2019, sixty-six patients (median age 60 years old; range 27-85, SD 12.26) affected by histologically confirmed diagnoses of high grade gliomas were treated in our institution. Fifty five patients (78%) were glioblastoma (GBM) and 11 (12%) resulted anaplastic astrocytoma and anaplastic oligodendroglioma (Grade III WHO). Of them 48 patients (73%) underwent chemo radiotherapy according to Stupp et al. regimen and 18 pts were treated with short course radiotherapy (40,05 Gy in 15 fractions) according to Perry et.al protocol due to low KPS or unfit to Stupp protocol. RT treatment was performed with LINAC Synergy of Elekta company using 3DCRT or VMAT technique.

Results: At analysis 44 pts (67%) were male and 22 (33%) female. The median KPS was 80 (range 50-100). In patients underwent Stupp regimen the overall survival was 18 months and 4 years survival was 25%. Total resection, KPS (≥80), the response/absence of tumor at RM evaluation after RT-CT treatment (according to RANO criteria), adjuvant TMZ > 6 cycle and young age were prognostic factors regarding OS (p-value < 0,05). Patients with > 80% PTV coverage of prescribed dose (100%) had a benefit in terms of OS compared to patients with a lower dose coverage (21 mths vs 16 mths. In patients treated with short course RT+/-TMZ the median OS was 6 months. One year survival was reached only in 10% of patients. Pts with KPS ≥ 70 had a longer median survival compared with pts with KPS < 60 (8 mths vs 5.5 mths). Finally, addition of TMZ with RT treatment was associated with a longer median OS (10 mths vs 5 mths). There were not other prognostic factors influencing OS.

Conclusions: The results of our retrospective study showed that in high grade gliomas underwent Stupp regimen young age, PTV coverage >80% of prescribed dose, KPS, total tumor resection and CR/PR after radiotherapy treatment and CT association were prognostic factors in terms of OS. Pts with low KPS underwent short course radiotherapy had a poor prognosis; only KPS ≥ 70 and association of TMZ with RT was associated with higher OS.

P065

RETREATMENT IN RECURRENCES OF HIGH GRADE GLIOMAS: FEASIBILITY OF RE-IRRADIATION AND CONCOMITANT CHEMOTHERAPY

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Aim: Glioblastoma is the most common primary malignant brain tumor in adults, counting 16% of all primary CNS tumors, with poor prognosis. Almost all patients undergo disease progression/recurrence: actually no standard of care is established for recurrent or progressive GBM (rGBM). Treatment approaches for tumor recurrences include second surgery, re-irradiation, systemic therapies, combined modality and supportive cares. The treatment must be tailored to each single patient, considering tumor size and location, previous treatments, age, Karnofsky performance score (KPS), patterns of relapse, and prognostic factors. We retrospectively investigated the feasibility of a second irradiation associated with or without chemotherapy for patients with disease progression/recurrence of glioblastoma.

Methods: Thirty patients with recurrence of high-grade gliomas received a median re-irradiation dose of 36 Gy (34 – 41.1 Gy) with conventional fractionation (1.8 – 2 Gy/die) at our institution. Median age at the recurrence was 53 years (range 21-75 years). Twelve patients received chemotherapy (Temozolomide) as concomitant and adjuvant treatment, 8 patients received re-irradiation followed by adjuvant chemotherapy (Fotemustine), 10 patients received re-irradiation alone. Overall survival was calculated with Kaplan-Meier method. Neurocognitive evaluation (Minimental test and quality of life evaluation) was carried out with psycho-oncologist and patients underwent a neurocognitive rehabilitation therapy.

Results: Mean time between radiation therapies was 36 months (6-176 months). All patients carried out re-irradiation, with no cases of Grade ≥3 toxicity. At a follow up of 15 months, overall survival was 8 months (1-95 months). The group treated with concomitant chemoradiotherapy shows a better overall survival compared with the group treated with only re-irradiation (16 vs. 7 months); 1 year-OS was 57.1% vs 35.7% and 2 years-OS was 47.6% vs. 26.8%. From neurocognitive evaluation we report a good feasibility of re-irradiation, with good compliance to neurocognitive rehabilitation therapy

Conclusions: In our experience, re-irradiation associated with chemotherapy (Temozolomide) for recurrent high grade gliomas represents a good treatment option, with better OS. Patients selection is important to identify those patients who benefit from this approach

P066

MULTISESSION RADIOSURGERY IN RESIDUAL/RECURRENT ATYPICAL MENINGIOMAS: MONOINSTITUTIONAL PROSPECTIVE STUDY

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Aims: Meningiomas represent approximately 15-20% of all primary brain tumors in adults. Only a minority (around 10%) is classified as high-risk tumors, and among them are atypical meningiomas (ATM). Gross total resection (GTR) is the goal of meningioma treatment. However, even when complete resection is achievable, the lesions can relapse. In fact, the optimal management of ATM has yet to be established and the role of adjuvant radiotherapy and stereotactic radiosurgery (SRS) remains controversial. Literature data suggest that adjuvant SRS may greatly improve outcomes. In this scenario, we designed a prospective study, to evaluate the efficacy and safety of SRS in terms of toxicity and local control for patients diagnosed with ATM and never treated by radiotherapy.

Methods: This is a Simon Design phase II study for patients with residual or recurrent ATM. Between 2017 and 2019, a total of 25 patients were recruited. Twenty patients were treated for relapse after GTR and 5 after subtotal resection (STR). All treatments were delivered with hypofractionated schedule (multisession SRS), performed using a CyberKnife® system. The most common tumor location was convexity (40%), followed by parasagittal/parasinus (36%) and skull base (24%). The primary endpoint is the treatment-related toxicity, classified according to NCI Common Toxicity Criteria (CTCAE) version 5.0. The secondary endpoint is local control at 3 years. A radiological follow-up with MR imaging was scheduled at 4 months after mSRS procedure, then every 6 months. The radiological response was assessed using RECIST guidelines (vers 1.1).

Results: Of 25 pts, 12 were males and 13 females. The average age at treatment time was 61 years (range 37-87). The median follow-up was 22 months (range 9-36 months). The median pre-SRS tumour volume was 2859 mm3 (range 572 - 24992 mm3). The prescription dose was 28 Gy in 4 fractions with median prescription isodose line of 81% (range 78 - 84%). Only one patient developed toxicity G2 (brief generalized seizure) according to CTCAE scale. No severe adverse events occurred (CTCAE ≥III). Two patients (8%) developed a recurrence, 11 (48%) showed stable disease and 12 (44%) partial response.

Conclusions: SRS for adjuvant and salvage treatment of ATM seems a safe and effective treatment in terms of toxicity and local control. Our preliminary results confirm that SRS can be a viable treatment for ATM, especially for those patients who develop frequent relapses.

P067

PROGNOSTIC VALUE OF EARLY RELAPSE AFTER SURGERY IN PATIENTS WITH GBM

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Purpose: To evaluate the role of progression before adjuvant chemo-radiotherapy (early progression, EP) in glioblastoma patients.

Methods: We included all patients with glioblastoma undergoing adjuvant radiotherapy/TMZ at our Department between January 2019 and December 2019. We selected only patients that underwent gross total resection or subtotal resection that performed early MRI within 72 hours from surgery and a subsequent MRI before starting RT/TMZ treatment. Early progression (EP) was defined as a progression of disease at the MRI before adjuvant therapy. We retrospectively evaluated the EP in terms of progression free survival (PFS) and overall survival (OS) with Kaplan Meier analysis.

Results: We included 48 patients (31 males and 27 females), with a median age of 64 years (range 35-78 years). Twenty patients (41%) showed EP. Median PFS for the whole population was 8.6 months, median OS was not reached. Patients with EP showed a significant decrease in PFS (median 180 days versus 280 days, p-value: 0,034) and a trend towards a decreased OS (median 311 days versus median not reached, p-value: 0,064). Patients with EP tend to progress in field.

Conclusions: EP seems to be associated with a worse outcome and could characterize a subset of patients resistant to current standard of care. Further analysis is necessary in order to confirm these results.

P068

LONG TERM OUTCOMES IN RADIOSURGERY FOR CRANIOPHARYNGIOMA: MONOISTITUTIONAL EXPERIENCE

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Aims: The use of radiosurgical treatment (SRS) in patients with craniopharyngioma has been documented, but long-term follow-up reports are rare. The purpose of this study was to analyze the long-term outcomes of the SRS in patients (pts) with craniopharyngioma, reviewing a series of patients consecutively treated in a single institution.

Methods: 27 pts were treated for residual or recurrent craniopharyngioma between 2005 and 2018 with CyberKnife SRS. Patients underwent magnetic resonance imaging, visual and neuroendocrine evaluations before and after SRS at regular intervals.Both a multisession treatment regimen and a single fraction were used. A non-isocentric treatment plan was developed for each patient. The radiological response to treatment was assessed using RECIST guidelines(vers 1.1).

Results: Of 27 pts, 16 were males and 11 females. The average age at treatment was 46 years old, and the follow-up period was 10 to 150 months (80 mean, 48 median). The treatment was delivered to 10 pts with single fraction, to 17 pts with multiple fractions (median dose 25 Gy). 16 pts were treated for relapse after radical surgery and 11 pts received treatment after non-radical surgery. A partial reduction of the disease was observed in 8/27 pts (mean response 5,5 months). 3 pts achieved total tumor regression. Only 1 patient underwent new surgery due to disease progression. 15 patients maintained disease stability after treatment. No patient showed deterioration of visual or neuroendocrine function after SRS.

Conclusions: SRS has proven safe and effective, with no evidence of long-term complications. The use of SRS will be increasingly evaluated in the future, also in combination with conservative surgical resection.

P069

SMALLER CONTOURING OF HIGH GRADE GLIOMA DOES NOT INCREASE OUT OF FIELD RELAPSE

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Aims: High grade glioma (HGG) target definition is still discussed in radiation oncology. European Organisation for Research and Treatment of Cancer and Radiation Therapy Oncology Group published the most used guidelines; compared to the literature, we reduced planning target volume (PTV) expansion on clinical target volume (CTV) according to the treatment techniques, obtaining a progression free survival (PFS) comparable to literature data. We hypothesized a more frequent in-field involvement and less frequent out of field relapse for smaller-than-standard CTV-PTV margins by observation.

Methods: We retrospectively gathered data about 27 HGG patients (pts) treated from March 2017 to March 2020, calculating median and average progression-free survival from the end of radiation treatment and median and average follow-up (f.u.) time from histological diagnosis. Thirteen out of 17 received 60 Gy in 30 fractions, 14/27 50 Gy in 20 fractions. We have identified treatment volumes using fused pre- and post-operative axial T1 post-contrast and axial T2-FLAIR MRI sequences co-registered to the planning CT image set for contouring. We defined gross tumor volume (GTV); CTV, comprehending peri-lesional edema, trimming the margin according to anatomical barriers and organs at risk (OaRs); PTV, adopting a CTV-PTV margin of 0.3 cm for image guided radiation therapy (IGRT), or 1 cm if 3D conformational radiation therapy (3DCRT) technique was used (Table 1). The progression site margin was investigated via f.u. MRI exams, marking in-field and out-of-field progressions. At last we compared our contouring method to literature to show how it is possible to reduce volume target dose delivered while guaranteeing target irradiation objective.

Table 1.

	MRI sequences co-registered to the planning CT image	Target Volume
GTV	Axial T1 post-contrast	Surgical resection cavity plus any residual enhancing tumor OR Primary lesion
CTV	Axial T2 FLAIR	Edema modulated on OARs and anatomical barriers
PTV		CTV plus a 1 cm margin (3DCRT) CTV plus a 0,3 cm margin (IGRT)

Results: HGG pts in our center showed a PFS median time of 5 months and an average time of 6 months, over a median f.u. time of 12 months and an average time of 13 months. 18 pts treated with 3DCRT got a PTV expansion of 1 cm, as 9 pts treated with IGRT went through a PTV expansion of 0.3 cm. The progression site resulted in-field for 21 pts, out of these pts 2 manifested distant dissemination; whereas 1 pt showed out-of-field disease progression, 2 pts relapsed at PTV margin, 1 of these evidenced distant dissemination, and 4 pts did not relapse after chemoRT.

Conclusions: As no difference in terms of PFS was evidenced utilizing smaller margins, it may be possible to apply this contouring method to reduce total irradiated volume, causing fewer side effects and opening to re-irradiation possibilities with high doses.

P070

CLINICAL EVALUATION IN A MONO-INSTITUTIONAL CASISTIC: TOXICITY AND SURVIVAL DATA IN MESOPHARYNX AND HYPOPHARYNX CANCER

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Aim: To evaluate survival profile and toxicity data in patients (pts) affected by oropharyngeal/hypopharyngeal carcinoma, treated with chemo-radiotherapy (CHT-RT).

Methods: The clinical series included 34 pts, who underwent radical RT between 2012 and 2018. We evaluated toxicity data according to CTCAE v5.0. Statistical assessment was performed with SPSS®.

Results: Our casistic included 31 male/3 female. The median age was 69 years (range 45-84). Eighteen pts (53%) smoked during RT, 7 pts had stopped previously (21%). Eighteen pts (53%) had alcohol during RT, 3 in the past. In 27 cases (79%) the principle site was mesopharynx, in 7 (21%) was hypopharynx. Four pts underwent neoadjuvant chemotherapy (TPF schedule). Sixteen pts (47%) were classified at stage IVa, 3 pts (9%), 9(26%) and 6 (18%) were at II, III and IVb stage, respectively. Twenty-four pts (71%) received concomitant chemotherapy (weekly cisplatin, with a dose of 40 mg/mq). RT was delivered with IGRT-VMAT tailored plan. The prescribed dose to the precautionary PTV was 50 Gy/2 Gy per fraction and to the radical PTV T/N was 70 Gy and 60 Gy respectively. All patients underwent a local protocol for oral cleaning and sterilization, before treatment. Regarding acute toxicity we registered 20 cases of G1 mucositis (58%) and 14 (42%) grade G2. Twenty pts (59%) did not show any degree of dermatitis. Twenty-one pts (62%) showed xerostomia G1, 11 (32%) G0 and only 2 (6%) G2. Fifteen pts reported G1 dysphagia, 12 (35%), 3 (9%) and 4 (12%) showed G2, G3 and G0 respectively. Regarding chronic toxicity, 25 pts (73%) did not show any degree of dysphagia and 29 pts (85%) had no dysgeusia. Nineteen pts (56%) showed xerostomia G0, while 14 (41%) registered only G1 events. After a median follow up of 18 months, 2 and 5 years overall survival (OS) was 72% and 65% and disease specific survival was 80% and 70% respectively. We registered 4 events (12%) of local persistence/relapse and 8 events (23%) of nodal persistence, with rescue surgery. At the stratification analysis, we found worse OS and DSS in pts with local/nodal event (p=0.002 and 0.003, respectively and p=0.000). Only 3 pts showed metastatis (9%). At Chi-square analysis there was no statistical correlation between these events and initial risk factors/concomitant chemotherapy.

Conclusions: Our casistic evalutation showed opti-

mal toxicity data, due to treatment personalization and oral cleaning, and few recurrences, also with a concomitant weekly chemotherapy.

P071

A PET RADIOMICS STUDY OF PATIENTS WITH BRAIN METASTASES UNDERGO RADIO-TREATMENT

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Aims: This study aims to i) obtain the biological target volume from cerebral metastases in patients who underwent L-[11C]methionine (11C-MET) Positron Emission Tomography (PET), using a fully automatic procedure, and ii) extract radiomics features to stratify between patients who respond to radio-treatment or not. Specifically, although magnetic resonance imaging (MRI) remains the gold standard for diagnosis and follow-up after radiation therapy, 11C-MET PET can discriminate between cancer and healthy tissue, with great power of sensitivity and specificity.

Methods: The proposed segmentation system performs all steps automatically by individuating an optimal, operator-independent, initial region of interest located around the metastasis on an automatically selected PET slice. So, once the region has been identified, the tumour is delineated using an enhanced local active contour segmentation algorithm. Thirty-one brain metastases (15 men and 16 women without other organ or/and bone metastases) were segmented using the proposed method for predictive evaluation. Successively, 108 quantitative features were automatically extracted using the open-source toolbox "Chang-Gung Image Texture Analysis". A novel statistical system based on correlation matrix and point-biserial correlation coefficient was implemented for feature reduction and selection, while discriminant analysis was used as a method for feature classification. A clinical evaluation was carried out by our medical staff to differentiate between responder and non-responder patients 6 months after the treatment.

Results: Three features (asphericity, low-intensity run emphasis, and complexity) were able to discriminate between responder and non-responder patients, after feature reduction and selection. Optimal performance in patient discrimination was obtained using the combination of the three selected features (sensitivity > 81%, specificity > 73%, and accuracy > 78%).

Conclusions: The proposed system was able to i) automatically obtain the biological target volume from cerebral metastases from 11C-MET PET studies, and ii) extract 108 11C-MET PET features for each metastasis in order to identify a sub-panel of radiomics features with valuable association with patient outcome. We believe that our model can be useful to improve treatment response and prognosis evaluation, potentially allowing the personalization of cancer treatment plans.

P072

XEROSTOMIA INDUCED BY SUBMANDIBULAR GLANDS IRRADIATION IN EARLY GLOTTIS CANCERS: A RETROSPECTIVE DOSIMETRIC ANALYSIS

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Aims: Saliva deriving from submandibular glands (SMG) is necessary to minimize xerostomia in H&N radiotherapy (RT). In early glottis cancer (EGC) xerostomia represent an uncommon but possible sequel and this could be particularly related to SMGs irradiation. The aim of the study was to evaluate the correlation between xerostomia and submandibular gland (SMG) irradiation in patient affected by EGC submitted to primary 3D-CRT.

Methods: A retrospective dosimetric analysis was performed on 20 EGC patients treated with RT doses from 66 to 70Gy (2 Gy/die) between January 2013 and April 2020. Original plans did not include SMGs as avoidance structure in optimization criteria; SMG were retrospectively delineated on planning CT, according to Van de Water TA et al 2009. Volume in cc of SMGs and PTV was recorded and an overlapping volume of each SMG with PTV was created and measured both in cc and%. Constraints analyzed in respect to SMGs were V15 <66%, mean dose (MD) <35 Gy. For parotid glands (PGs) a MD <25 Gy was considered as cut-off. Xerostomia was evaluated according to CTCAE scale and its impact on quality of life was assessed using "Xerostomia quality of life (XeQols)" and Oral Health Impact Profile (OHIP14) questionnaires administered at the time of the last visit.

Results: Out of 20 patients 11 (55%) had xerostomia (only G1 toxicities were observed) at any time after RT. Dose constraints were respected in all case but one for both PG. About SMGs, 8/20 patients had a MD>35 Gy on both SMGs and 4/8 experienced xerostomia; one patient had a MD on SMGr near to the threshold (34.9 Gy) and still developed xerostomia. In 9/11 patients, SMGs received a dose ≥20 Gy. SMGr mean volume was 8.2 cc (range 4.6-12.5) and 7.9 cc (range 3.9-12.9) for SMGl. We found an overlap PTV-SMG in 10 patients (6/10 had bilateral overlap) and 8/10 developed xerostomia. Mean overlap volume was 0.14 cc (1.5%). XEQols and OHIP14 questionnaires were filled in by 14/20 patients. In symptomatic patients mean score was 0.7 points (indicating mild xerostomia) on the XEQols while 5.4 in OHIP14, with possible scores ranging from 0 to 56.

Conclusions: Despite the small sample size, we observed that even small volume of SMG can be associated with a some degree of xerostomia. In our study, patients experiencing xerostomia had worse Qol and their SMG received higher doses, validating the idea that sparing SMG may improve toxicity and Qol outcomes for those patients.

Table 1.

	Asymptomatics Mean - (range)		Xerostomia Mean (range)	
Mean dose to parotid glands (PG)				
right PG	3.7 (0.53 – 25.2)		10.2 (0.7 – 36.7)	
left PG	1.0 (0.62 – 25)		10.8 (0.70 – 36.29)	
Mean dose to submandibular glands (SMG) (Gy)				
right SMG	19.3 (0.19 – 47.34)		30.1 (8.80 – 55.16)	
left SMG	18.5 (2.54 – 45.74)		31.8 (10.21 – 61.31)	
Overlap PTV - SMG (Absolute in cc and relative in %)				
right	0.01 (0 – 0.3)	0.91 (0 - 8)	0.21 (0 – 0.62)	2.11 (0 – 5.05)
left	0.03 (0 – 0.3)	1.24 (0 - 9)	0.22 (0 – 0.76)	2.08 (0 - 6.9)
Questionnaires scores				
Xeqols score	0.01 (0 – 0.06)		1.00 (0 – 2.4)	
OHIP - 14	1.6 (0 – 5)		5.44 (0 - 28)	

P073

ROLE OF PET/CT IN RADIOTHERAPY PLANNING FOR LUNG AND HEAD AND NECK CANCER PATIENTS

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Aims: In this study, we investigated the benefits of simulation with 18F-deoxyglucose positron emission tomography/computed tomography (FGD-PET/CT) for staging and radiotherapy (RT) planning in patients with lung (LC) and head and neck cancers (HNC) undergoing radiotherapy with simultaneous integrated boost (SIB).

Material and methods: Forty-six patients (twenty-six lung and twenty head and neck) who had undergone RT with PET/CT simulation at the "REM Radioterapia" center were examined. The metabolic information provided by PET study was utilized to characterize the anatomical gross tumor volume (GTV) by identifying functional sub-volumes leading to the definition of a biological target volume (BTV), adopting the 40% SUV max threshold.

Results: With PET/CT imaging, the stage of all LC patients remained the same while for 4 HNC patients (20%) the stage changed. PET didn't influence our choices regarding primary tumor determination but it helped in the detection of lymph nodes for SIB delivering. We found that BTV of lymph nodes identified by PET/CT was smaller in 10 lung cases (38.5%) and in 6 head and neck cases (30%) when compared to GTV determined only by CT. One head and neck case (5%) showed an increased high-risk volume determined by means of PET imaging.

Conclusions: PET/CT has a high impact when used for SIB treatments. The BTV introduction paves the way to the concept of "dose painting", where target volume receives an inhomogeneous dose distribution according to its functional activity and all this allows to apply dose escalation. In our study, PET/CT changed the treatment planning in 37% of patients. PET/CT imaging can increase the accuracy of the staging and defining target volumes for RT treatments in LC and HNC patients. We recommend the use of simulation with PET/CT before RT treatment for both a more correct identification of treatment volumes than CT and for an accurate delivery of SIB treatment.

P074

PROGNOSTIC NUTRITIONAL INDEX IN HEAD AND NECK CANCER: A LOW-COST BIOMARKER FOR TOXICITY AND SURVIVAL AFTER INTENSITY MODULATED RADIOTHERAPY

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Aims: Several nutritional and systemic inflammation biomarkers have been associated with the risk of toxicity and complications after cancer therapy. However, very few studies focused on patients with head and neck cancer (HNCa). The purpose of this study was the evaluation of the association between the Prognostic Nutritional Index (PNI) and the risk of toxicity and death in a cohort of HNCa patients.

Methods: A retrospective cohort of 163 HNCa patients treated with definitive chemo-radiotherapy between 2010 and 2017 was followed-up for toxicity and vital status (median follow-up: 38 months). PNI was calculated according to Onodera formula; the optimal cut-off of PNI was calculated through a recursive algorithm that maximises predictivity in overall survival (OS). Survival analysis and toxicity-free survival was conducted with Kaplan-Meier method and hazard ratios (HR) were calculated through the Cox hazard model, accounting for competing risks.

Results: Patients with PNI≥55 reported better 5-year OS than those with PNI<55 (85.8% and 69.7%, respectively; HR=0.40, 95% CI: 0.17-0.96) and a better progression-free survival, thought not significant

(HR=0.51, 95% CI: 0.23-1.10). However, PNI≥55 was associated with a 3-fold increased risk of late severe dysgeusia (HR=3.14, 95% CI: 1.08-9.17) and to late severe xerostomia (HR=2.06, 95% CI: 1.02-4.16).

Conclusions: Higher levels of PNI identify HNCa patients with improved survival but at increased risk of late radiation-induced toxicity as well. Further validation in a prospective study with a larger number of cases is needed for its application in daily clinical practice.

P075

OFF-LABEL USE OF ANTI PD-1 IN A YOUNG WOMAN AFFECTED BY SINONASAL UNDIFFERENTIATED CARCINOMA: A CASE REPORT

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Introduction: Sinonasal undifferentiated carcinoma (SNUC) is a rare and aggressive malignancy. Multimodality approach including surgery, chemotherapy (CT), and/or radiotherapy (RT) is recommended, due to the high risk of local recurrence, advanced stage at presentation and proximity to critical structures.

Case: We report the case of 40 years-old woman presenting on May 2016 with reduced vision, diplopia, left proptosis, anosmia, ipogeusia, and vomiting. Brain MRI demonstrated a mass lesion in the anterior cranial fossa extending through the cribriform plate in the anterior nasal fossa, with invasion of the left orbit and unilateral grade II proptosis. The patient underwent surgical resection of disease with ethmoidectomy and bifrontal craniotomy. Histological examination showed a SNUC with infiltration of the mucosal corion, brain parenchyma, soft and bone tissue (pT4N0MX). Postoperative PET/TC revealed hypercaptation (SUV25) on the left retrobulbar space and brain MRI confirmed an intra-orbital lesion. On July 2016, patient received docetaxel-cisplatin-fluorouracil (2 cycles) chemotherapy. Restaging MR showed a left frontobasal recurrence. Thus, the patient received RT to the resection cavity and the recurrence (65.92 Gy), with concomitant weekly cisplatin, until December 2016. On Febraury 2018, PET/TC showed a liver metastasis and 5 cycles of Paclitaxel and Cisplatin were administered. On June 2018, the patient were treated with SBRT to the liver lesion (56.25 Gy, 3 fractions). On November 2018, PET/ TC demonstrated a good response in the liver and stable disease on primary site. Then patient was treated with capecitabine maintenance, but on June 2019 an abdomen MR showed new liver lesions. We switched CT with Carboplatin and Vinorelbine but there was a further progression on liver disease. Then was proposed a treatment with Nivolumab, an anti-programmed cell death-1 monoclonal antibody, used for patients with recurrent or metastatic squamous cell carcinoma of the head and neck after platinum CT. AIFA authorized off label use. Currently, the patient completed 9 cycles of Nivolumab (240 mg every 2 weeks) without side effects and with stable disease.

Conclusion: Due to the rarity of metastatic SNUC, there is a lack of randomized clinical trials and the optimal treatment strategy remains undefined. In our case, an anti-PD1 antibody provided stable disease. Studies are required to define genetic aberrations in SNUC that can be targeted with biological agents.

P076

BODY MASS INDEX (BMI) AS A PREDICTIVE FACTOR OF SURVIVAL AND LOCAL CONTROL IN A COURT OF ELDERLY PATIENTS TREATED FOR HEAD & NECK CANCER

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Aims: Head & neck cancer among the elderly patients is showing a continuous increase, with an estimate incidence between 24% and 40%. Stratification of these patients and the identification of those who can be more prone to local therapeutic failure or to the development of distant metastasis, besides the biological and histopathological features of the neoplasia, is primary in the right choice of the most appropriate therapeutic course.

Methods:199 patients over 65 years of age affected by HNSCC at any stage who were treated with radical exclusive RT or RT-CHT between 2007 and 2017 at Radiation Oncology Department of Spedali Civili and University of Brescia were evaluated. Among the other characteristic we focused our analysis on Body Mass Index (BMI), datum available for 146 patients, and its relation with local control (LC), nodal control (NC), locoregional control (LRC) and metastasis free survival (MFS). Correlation of this characteristic with overall survival (OS) and cancer specific survival (CSS) were also analyzed.

Results: The univariate analysis showed a correlation of this datum with NC. Correlation that even with Cox regression multivariate analysis maintained its statistical association with NC with 0,11 of relative risk (RR) of local relapse in obese patients and 0.15 in overweight and normal weight patients. LRC showed the same association with BMI (p=0.002) in the univariate analysis, even if this finding was not confirmed in the multivariate analysis. MFS showed a statistically significant association (p=0.005) with BMI, with 95.5% of obese patients alive without metastasis at 12 months, compared to the 80% MFS at 10 month for the 5 underweight patients in our cohort. Finally, CSS were also related with BMI, correlation that, in the multivariate analysis showed a RR for over-weight patient of 0.12 while normal weight patient showed a RR of 0.31.

Conclusions: In our cohort of patients, a high BMI was in conclusion associated with a better control of locoregional and metastatic disease. Despite the limits of this study, these findings are comparable to the know

obesity paradox, that can be explained with the energy reserve function of the fat tissue, expendable by the organism in stress conditions; the impairment of immune system in malnutrition state and the role of the loss of lean body mass in pro-inflammatory status and cachexia, factors that brings to a poorer prognosis and a worse locoregional and distance control of the disease.

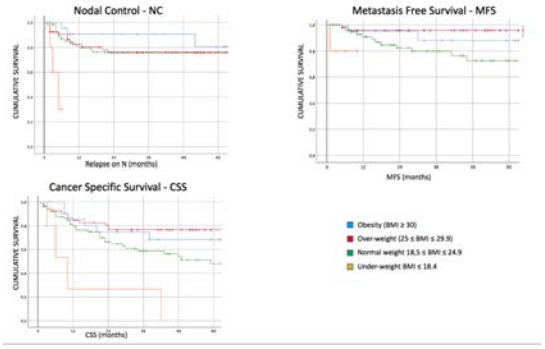

Figure 1.

P077

PROGNOSTIC SIGNIFICANCE OF PRETREATMENT NEUTROFIL TO LYMPHOCYTE RATIO IN 36 PATIENTS WITH HEAD NECK SQUAMOUS CELL CARCINOMA TREATED WITH DEFINITIVE SIB-IMRT

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Aims: to explore the prognostic value of pretreatment NLR (neutrophil to lymphocyte ratio) to predict overall survival (OS) in patients with Head and neck squamous cell carcinoma (HNSCC) treated with definitive definitive radiotherapy.

Methods: Retrospectively collected data of 70 patients that received definitive radiotherapy for HNSCC at our radiation oncology centre and treated between 2011 and 2017 were included in this analysis. The median age was 60 years (range 43-86), 83% males and 17% females, ECOG PS 0-2. The primary tumor sites were 40% oropharynx, 23% larynx, 17% hypopharynx, 7% oral cavity, 6% unknown primary cancer, 4% nasopharynx, 3% others; PET-staged 67% IV a-b, 19% III, 10% II, 4% I (AJCC-7 th edition). Radiotherapy was delivered by simultaneous integrated boost intensity-modulated radiation therapy (SIB-IMRT) technique. Levels of dose were 67.5 Gy (2.25 Gy/fr), 60 Gy (2 Gy/fr), 54 Gy (1.8 Gy/fr) for the high risk, intermediate risk and low risk PTVs respectively in 30 daily fractions in 40 days. The median follow-up of patients still alive was 21 months (range 4-96). Overall survival (OS) was estimated by using the Kaplan-Meier method and it was measured from the date of diagnosis until death from any cause. At baseline, the pretreatment blood routine were performed in all 70 patients within 15 days before treatment.

Results: A total of 36 patients were eligible for this analysis. The NLR ranged from 1 to 7.2. Median cut-off value of 2.78 was used to stratified the patients into two groups (NLR $\leqq$ 2.78 vs NLR >2.79 respectively). As shown in fig 1, patients with high NLR had poor OS: 3 years OS were 36% and 62% respectively while median OS value was 1.93 for high NLR group (for the low NLR group the median OS was not reached), p=0.265

Conclusions: In our work we showed that NLR in locally advanced HNSCC treated with moderate hypofractionated SIB-IMRT, had a trend toward improved long term OS but this did not reach statistical significance.

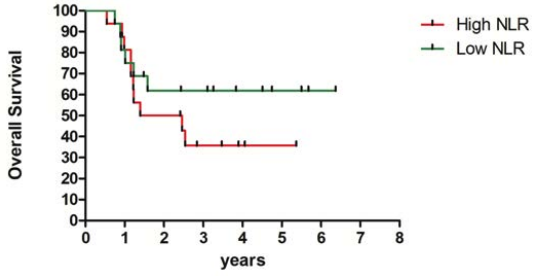

Figure 1.

P078

THE REDUCTION OF CLINICAL TARGET VOLUME AND ITS DOSIMETRIC IMPACT ON THE CAROTID ARTERIES SPARING IN EARLY GLOTTIC CANCER: COMPARISON BETWEEN VOLUMETRIC MODULATED-ARC THERAPY AND 3D-CONFORMAL RADIOTHERAPY

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Aim: 3DCRT is a treatment option for T1 glottic cancer (GC). VMAT provides, however, dosimetric advantages in carotid arteries (CAs) sparing. The reduction of CTVs, recently proposed in a consensus contouring guide of Gregoire and colleagues, would change CAs sparing of VMAT over 3DCRT. Although this guide was not specifically developed to spare CAs, the reduction of the contoured primary CTVs parallels with the greater distance of targets from contralateral and, in less measure, from ipsilateral CAs. In this dosimetric study we investigated if anatomical factors (the increased anatomical distance between target volumes and OARs) can prevail over advanced planning strategies (conformal properties of IMRT/VMAT) in sparing contralateral CAs and CBs. This hypothesis was tested comparing the plans generated by VMAT or 3DCRT under reduced primary CTVs delineation in T1 GC.

Methods: Ten CT of patients with T1a GC were contoured using the new consensus contouring guide of Gregoire and colleagues. The CAs and bulbs were separately outlined and 3DCRT and VMAT plans were generated. Bulbs and CAs D0,1cc, Dmean, V35, V50 were comparatively assessed. Plan quality indices and organs at risk (OAR) doses were also compared.

Results: contralateral bulb ($p<0,0001$) and CA D0,1cc ($p<0,0001$) were lower in VMAT than in 3DCRT plans. Moreover, contralateral bulb ($p=0,0002$) and CA Dmean ($p<0,0001$) and contralateral bulb ($p=0,02$) and CA V35 ($p=0,005$) were higher with 3DCRT. Similarly, mean ipsilateral bulb and CA Dmax significantly decreased from 51,8 Gy to 32,8 Gy ($p<0.0001$) and from 54,0Gy to 44,0 Gy ($p=0,0005$) for 3DCRT and VMAT, respectively. VMAT significantly lowered ipsilateral bulb Dmean ($p=0,0001$) and V35 ($p=0,005$) and ipsilateral CA V35 ($p=0,0002$). VMAT significantly reduced the dose to pharyngeal constrictor muscles, thyroid gland and supraglottic larynx.

Conclusions: VMAT maintains its dosimetric advantages in contralateral CA and CB sparing over 3D-CRT even when the delineation of the primary CTVs is significantly reduced. These dosimetric sparing advantages were evident for ipsilateral CAs and CBs. All these dosimetric benefits were achieved without compromising the target coverage or plan quality indices. The dosimetric data here provided, once more, confirm that VMAT could be considered a new standard of care in the treatment of early GC even when the delineation of the primary CTVs is significantly reduced.

P079

ELDERLY HEAD AND NECK CANCER: A GERIATRIC ASSESSMENT COULD PREDICT TREATMENT TOLERANCE AND CLINICAL OUTCOME IN PT ≥ 75 YEARS OLD?

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Aims: The majority of HNC patients(pts) are over 50 years(ys) odl and about 20–25% of HNC pts is over the age of 65 ys. The National Institute of Health divided old aged pts in three categories: young old (65-74ys), older old (75-84ys) and oldest old (over 85ys) but there is no shared definition of elderly pts. HN pts often present multiple comorbidities and frailties. Here, pts over 75ys were examined.

Methods: Since June 2017 we started a research project in collaboration with geriatric colleagues. The pts are examined according to a multidimensional geriatric evaluation with comprehensive geriatric assessment (CGA) and divided into categories of fragility. From June 2017 to June 2020,215 HN pts were treated with a mean age of 67ys (range 32-92).58pts(27%) were over 75ys (mean age 81 ys). All pts underwent RT +/- systemic therapy.

Results: 58pts underwent RT, 9pts(16%) were treated with concomitant Cetuximab, 1pt received concomitant CDDP. RT was administered as adjuvant therapy in 12 cases(21%) range dose (60-66Gy), as radical treatment in 37 (64%) range dose (66-70 Gy) and with palliative intent in 9 cases(16%) range dose (30-40Gy). The main sites were 26(45%) oropharynx and 13(22%) larynx, 6pts(10%) were treated for a relapsed cancer. 43/58pts (74%) were evaluated by geriatricians before treatment and according to the frailty index (FI) patients were classified as fit 6 (15%), pre-frail 22 (50%) and frail 15 (35%). 20/43 pts (47%) received a corrective action (nutrition, pain control, psychological support). 39/58pts were evaluated for response. We observed 23 (40%) CR, 2 (3%) PR, 14(24%) PD, 9(16%) have not been evaluated or lost at follow up, 9(16%) are waiting for revaluation and 1pt is in treatment.4 pts(7%) had to interrupt RT. 29 pts (50%) needed nutritional support: oral supplement (16 pts), PEG(3 pts), parenteral nutrition (5 pts) and SNG (5pts). 7/58 (12%) have requested hospitalization. To date 19 pts (33%) died: 9 (16%)for disease, 10 (17%) other cause. 7 pts died within 3 months of the end of RT. 21/43 pts patients had geriatric revaluation about 3 months after the end of RT. 9/21 pts (43%) did not change their assessment grade, 5 pts (24%) worsened and 7 pts(26%) improved their status.

6pts are still waiting a second geriatric visit. In table 1 we see results divided according categories of FI.

Conclusions: In elderly HNC pts is extremely important implement evaluation to achieve a real tailored therapy. Geriatric evaluation with CGA could be a useful tool.

Table 1.

	Died	Died within 3 months of the end of RT	Hospitalized	Interrupted radiation	Nutritional support
Frail	7 (37%)	3	3	2	7
Pre-frail	6 (33%)	2	1	/	15
Fit	2 (10%)	/	/	/	5
Not evaluated by geriatrician	4 (20%)	1	3	2	2

P080

IMRT BASED RE-IRRADIATION FOR SECONDARY/RECURRENT HEAD AND NECK SQUAMOUS CELL CARCINOMA: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Limited data are available about reirradiation treatment of recurrent or second primary squamous carcinoma of head and neck. This study aims to evaluate the outcome and toxicity of patients treated in our experience at UO Radiotherapy of Arezzo.

Methods: Between June 2012 and March 2019, 26 patients, 23 male and 3 female, with recurrent head and neck cancers underwent fractionated intensity modulated radiotherapy (IMRT) re-irradiation (re-RT) with curative/adiuvant (18 patients) or palliative (8 patients) aims. 17 (68%) patients received chemotherapy. All patients were previously irradiated in adjuvant or radical setting, with a median total dose of 64 Gy (range 54-70 Gy). The effect of re-RT on overall survival (OS), locoregional control (LRC) and acute and late toxicity was assessed. Acute and late toxicities were evaluated according to CTCAE v. 4.0.

Results: The median time interval between first treatment and re-RT was 34.6 months (range 6-123 months) The median total dose delivered was 50.4 Gy (range 20-66 Gy). 10 (40%) patients underwent to surgery before RT and 19 (76%) patients underwent a chemiotherapy (10 patients with concomitant treatment), 73% of case platinum based. At a median follow-up of 18.3 months, the 1 year local LRC was 65,2%, OS was 48,3%. The rate of acute grade 1-2 toxicity was 80%, grade 3 16%. Late toxicity (fibrosis and osteonecrosis) was observed in 16% of patients.

Conclusion: re-RT is a feasible and well tolerated treatment option for loco-regionally recurrency of head and neck squamous cell carcinoma. Acute and late toxicity can be manageable but patients need to be carefully selected. Dose and irradiation schedule should be prospectively evaluated.

P081

QUALITY OF LIFE: AN INTERIM ANALYSIS OF PATIENTS WITH LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK TREATED WITH DURVALUMAB PLUS CETUXIMAB AND RADIOTHERAPY IN THE PHASE I/II DUCRO TRIAL (NCT03051906)

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Aims: To report a descriptive analysis of interim results concerning the quality of life (QoL) of patients enrolled in the DUCRO trial (NCT03051906).

Methods: In this multi-center, single-arm, phase I/II study, enrolled patients affected by locally advanced squamous cell carcinoma of the head and neck will receive RT (69.9 Gy in 33 fractions) with concurrent Cetuximab and Durvalumab followed by adjuvant Durvalumab to a maximum of 6 months. Primary endpoint of the study is 2-year progression-free survival (PFS). Assessment of QoL, an exploratory endpoint, was achieved through the administration of validated questionnaires (EORTC QLQ C-30 and QLQ H&N-35) at pre-specified time points (at registration and at weeks 9,19,31). The EORTC scoring manual was employed to analyze the results, which were transformed to a linear scale of 100, varying from 0 (no effect) to 100 (effect experienced all the time) in symptoms scales and 0 (complete loss of functioning) to 100 (full functioning) in functional scales.

Results: From June 2019 to July 2020, 8 patients were recruited in the trial and all of them had completed at least 1 QoL evaluation at the time of analysis. Three of them reached all the evaluation time points. Constipation, fatigue and appetite loss were the most frequent symptoms reported by patients (median scores throughout all evaluations were 24.10, 18.98, 18.61 respectively). Median global health status levels were 56.25, 63.33, 44.44 and 86.61 at baseline, week 9, 19 and 31 respectively. The most affected domains in all patients at the pre-specified timepoints were the emotional functioning (76.04 at baseline and 81.67 at week 9) and physical functioning (95.56 at week 19 and 86.67 at week 31).

Discussion: Patients had similar baseline scores in

global health status; the score was higher shortly after the end of treatment phase, showing a remarkable decrease at week 19. The first improvement in QoL could be explained by the relief of symptoms brought by the presence of a locally advanced mass, while the burden of late treatment effects may have had a severe impact on patients' health at week 19. Overall patients showed a good acute tolerance to the treatment and long-term adverse events were scarce.

P082

RADIOTHERAPY FOR ATYPICAL FIBROXANTHOMA OF HEAD AND NECK IN VERY OLDER PATIENT: A CASE REPORT

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Aims: Atypical Fibroxanthoma is a rare dermal mesenchymal neoplasm arising predominantly in the head and neck area of elderly patients. It is considered to be a benign tumor, rarely, metastases arise, but it 's characterized by a rapid and exophytic growth with (frequent) ulceration of the epidermis We present a rare case of very older women with atypical fibroxanthoma of the face, with a positive history of sun exposure skin.

Methods: In april 2020 a 92-years-old female patient, PS ECOG 1, affected by atypical fibroxanthoma of the face, was referred to our Radiation Oncology Unit after a multidisciplinary evaluation. The patient was also affected by cardiological and neurological comorbidity. In february 2020 she presented a rapidly and exophytic growth left zygomatic lesion of 3 centimetres with ulceration of epidermidis. An incisional biopsy showed "atypical fibroxathoma" infiltrating the deep margin of surgical excision. The case was submit to multidisciplinary evaluation: given the age and extent of the disease, radical surgery of the lesion was escluded. Patient was treated with palliative radiotherapy (10 fractions for a total dose of 30 Gy).

Results: The treatment was well tolerated. The patient presented moderate (G2) erythema on the skin, without severe toxicity.

Conclusions: Palliative radiotherapy could allow a satisfactory local control, as well as an improvement of patient's quality of life, in very older patient. This approach could be considered for selected patients and should be evaluated in the multidisciplinary management of these rare tumors.

P083

PILOT PROSPECTIVE ASSESSMENT OF PATIENT-REPORTED TASTE ALTERATIONS IN HEAD AND NECK CANCER: PREDICTIVE IMPACT OF DOSE DISTRIBUTION TO THE MOBILE TONGUE

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Aims: Radiotherapy (RT), plus concomitant chemotherapy, is a major treatment modality for patients with Squamous Cell Carcinoma of the Head and Neck (HNSCC). Despite many of these patients develop a taste disorder during treatment, data about the evaluation of taste changing are still poor. We report a longitudinal assessment of patient reported taste alterations and QoL scores in head and neck cancer. We also performed an explorative analysis on predictive impact of dosimetric factors, relating dose for tongue and time-trend of PROs scores.

Methods: We evaluated 22 patients with locally advanced HNSCC treated in our institution from September 2019 to June 2020. Patients received adjuvant or curative IMRT, alone or with concurrent chemotherapy. Patients with tumor of the oral cavity submitted to surgery excision have been excluded. We collected data from CiTAS, EORTC QLQ C30 and EORTC QLQ HN43 questionnaires at baseline (T0), 3 weeks after RT conclusion (T1) and at 3 months (T2) to assess change over time. An explorative contouring of the tongue was conducted (apex, central portion and base). The mean dose received was related with the subdomain "general taste alterations", "global health status" and "dry mouth" of CiTAS, EORTC QLQ C30 and EORTC QLQ HN43, respectively.

Results: We report a preliminary analysis on 17 patients treated for SCC of the oropharynx (n=12; 70,6%), hypopharynx (n=2; 11,8%), nasopharynx (n=2; 11,8%) and larynx (n=1; 5,9%). 11 patients received concurrent chemoradiation (64,7%) and 6 RT alone (35,3%). The mean values of the subdomain "general taste alteration" at CiTAS was 1.24, 2.29, 1.90, the mean scores of "global health status" at EORTC QLQ C30 was 67.65, 66.18, 69.61 and the mean values of "dry mouth" at EORTC QLQ HN43 was 14.71, 45.10, 48.04 at T0, T1 and T2, respectively. The mean dose to the apex of the tongue was 24.52 Gy (range 15.5-39.4 Gy), to the central portion was 37.17 Gy (range 18.7-63.9 Gy) and to the base was 49.1 Gy (range 19.4-50.1 Gy). At statistical univariated analysis we found a significant correlation between mean dose at the anterior portion of the tongue (apex and central portions) and worsening across time of values of general taste alteration (CiTAS) and dry mouth (EORTC QLQHN43).

Conclusions: Even in a pilot experience, with few patients included in the study, we demonstrated an early signal of correlation between dose distribution to the oral cavity and dysgeusia, in particular with the anterior segments of the tongue.

P084

GLIOBLASTOMA: PROLONGED SURVIVAL BY TREATING THE RECURRENCE WITH STEREOTACTIC RADIATION THERAPY

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Introduction: Glioblastoma multiforme (GBM) (WHO grade IV) is the most common malignant brain tumor, is a fatal illness that is associated with a median survival of less than 2 years. The recurrence is systematic and prognosis poor. Many years ago we analyzed the survival of a group of patients (pts) with GBM treated in our center between 1998 and 2003; the purpose of our work today is to compare survival, analyze the influence of prognostic factors and if there is a difference after 15 years.

Material and methods: 53 consecutive pts treated from 2012 to 2018. The mean age was 70 years, median 68 (range 32-82). 31/53 (58%) are of male sex. 45/53. (85%) underwent surgical (S) and of these 27/53 (51%) macroscopically radical, 8/53 (15%) only the biopsy. All pts treated with accelerator 6MV 3DCRT or VMAT and standard or hypo fractionated dose.

Results: The median overall survival from the diagnosis to the death was 13,4 months (mean 16; range 4-41). The median survival of pts undergoing biopsy alone was 9 months. At the time of observation (48 months of median follow-up) 9 pts were alive and 44 died. The median of survival in pts treated with stereotactic radiotherapy (SRT) at the recurrence of disease was 20m, median 27m (range 6-31). Discussion Comparing the data of this study with those of 2008, there is a improvement in the survival of patients treated with SRT. Similarly, a better prognosis is correlated with the relatively younger age, with radical S, with doses of radiation (≥ 60 Gy) and with the use of temozolomide in concomitant with radiotherapy (RT) and subsequently in adjuvant.

Conclusion: Radical surgery is a determining factor, particularly if associated with RT, and temozolomide. The use of SRT to treat the recurrence has improved the survival of these pts. Many steps must be taken.

P085

A DOSIMETRIC COMPARISON BETWEEN TOMOTHERAPY AND VMAT FOR OROPHARYNGEAL CANCER IRRADIATION

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Aims: The aim of this study is to compare a volumetric-modulated arc therapy (VMAT) and helical TomoTherapy (HT) for the irradiation of oropharyngeal cancer in terms of target coverage and doses to OAR, both for sequential (SBT) than for simultaneous integrated boost technique (SIB). A prescription of 54-60 Gy in 30 fractions followed by a 10 Gy boost in 5 fractions was used in SBT and 54-60-66 Gy in 30 fractions in SIB regimen.

Table 1. Statistical analysis in terms of two tailed paired sample t-test(α=0,05); * where p<0,05.

	MEAN± SD	MEAN± SD	
SBT			
PTV 54 Gy	HI= (0.18±0.03)	HI=(0.16±0.04)	p=8.3E-1
	CI= (0.990±0.003)	CI= (0.993±0.006)	p=9.5E-1
PTV 60 Gy	HI = (0.18±0.04)	HI=(0.241±0.02)	p=7.1E-1
	CI= (0.989±0.014)	CI= (0.990±0.008)	p= 9.9E-1
PTV 70 Gy	HI = (0.040±0.016)	HI=(0.12±0.02)	p= 5.4E-1
	CI= (0.990±0.010)	CI= (0.984±0.006)	p=9.4E-1
Trunk	D_{max}= (17.73±1.78) Gy	D_{max}=(24.43±7.26) Gy	p=4.5E-2*
Spine	D_{max} (22.33±1.83) Gy	D_{max}=(33.89±1.35)Gy	p=2.3E-3*
Parotid glands	V_{30Gy}= (34.61±6.11)	V_{30Gy}= (54.80±7.20)	p=9.4E-3*
	D_{mean}= (27.91±3.13) Gy	D_{mean}=(35.18±4.18) Gy	p=4.2E-2*
SIB			
PTV 54 Gy	HI= (0.13±0.03)	HI=(0.19±0.06)	p=7.7E-1
	CI= (0.987±0.006)	CI= (0.973±0.009)	p=8.6E-1
PTV 60 Gy	HI = (0.15±0.03)	HI=(0.203±0.024)	p=7.5E-1
	CI= (0.991±0.032)	CI= (0.950±0.008)	p= 7.5E-1
PTV 70 Gy	HI = (0.047±0.009)	HI = (0.096±0.021)	p= 6.5E-1
	CI= (0.998±0.001)	CI= (0.974±0.012)	p=7.2E-1
Trunk	D_{max}= (30.00±8.17) Gy	D_{max}=(23.70±0.94) Gy	p=5.1E-2*
Spine	D_{max} (24.30±1.59) Gy	D_{max}=(31.98±3.64) Gy	p=2,8E-2*
Parotid glands	V_{30Gy}= (41.41±9.67	V_{30Gy}= (52.36±12.86)	p=2.5E-2*
	D_{mean}= (28.48±3.24) Gy	D_{mean}=(33.29±6.08) Gy	p=5,1E-2*

Materials: 20 patient planning CT were segmented. For every patient two plans were generated: one for TomoTherapy and the other for VMAT. For Tomotherapy plans 6 MV photon beams were used and the optimization was performed by the TPS using the least squares optimization method. For planning a field width of 2.5 cm, a pitch value of 0.287, a modulation factor of 2.7 and a fine dose calculation grid were applied. VMAT plans were instead calculated using Elekta Monaco TPS with 6 MV photon beams, using the Monte Carlo algorithm on a 3 mm calculation dose grid. A single isocenter and three coplanar arcs (one of 360° and two <180°) were used for the plans calculated on 30 fractions, both for SBT than SIB; for the sequential boost a single 360° arc with the isocenter at the center of the boost volume was used. The accumulated dose of the two SBT plans was calculated using MIM Maestro both for TomoTherapy and VMAT: the two DVHs obtained were analyzed and compared. Both TomoTherapy and VMAT plans were optimised to obtain the best compromise between targets coverage (in terms of CI and HI) and OAR sparing (maximum dose (Dmax) for spinal cord and trunk; mean dose (Dmean) and V30 for parotid glands). In order to encompass the inter-subjects variability, for each planning CT the differences of each parameter in the two competitive plans were evaluated by means of two

tailed paired t-test.

Results: Mean±SD of each dosimetric parameter both for TomoTherapy and VMAT and for SBT and SIB are reported in Table, together with the statistical analysis. OAR sparing is slightly significant in TomoTherapy plans: V30 and Dmean of parotid glands, Dmax of spine and trunk are slightly significant lower in TomoTherapy than in VMAT, both for SBT than SIB. No relevant differences for target coverage were observed.

Conclusion: Our results show that TomoTherapy technique for the irradiation of oropharyngeal cancer offers better sparing of OAR than VMAT. The target coverage is very similar in terms of CI and HI for the two techniques both for SIB and SBT plans.

P086

PRELIMINARY RESULTS OF QUALITY OF LIFE AND SKIN TOXICITY IN HEAD AND NECK CANCER USING EORTC QLQ-C30, QLQ-H&N43 QUESTIONNAIRES AND SKINDEX 29

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Aims: To evaluate quality of life (QoL) and skin toxicity in patients with head and neck cancer (HNC)treated by combined modality therapy and longitudinally evaluated with EORTC QLQ-C30, QLQ-H&N43 and Skindex 29 questionnaire.

Methods: From February to June 2020 we enrolled 9 patients with diagnosis of head and neck cancer (HNC) who underwent exclusive radiotherapy (RT) or radiotherapy plus chemotherapy (Cetuximab or Cisplatin) both with radical or adjuvant intent. All patients underwent IMRT (VMAT or Tomotherapy) with a range dose from 52.8 to 69.9 Gy and completed the questionnaire at baseline, onset of Radiation dermatitis (RD) ≥G2, and 4 and 8 weeks after the onset of RD.

Results: The mean score for global health status (GHS) QoL was 54.6. The mean value of the five scales of functioning ranged from 71.39 (emotional functioning) to 90 (cognitive functioning). The highest symptom score on QLQ-C30 was for fatigue, followed by appetite loss, constipation and pain. In the H&N 43 module, opening, dry mouth, senses problems, and speech problems ranked as the four worst symptoms of 19 items subgroup. Effects of skin disease evaluated with Skindex-29 were more significant for symptoms scale.

Conclusion: QoL is adversely affected in HNC patients treated with combined therapies. Many factors adversely affect QoL, in particular skin toxicity is one of the key element within this context. The possibility to reduce skin dose with IMRT for advantages in terms of QoL is warranted and the correlation between skin dosimetry and QoL will be further evaluted in the framework of this study.

P087

PILOT ASSESSMENT OF GLIM CRITERIA IN HEAD AND NECK CANCER: PREDICTIVE ABILITY OF WEIGHT LOSS AT THE END OF CHEMO-RADIOTHERAPY

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Aims: Evaluation of the ability of GLIM SCORE in predicting risk of weight loss at the end of a radiochemoterapy (RCT) treatment for head and neck cancer in an homogeneous cohort of patients submitted to prospective standardize nutritional counseling.

Methods: From October 2019 to March 2020 we selected 20 patients with new diagnosis of head and neck cancer (HNC) who underwent radiotherapy (RT) or radiotherapy plus chemoterapy (CTX) both with radical intent, preoperative intent or postoperative intent if lymph node stations were included in the radiation field. IMRT (VMAT or tomotherapy) was administered to all patients with a range doses from 50 to 69.9 Gy. Nutritional counseling was provided at baseline, 3-4 weeks after treatment, at the end of RT, one month and three months later. It consisted of dietetic history, estimated total daily energy requirements, protein-calorie requirements, anthropometric measurements, GLIM score malnutrition and PG-SGA score, prescription of oral nutritional supplements (ONS) if indicated. The primary endpoint was to evaluate prospectively the correlation between GLIM SCORE and weight loss at the end of treatment.

Results: At baseline nutritional counseling all patients had oral intakes, 2 patients (10%) had already received ONS prescription and one patient (5%) had gastrostomy tube feeding. Mean weight was 63,5 kg (63,5 ± 13; 35,7 kg- 92,8 kg). Mean BMI was 23,5 kg/m^2 (23,5 ± 3,9; 15,9 kg/m^2- 29,7 kg/m^2). According to GLIM score, 5 patients (25%) had stage I malnutrition, 3 patients (15%) had stage II malnutrition, 12 patients (60%) were normonourished. At the end of RT, we reported a mean weight of 60.5 kg (60.5 ± 13; 36.6 kg -90.3 kg), a mean weight loss of 3,5 kg (3,5 ± 2,75; 0 kg -10,5 kg), a mean percentage of weight loss of 5,67% (5,67 ± 5,02; 0-20,19%). We found no correlation between basal GLIM SCORE and weight loss at the end of treatment (Pearson correlation coefficient p = 0.15 ; chi-square test p=0.22) neither in the ability to predict the risk of weight loss using Pearson correlation

coefficient and chi-square test. The little sample of patient enrolled could be a strong limitation.

Conclusions: In patients with HNC who undergo RCT, GLIM score could be an interesting tool to consider during nutritional counseling to follow and predict malnutrition and weight loss. Up to now there is not yet a validation of this score, we need further studies to investigate it.

P088

A COMPARISON BETWEEN RADIATION ONCOLOGISTS AND THERAPISTS WITH THE AIM OF PARTIAL DELEGATION OF SET-UP CONTROL IN HEAD AND NECK CANCER PATIENTS.

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Aims: To evaluate the partial delegation from the radiation oncologist(RO) to the radiation therapist(RT) of the on-board imaging (OBI) and cone beam CT (CBCT) imaging position control in patients with head and neck (H&N) cancer treated with SIB-IMRT (Simultaneus Integrated Boost-Intensity Modulated Radiation Therapy).

Methods: From June 2019 to May 2020, 45 histologically confirmed patients with H&N cancer stage III-IV were treated with SIB IMRT (69,96/59.4/54 Gy in 33 fr). Imaging set-up control was evaluated (during irradiation/treatment) with kV CBCT images once a day for three days and thereafter once a week. The rest of the days we evaluated kV OBI images. Evaluation was performed between 11 RTs and 2 ROs. The RTs and the ROs double - blind reviewed daily images. The mean and standard deviation (SD) of all measures and the concordance of decisions between RTs and ROs were calculated.

Results: About 360 CBCT and 990 OBI images were analysed. In the first six months, the concordance of measurements (difference of 3mm or less) was 86% with CBCT images, and 87% with OBI images. Instead, in the next five months, thanks to the skills acquired by the radiation therapists, the concordance of measures (with a difference of 2mm or less) was 95% with CBCT images and 98% with OBI images. The mean of the difference of the measures was 90, 5% with CBCT images and 92, 5% with OBI images.

Conclusion: The small gap between the radiation oncologist's and the radiation therapist's measures allows a partial delegation of positioning images control, ensures safety of the treatment and reduction of therapy time.

P089

AUDIT ON THE TREATMENT WITH UPFRONT RADIOTHERAPY OF 214 CONSECUTIVE PATIENTS WITH HEAD AND NECK CANCER. PART 1: TREATMENT DELIVERY AND ACUTE TOXICITY

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Aims: The treatment of Head and Neck cancer (H&Nc) involves complex resources and multiprofessional expertise. To monitor the quality of the whole process, well designed audits should be performed on a regular basis. We describe the results of a three-stage audit performed at our Radiotherapy (RT) Unit addressing the non-surgical treatment of H&Nc patients (pts) from 2009 to 2018. In this abstract we describe the target population and report on the findings of the first stage of the audit process.

Methods: From 2/2009 to 12/2018 820 H&Nc pts were treated with RT. We excluded 441 pts diagnosed at other hospitals,146 pts treated with post-operative or palliative aim, and 19 pts for other reasons: 214 pts are left representing the study population. Inclusion criteria are 1) confirmed histology of squamous cell or unspecified carcinoma of pharynx, larynx, oral cavity, sinonasal region or unknown primary, 2) diagnosis and treatment fully at our Hospital 3) upfront RT with curative intent. Male/female ratio was 169/45, age ranged between 18 and 90 (median 66). Primary sites were larynx (34%), oropharynx (31%) and nasopharynx (18%). Stage mix (7th ed.) was: stage 1=26%; stage 2=14%; stage 3=20%; stage 4=41%. Acute toxicity was resumed from clinical charts in 46 of all 48 pts treated from 2016 to 2018.

Results: Delivered RT dose ranged between 60 and 76 Gy (median 70 Gy), with all but one patient receiving at least 64 Gy; 76% of pts received a total dose ≥ 70 Gy or equivalent. 180 pts received 2-Gy daily fractions, 34 pts were treated with mild acceleration (2.1 Gy daily). Duration of RT ranged between 42 and 116 (median 50) days; ratio of actual duration of RT as compared to optimal duration ranged between 0.89 and 2.47 (median 1.09); in 100 pts this value was ≥1.10. Opioids were prescribed for acute mucositis in 27 pts (59%), with a median time to prescription of 33 days. Weight loss ranged between 0.80 and 1.01 (median value 0.93). A value ≥10% was found in 28% of cases. In-patient supportive therapy was prescribed in 7 pts (15%) and a feeding tube was positioned in 3 pts (7% of total cases).

Conclusions: In our study, prescription and delivery of RT were appropriate in terms of total dose, but treatment time prolongation was recorded in a significant proportion of pts. Acute toxicity was substantial with 59% of cases receiving opioids during RT, invasive procedures to support nutrition were not frequent while weight loss was relevant in one third of cases.

P090

AUDIT ON THE TREATMENT WITH UPFRONT RADIOTHERAPY OF 214 CONSECUTIVE PATIENTS WITH HEAD AND NECK CANCER. PART 2: LONG-TERM SURVIVAL AND DISEASE CONTROL RATES

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Aims: The treatment of Head and Neck cancer (H&Nc) involves complex resources and multiprofessional expertise. To monitor the overall quality of the whole process, well designed audits should be performed on a regular basis. We describe the results of a three-stage audit performed at our Radiotherapy (RT) Unit addressing the non-surgical treatment of H&Nc patients (pts) treated from 2009 to 2018. In this abstract we report the results of the 2nd Stage of the audit dealing with long-term survival and disease control rates.

Methods: 214 consecutive pts fully managed at our Hospital and treated with curative intent RT with a diagnosis of squamous or unspecified carcinoma of H&N sites were included. Male to female ratio was 169:45, age was 18-90 years (median 66). Most frequent primary sites were larynx (34%), oropharynx (31%) and nasopharynx (18%). TNM stage (7th ed.) was I in 25%, II in 14%, III in 20% and IV in 41% of cases.

Results: Outcome rates are reported as 3-y and 5-y actuarial rates (Kaplan-Meier estimates). In the whole group survival rates were 78% and 73% and rates of any failure 72% and 68%. Survival by stage were 98% and 92% for stage I, 80% and 69% for stage II, 84% and 84% for stage III, 60% and 58% for stage IV. Rates of any failure by stage were 87% and 83% in stage I, 72% and 72% in stage II, 88% and 82% in stage III, 55% and 50% in stage IV. Survival by site was worst for oral cavity (22% and 16%), best for larynx (91% and 88%) and nasopharynx (85% and 80%), intermediate for oropharynx (74% and 68%) and hypopharynx (75% and 75%). In pts with stage I larynx cancer (n=44) local failure rates were 93% and 86%. In pts with oropharyngeal cancer, rates of any failure by p16 status were 76% and 59% for p16+, 52% and 52% for p16-, 84% and 78% for p16 unknown cases.

Conclusions: Outcome of our study population compares favorably with published data in terms of overall survival and control rates. The worst outcome was in cancers of the oral cavity: all these cases were actually excluded from upfront surgery due to advanced disease and/or severe comorbidities. Cancers of pharynx and of larynx showed good 5-year survival and control rates far greater than 50% (range 68-88%). Both the unexpected inversion of outcome in stage II and stage III, and the slightly higher than expected local failure rates in stage I larynx cancers deserve further analyses.

P091

RADIOTHERAPY IN FRAGILE ELDERLY HEAD AND NECK CANCER PATIENTS: A SINGLE CENTRE EXPERIENCE

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Aims: Elderly patients with head and neck cancer presenting with multiple comorbidities - diabetes, cardiac disease, renal insufficiency, poor nutritional status, immobility, and cognitive decline - represent a challenging clinical dilemma. The purpose of the study was to assess the impact of pretreatment evaluation to assess factors that increase morbidity during radiotherapy, ensuring durable outcomes with an acceptable treatment toxicity.

Methods: In our preliminary analysis, we selected pts, aged ≥75 years, treated with IMRT (Intensity-modulated radiation therapy) or VMAT (Volumetric modulated arc therapy) for head and neck cancers from 2008 to 2019. All pts were screened with Geriatric-8 tool (G8) test.

Results: We included 50 pts, 38 males and 12 females, with a mean age of 81,16 (range: 75-94) at diagnosis. Tumor locations were larynx (18/50, 36%), oral cavity (12/50, 24%), oropharynx (11/50, 22%), hypopharynx (4/50, 8%), nasopharynx (3/50, 6%) and major salivary gland (2/50, 4%). All patients were defined as frail according to G8 score. Pts received radiotherapy with curative intent, either in definitive or adjuvant setting, with a total dose to high risk CTV between 54 Gy and 70 Gy with standard fractionation (1,8-2,0 Gy/day). Two out of 50 pts (4.0%) received concurrent chemotherapy based on weekly cisplatin. Nine pts required preventive PEG (percutaneous endoscopic gastrostomy) to ensure adequate nutrition during treatment. Eight patients (16%) experienced G1 acute skin toxicity according to RTOG scale, while 18 patients (36%) experienced G2 toxicity. Ten patients

(20%) developed G3 toxicity, while 14 patients (28%) completed the treatment with no skin toxicity. Six patients (12%) experienced G1 acute mucosal toxicity, 17 (34%) G2, 6 (12%) G3. Twenty-one pts (42%) had no mucosal toxicity. Only two pts needed hospitalization. The median follow-up was 14 months (range: 6-58) with 54% of complete response. Ten patients were lost at follow-up immediately after the end of radiotherapy course. The analysis of overall, disease-specific and disease-free survival are ongoing.

Conclusions: From our analysis, radiotherapy with curative intent, even combined with concurrent chemotherapy, can be appropriate in elderly patients. The results are promising in terms of efficacy and tolerance, with a good toxicity profile and favorable disease response.

P092

AUDIT ON THE TREATMENT WITH UPFRONT RADIOTHERAPY OF 214 CONSECUTIVE PATIENTS WITH HEAD AND NECK CANCER. PART 3: LATE EFFECTS AND QUALITY OF LIFE

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Aim: The treatment of Head and Neck cancer (H&Nc) involves a multidisciplinary effort that should be submitted to regular auditing. We report the results of the 3rd part of our audit concerning late effects and Quality of Life (QoL) in long-term survivors after upfront radiotherapy (RT).

Methods: The original population included 214 consecutive patients (pts) fully managed at our Hospital with upfront RT after a diagnosis of carcinoma of H&N sites. Overall clinical outcome was favourable with a survival probability of 73% at 5 years (y). For the present analysis we selected pts matching the inclusion criteria: complete response after RT+/-chemotherapy, follow-up duration >2 y, no disease recurrence at any sites. Three questionnaires were administered: the EORTC C-30 module (we report only the results of the item "overall functioning"), the EORTC Head & Neck 35 (H&N 35) module and the Hospital Anxiety and Depression Scale (HADS) module. Questionnaires have been delivered through telephone interview to several pts during the Covid-related health emergency.

Results: Have been compared with reference values taken from literature (Hammerlid et al, 2017). Results Sixty-eight questionnaires have been analysed. Male:female ratio was 49:19, age was 26-89 y (median 64.5), interval range between RT completion and survey was 2.3-11.2 y (median 4.9), most frequent primary sites were oropharynx and larynx, stage at diagnosis was III or IV in 61% of cases. Average score for Global Health in the C30 module was 80.1%, higher (better) than the reference value of 64.1%. Several average scores for symptom scales/items in the H&N 35 module were higher (worse) than reference. Symptoms showing the worst outcome were xerostomia (39,4% vs 12,0%), sticky saliva (28,3% vs 5,9%), teeth discomfort (23,2% vs 8,8%), dysgeusia (15,2% vs 4,5%), mouth opening (9,1% vs 2,0%), dysphagia (12,6% vs 1,6%) and local pain (7,1% vs 3,4%). A very low score for the item "malaise" was recorded (1.0% vs 13.6%). Concerning HADS scale, 8 cases were at risk for depressive syndromes and 3 cases had a score higher than cutoff, whereas for anxiety complains 5 cases reported a borderline score and 5 cases exceeded cutoff.

Conclusions: Our results show that late effects after RT+/-CT are significant but acceptable in the context of a good residual overall health. The most relevant late effects are related to salivary gland damage. The global health status, malaise and mental status are only minimally affected.

P093

EVALUATION OF LIFETIME AND FUNCTIONALITY OF VOICE PROSTHESIS

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Aims: Voice prosthesis is the most preferred method for postlaryngectomy voice rehabilitation . Provox® is currently the most widely used voice prosthesis. The purpose of this study is to assess factors influencing Provox voice prosthesis lifetime and quality of voice.

Methods: We included all patients that underwent Total Laringectomy with implanted Provox voice prosthesis from January 2019 till March 2020. Patients were evaluated every month for the first year, then every three months. The voice prostheses were replaced if complications were observed, as salivary leakage or prosthesis deterioration. Functionality of the voice prosthesis was scored by an expert logopedist with a scale from 0 (poorer functionality) to 10 (better functionality). Time to substitution (TTS) was calculated from surgery till the replacement of the prosthesis and Kaplan Meier analysis was used for survival analysis. Clinical variable (sex, age) as well as adjuvant therapies

(radiotherapy with or without chemotherapy) were taken in consideration. Differences in functionality were calculated with Chi-Square test.

Results: A total of 25 patients were included in our analysis and 17/25 patients underwent adjuvant therapies. Median TTS was 208 +/- 17 days (mean 240 days, range 39-552 days). Percentage of patients who did not underwent replacement were 80% at three months, 66% at six months and 40% at nine months. Median functionality was 8 (range 5-10). None of the clinical variables or adjuvant therapies correlated at survival analysis (p:0,613 for RT and p:0,617 for CHT). Females showed a poorer functionality than males (p:0,025).

Conclusions: Adjuvant therapies don't seem to modify the functionality of voice prosthetic, whereas females show a poorer voice quality than males. Our preliminary results need to be confirmed in large series with a greater follow up period.

P094

PROGNOSTIC ROLE OF SARCOPENIA AND PNI IN HNSCC PATIENTS UNDERGOING RADIOCHEMOTHERAPY

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Purpose: To evaluate the role of Sarcopenia and Onoderàs Prognostic Nutritional Index (PNI) as a prognosticators of poor compliance to concurrent chemotherapy with cisplatinum in patients with HNSCC.

Methods: We included all patients with locally advanced HNSCC undergoing concurrent chemoradiotherapy with cisplatinum (CDDP) at our Department betweeen January 2019 and May 2020. We contoured on simulation CT right and left Sternocleidomastoideus volumes, from the cranial to caudal muscle border and we calculated the mean intensity (MI). MI value was used as diagnostic tool of cancer sarcopenia. PNI is an indicator of both nutritional and immunological status of patient and was calculated according to the formula: 10 x Alb + 0.005 x TLC (total lymphocyte count). It is assumed to be a significant predictor of severe adverse events in HNSCC treated by radiotherapy. We considered patients receiving a cumulative dose of CDPP < 240 mg/m2 having poor compliance (PC). We correlated PC with clinical prognosticators (age, ECOG, sex, BMI, PNI) and MI, with Chi-square method (univariate) and Binary Regression Analysis (multivariate). ROC curve was also calculated.

Results: We included 51 patients (33 males and 18 females), with a median age of 64 years (range 48-84 years). The parameters that results significantly correlated with PC were MI (p: 0,005), ECOG (p: 0,034), PNI (p:0,011). At multivariate analysis, both MI and PNI remained significant (respectively p: 0,011, OR 0,78, and p:0,035, OR: 1,31). ROC curve area for the prediction of PC was 0,803 (0,680-0,931).

Conclusions: Both MI and PNI could represent an independent prognosticator of poor compliance to concurrent chemotherapy with cisplatinum in locally advanced HNSCC patients and deserve further investigations.

P095

ABSTRACT WITHDRAWN

P096

RADICAL HYPOFRACTIONATIONATED RADIOTHERAPY AND CONCURRENT CARBOPLATIN-PACLITAXEL IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (LA-NSCLC) PATIENTS: TOXICITY PROFILE AND OUTCOME

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Aims: The purpose of this phase II study is to investigate treatment related toxicity and tumor control in locally advanced NSCLC (LA-NSCLC) patients who received curative radio-chemotherapy (RCHT). Concomitant RCHT with 60 Gy in 30 fractions and double-agent chemotherapy is the standard treatment for LA-NSCLC patients not candidate for surgery1-3. In the RTOG 0617 trial, RCHT with Carboplatin plus Paclitaxel followed by consolidation therapy achieved a median overall survival (OS) of 28 months4. Dose escalation studies failed to demonstrate any benefit by increasing the total dose up to 74Gy. Hypofractionation, due to the higher biologically effective dose to the planning volume, might be associated to better loco-regional control and acceptable toxicity profile. So far, there are no trials investigating concomitant hypofractionated radiotherapy and doublet carboplatin-paclitaxel chemotherapy.

Methods: Consecutive LA-NSCLC patients were prospectively evaluated. Target volumes have been defined according to ICRU report 50, there was no expansion from gross tumor volume to clinical target volume (CTV). The planning target volume (PTV) has been created by adding 5 to 10 mm margins to the CTV. A total dose of 60 Gy (2.4 Gy per fraction) was prescribed to the 95% of PTV by using intensity-modulated radiation therapy (IMRT) technique. Treatment was

delivered daily, in 25 fractions, in 5 weeks. During radiotherapy was administered a weekly chemotherapy infusion of Carboplatin (AUC= 2) and Paclitaxel (45 mg/m^2). Finally, fit patients received consolidation therapy with the anti-PD-L1 Durvalumab or with Carboplatin (AUC= 6) and Paclitaxel (200 mg/m^2).

Results: Twenty patients were included. The median age was 69 (range 47-79), 80% had 0-1 performance status, 7 were active smokers. At diagnosis, 7 patients had Stage IIIA, 13 had Stage IIIB. Seven patients received adjuvant Durvalumab, 4 patients had 1 or 2 cycles of chemotherapy, 7 did not receive any further treatment after RCHT. Only 1 patient interrupted radiotherapy treatment due to toxicity. Nine patients experienced Grade 3-4 haematologic toxicity, 13 patients had mild/moderate lung toxicity (Table 1). After a median follow-up of 14.7 months the crude loco-regional control was 90%. Seven (35%) patients had distant disease progression.

Conclusions: Hypofractionated RCHT was associated to an acceptable toxicity profile and an excellent loco-regional control rate. The prominent pattern of failure was distant.

Table 1. Treatment related Adverse Events*.

	Severity	Nr of patients
Neutrophil count decreased	Grade 1	2
	Grade 2	4
	Grade 3	3
	Garde 4	/
Lymphocyte count decreased	Grade 1	/
	Grade 2	6
	Grade 3	9
	Garde 4	2
Platelet count decreased	Grade 1	5
	Grade 2	/
	Grade 3	1
	Garde 4	/
Anemia	Grade 1	1
	Grade 2	1
	Grade 3	/
	Garde 4	/
Cough	Grade 1	2
	Grade 2	6
	Grade 3	/
	Garde 4	/
Pneumonitis	Grade 1	2
	Grade 2	3
	Grade 3	/
	Garde 4	/
Fatigue	Grade 1	2
	Grade 2	4
	Grade 3	/
	Garde 4	/
Esophagitis	Grade 1	2
	Grade 2	10
	Grade 3	/
	Garde 4	/
Nausea	Grade 1	3
	Grade 2	3
	Grade 3	/
	Garde 4	/
Sepsis	Grade 4	1
Neuropathy	Grade 2	1

**Adverse Events are defined according to Common Terminology Criteria for Adverse Events v4.0 (CTCAE)*

P097

A MULTI-INSTITUTIONAL ANALYSIS OF FRACTIONATED VERSUS SINGLE FRACTION STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN THE TREATMENT OF PRIMARY LUNG TUMORS: A COMPARISON BETWEEN TWO ANTIPODAL FRACTIONATIONS

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Objectives: Stereotactic body radiotherapy (SBRT) is a consolidate treatment for inoperable early stage lung tumors, usually delivered in single or multi-fraction regimens. We aimed to compare these two approaches in terms of local effectiveness, safety and survival.

Material and methods: Patients affected by medically inoperable early stage lung tumor were treated at two Institution with two different schedules: 70 Gy in 10 fractions (TF) (BED: 119 Gy10) or 30 Gy in single fraction (SF) (BED: 120 Gy10).

Results: 73 patients were treated with SBRT delivered with two biological equivalent schedules: SF (44) and TF (29). The median follow-up was 34 months (range 3-81 months). Three-year Overall survival (OS) was 57.9%, 3-year cancer-specific survival (CSS) was 77.2%, with no difference between treatment groups. Three-year progression-free survival (LPFS) was 88.9% and did not differs between SF and TF. Overall, 4 cases (5.4%) of grade ≥3 pneumonitis occurred. No differences in acute and late toxicity between the two groups were detected.

Conclusion: SF and TF seems to be equally safe and effective in the treatment of primary inoperable lung tumors. TF schedule seems to be more appropriate for large lesions, while tumors smaller than 25 mm may benefit from the SF.

P098

ROLE OF CONE BEAM CT (CBCT) FOR INTERNAL TARGET VOLUME DEFINITION IN STEREOTACTIC BODY RADIOTHERAPY OF LUNG TUMORS

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Aims: To determine Internal Target Volume (ITV) using CBCT system in Stereotactic Body Radiation Therapy (SBRT) of lung cancer.

Materials and Methods: A retrospective analysis

was carried out for lung cancer patients who underwent SBRT from December 2017 to May 2020. All patients were immobilized using a wing board system, and a free-breathing CT scan was acquired. Thereafter, 2 CBCTs in free-breathing, with at least two hours period, were acquired. Reconstructed images were exported to the TPS image fusion module (Syntegra-Pinnacle) and have been used to delineate the GTV and ITV. We delineate the GTV-CT, and two other contours named GTV-CBCT. Internal Target Volume at time 0 (ITV0) was obtain by combination of GTV-CT and GTV-CBCTs. An additional margin was added for PTV. All Patients underwent 3D-CBCT scan for verification before each fraction of SBRT, using automatic or manual registration when appropriate. Pre-treatment CBCTs images were sent to Syntegra-Pinnacle and were co-registered to the reference planning CT images. ITVdf (date of fraction) were delineated comparing this volumes with planned ITV and PTV. Therefore, two new contours were generated, named ITVdf-ITV0 and ITVdf-PTV. Finally, the percentage of ITVdf that exceeds from ITV0 (%ITVdf-ITV0) was extracted.

Results: Among 50 treated patients, 9 patients with primary (89%) or metastatic (11%) lung tumours were available for this analysis. Seven tumors were located in the upper right lobe, 1 in the lower right lobe and 1 in the upper left lobe. Forty-four pre-treatment CBCTs have been evaluated. All daily ITV were included in PTV (ITVdf-PTV was null in all cases), while in all but 3 cases%ITVdf-ITV0 exceeded more than 5% (see enclosed Figure 1).

Conclusion: These preliminary results provide data on the ability of CBCT to generate an ITV if a 4D-CT is not available. The inclusion of more patients along with lower lobe site are needed to confirm this ability.

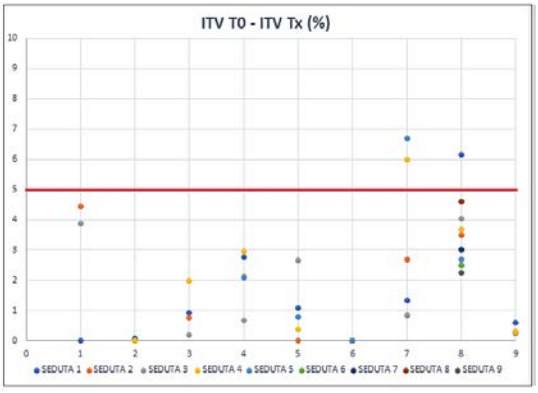

Figure 1.

P099

EVALUATION OF PLAN QUALITY AND TREATMENT EFFICIENCY USING VOLUMETRIC-MODULATED ARC THERAPY FOR SINGLE- VS. MULTI-ISOCENTER STEREOTACTIC ABLATIVE IRRADIATION OF SYNCHRONOUS MULTIPLE LUNG NODULES

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Aims: To evaluate the plan quality and efficiency of single- versus multi-isocenter volumetric-modulated arc therapy (VMAT) for multiple lung lesions with stereotactic irradiation technique (SABR).

Methods: Since 2019, six patients with two or more lung lesions (three multiple metastases and three multiple primary NSCLC) underwent VMAT SABR treatment in our institution. Doses were 36 Gy/60 Gy in 5/8 fractions prescribed to 100% isodose. Four patients were treated for two lesions, and 50% had bilateral disease. Each patient performed a 4DCT with Anzai respiratory gating system on a Toshiba Aquilion LB CT and internal target volume (ITV) was evaluated with MiM Maestro v.6.7.5. Plans were optimized in the TPS Elekta Monaco v5.11 placing a single isocenter between the lesions. The mean isocenter to tumors distance was 6 cm and the mean combined planning target volume (PTV) was 54 cc. Treatments were performed with an Elekta Synergy Agility accelerator equipped with HexaPOD™, a robotic couch with six degree of freedom. For comparison, the VMAT plans were retrospectively re-optimized using identical constraints and planning parameters, but with separate isocenters placed in the center of each PTV. Both plans were normalized to receive the same target coverage. The conformity (CI) and heterogeneity (HI) indices, maximum dose in the lung at 2 cm away from the PTV and lungs doses were compared for both plans.

Results: Average values of CI, HI and maximum dose at 2 cm for single/multi-isocenter plan, were 0.32/0.34,1.13/1.12 and 77/73%, respectively. Dose to the lungs in terms of V20, V5 and mean lungs dose were 5.9/6.2%,45/43.5% and 6.51/6.50 Gy, respectively. The total number of MUs was increased by a factor of 1.65 (range 1.4-1.9) moving from single- to multi-isocenter approach raising the average beam on time from 8 to 13 minutes.

Conclusions: There was no clinically significant difference in the plan quality of single- and multi-isocenter evaluated according RTOG guidelines. Faster treatment delivery for single-isocenter approach can improve patient compliance and reduce the amount of intrafraction motion errors. The rotational errors could cause dosimetric changes in organs at risk and target coverage especially when the distance between nodules is wide but these errors can be compensated by robotic couch corrections.

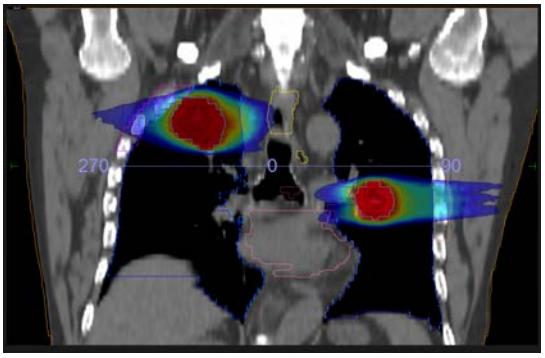

Figure 1.

P100

STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN STAGE I NON SMALL CELL LUNG CANCER (NSCLC): REPORT OF OUTCOME AND TOXICITY FROM A SINGLE ITALIAN CENTER

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Aims: SBRT is a curative approach in Patients with early-stage lung cancer unsuitable for surgical resection and may be soon become an equivalent curative tool also in Patients suitable for surgery. We report outcome and toxicity from our Center, showing how SBRT can allow Patients to achieve cure with an excellent toxicity profile.

Methods: 47 stage I NSCLC patients were treated in a single Italian center with SBRT with curative intent; most patients had been deemed unfit for surgery because of severe comorbidities and only a minority because of surgery refusal. Median age was 80 years (range 66-86 years). Prescription dose was normalized at isodose 65%. Median total dose was 40 Gy (range 28-50 Gy) in 3-5 fractions. Istology was adenocarcinoma (53%), squamous cell carcinoma (21%) and unspecified non small cell lung cancer (26%). Fluorodeoxyglucose positron emission tomography (FDG-PET) before treatment is routinely used in our Center. Pulmonary function was routinely assessed before SBRT. Planning met the constraints of organs at risk as in NCCN (National Comprehensive Cancer Network) guidelines. Response to treatment was assessed with computed tomography (CT) 6-8 weeks after SBRT and with FDGPET 3 months after SBRT. Data were collected retrospectively.

Results: Median follow-up was 14 months (range 4-55 months). Thirty-eight (81%) patients achieved complete response. Nine patients (19%) did not achieve complete response, meaning that SUVmax after treatment was such that it did not permit to exclude persistent disease. Median SUVmax before SBRT was 13 (range 25.44-2.25) for complete responders and 8 (range 28.2-1.9) for non-complete responders. Median prescribed total dose was 40 Gy (median number of fractions: 5) for both responders and non responders. No toxicity ≥ grade 3 was recorded.

Conclusions: Our report confirms SBRT can achieve excellent rates of cure with minimal toxicity for stage I NSCLC Patients. The limited number of fractions and the non-invasive nature of SBRT when compared to surgery are in favor of SBRT as a curative tool. We therefore advocate the need to directly compare SBRT and surgery as it is likely that they have a comparable rate of cure whilst the burden of toxicity expected with SBRT is less. A higher SUVmax before SBRT did not demonstrate to be a predictor for lack of response in our analysis. This is consistent with some reports, whilst others have advocated a role for SUVmax before SBRT for prognosis after treatment.

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DAILY ADAPTIVE STRATEGY SIMULATION FOR 10 LUNG CANCER PTS TREATED WITH RADIOCHEMOTHERAPY WITH REDUCED ICTV-PTV MARGINS

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Aims: To evaluate interfraction target coverage and primitive tumour GTV shrinkage in a cohort of lung cancer patients treated with radical intent radiochemotherapy (RTCHT) and planned with 4DCT with reduced iCTV-PTV margins.

Materials and Methods: 10 lung cancer patients treated from 2017 and 2019 with a diagnosis of NSCLC or SCLC were identified. 4D CT acquisition were performed, iCTV-PTV margin of 6 mm in cranial-caudal direction and 4 mm in radial direction were applied. Dose prescription were 60 Gy in 30 fraction, PTV coverage prescription was D95%≥95%. IMRT versus V-MAT RT plan were generated. Daily online CBCT images were acquired. We retrospectively recontured GTV_T, CTV and Organs at risk (OAR) for all 30 CBCT for all patients. A DVH representing each single fraction and a mean DVH representing all 30 fractions were generated using an in-house software (PRO-DVH). Mean plan_adaptive was compared to plan_reference. Z test was exploited to detect statistically significant differences between provisional and adaptive CVT coverage. A shrinkage GTV_T map was also generated.

Results: In seven of 10 patients, mean target coverage of plan_adaptive resulted equal or superior to plan_reference. In three cases CTV coverage resulted inferior to plan_reference (D95=90% versus D95=95%,

D95%=90% plan_adaptive versus D95%=94% plan_reference and D95%=87,5% versus D95=95%, respectively, all p<0,001). In two of three patients, the analysis of DVH_adaptive of each fraction showed a progressive reduction in target coverage in the last 10 fractions. No trends were identified for the second patient. Concerning GTV_T volumes, we observed a mean regression in the whole series of 48% (range 32%-65%), with a major trend of reduction between the VIII and the XX fractions.

Conclusion: Margin reduction does not underdoes clinical target volume in the majority of patients. GTV of primary tumour demonstrated a mean shrinkage of 48%. These observations lead us to prospectively select candidates for a complete adaptive replanning strategy. It could be of benefit in the second or third week of treatment, in particular when a suboptimal target coverage was accepted at the beginning due to volume complexity. Future studies should consider a prospective adaptive strategy with the aim of a better target coverage, sparing lung tissue and, if so, attempt to an isotoxic dose escalation.

P102

MANAGEMENT OF LUNG CANCER DURING THE COVID-19 PANDEMIC: THE EXPERIENCE OF ITALIAN CENTER

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Aims: New Coronavirus Disease (COVID-19) has had a devastating impact around the world and has rappresented a challenge to healthcare systems.The management of cancer care has become a crucial issue for clinical services to cancer patients. Patients with lung cancer was a particularly vulnerable population. The current challenge in treating patients with lung cancer is the need to balance the risk of a potentially life-threatening infection with COVID-19 against the dire consequences of delaying or not treating a life-threatening malignancy. The aim of trial was the evaluation of the change in the management of these patients.

Methods: We retrospectively reviewed the data relating of the number of lung cancer patients who assed to Our Radiation Therapy department and what types of treatement administered before and after COVID-19 pandemic. According to ESTRO & ASTRO raccomandations, where possible, alternative therapies can be used, such as stereotactic body radiation therapy (SBRT) for patients with stage I- II NSCLC. Postponement or interruption of radiotherapy treatment of COVID-19 positive patients is generally recommended to avoid exposure of cancer patients and staff to an increased risk of COVID-19 infection.

Results: Two window periods, 1/3/2019–30/4/2019 and 1/3/2020–30/4/2020, were chosen for comparison. No significant difference in terms of percentage of concomitant chemo-radiotherapy (cCTRT) in stage III NSCLC patients was observed, calculated as the ratio between the concomitant chemo-radiotherapy treatments and the overall chemo-radiotherapy treatments (concomitant plus sequential: csCTRT). We experienced 4(50%) out of 8 cCTRT in 2019 and 3(60%) out of 5 in 2020. Our Centre increased the percentage of hypofractionated regimens on the overall treatment plans: from 21%(10/48) to 31% (10/32) in the same time periods. Finally, a reduction of palliative treatments (meant as disease-symptoms relief on brain, bone, chest) was observed in COVID-time, 21 in 2019 and 17 in 2020.

Conclusions: The department reorganization, limiting the number of access to the hospital, involved also our Institution leading to a change in the management of lung cancer patients with an increased of hypofractionated treatments and a reduction of palliative treatments.Our approach was in line with the Italian experience recently reported by the Italian Association of Radiotherapy and Clinical Oncology. According to literature, hypofractionation could be considered as one of the basic strategies to efficiently cope with the pandemic disruption in lung cancer patients.

P103

TEMPORAL MUSCLE THICKNESS AS A POTENTIAL BIOMARKER FOR PREDICTION OF OVERALL SURVIVAL IN NSCLC PATIENTS WITH BRAIN METASTASTES TREATED WITH STEREOTACTIC RADIOTHERAPY

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Objectives: Temporal muscle thickness (TMT) was described as a surrogate marker of skeletal muscle mass. The purpose of this study was to evaluate the prognostic relevance of TMT in non- small-cell lung cancer (NSCLC) patients with newly diagnosed of single brain metastasis (BM) treated with stereotactic radiotherapy (SRS).

Methods: TMT was retrospectively assessed in 89 NSCLC patients (81 adenocarcinoma and 8 squamous cancer cell, median age 67,5, range 27-81,M:F 1,5:1) with a single newly diagnosed brain metastasis and which subsequently underwent to SRS between 2011 and 2019. The following were the inclusion criteria: available MRI examination of the brain or computer tomography (CT); the temporal muscle had to be depicted in its whole extension; BM were treated with SRS. TMT was assessed by an expert radiologist at the time of diagnosis of brain metastases on axial T1-weighted MR images or on axial CT scan with contrast. The measurements were taken perpendicular to the long axis of the temporal muscle using the orbital roof (cranio-caudal) and the Sylvian fissure (anterior–posterior) as anatomical landmarks as reported by Furtener et al. TMT was measured on the left and on the right side

in each patient and then a media was performed. Disease-specific graded prognostic assessment (DS-GPA), the presence of extracranial metastases, histology and survival times were evaluated. For the present study, overall survival (OS) was defined as days between the diagnosis of brain metastasis and death or date of last follow-up.

Results: Patients with a TMT above the median (7.39 mm) had a significantly improved survival prognosis compared to those who had a TMT > median (p= 0,003; HR 0.459,IC 0.274- 0.767). The risk of death was increased by 20% with every millimeter reduction in TMT. In the multivariate analysis, TMT (HR 0.479; 95% 0.279–0.825; p=0,008), histology adenocarcinoma (HR 0.411, CI 0.299-0.798,p=0.003) showed a statistically significant correlation with OS.

Conclusion: In our study we have demonstrated that TMT is an independent predictor of survival in NSCLC patients harboing BM, which is consistent with the present literature. This is based on the fact that muscle wasting is associated with cancer-related cachexia.This parameter may aid patient selection for the choice of different treatment options.

P104

MANAGEMENT OF ARTHRALGIA IN A PATIENT WITH LUNG ADENOCARCINOMA UDERGOING DURVALUMAB TREATMENT: A CASE REPORT

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Aims: This case report illustrates how we managed the appearence of arthralgia during immunotherapy with a multidsciplinary approach.

Materials and methods: We treated our 72 years old patient with lung adenocarcinoma TxN3M0 with chemotherapy and concurrent radiation therapy. The patient underwent volumetric modulated arc therapy with a dose of 60 Gy at 2 Gy per once-daily fraction. In addition we administrated six cycles of concomitant chemotherapy with paclitaxel 60mg/m^2 and carboplatin AUC=2 once a week, with good tolerability and low toxicity. In order to assess the clinical response we performed a total body CT at the 4th week by the end of the treatment. The imaging demonstrated a partial response. In consideration of the PDL1 >1% expression we started the anti-programmed death ligand 1 antibody Durvalumab as consolidation therapy. The patient showed no significative side effects until the 7th cycle, when he complained about pain, stiffness and problems in performing hand-related activities of daily living. We obtained relief of symptoms with Ibuprofen 400mg/die assumption. A rheumatological examination, including sierological analysis, high resolution ultrasonography of joints and capillaroscopy, diagnosed immuno-related hand osteoarthritis. A 4 mg per day metilprednisolone therapy leaded to the resolution of symptoms.

Results: The introduction of low dose corticosteroids showed a clinical improvement without interruption or drug switching. At the XXIInd cycle Durvalumab is still well tolerated.

Conclusion: An accurate clinical monitoring and a multidisciplinary collaboration leaded to prompt and timely improvement of symptoms. A cross-sectoral approach coul be the key for the management of the immunotherapies' wide range of side effects.

P105

REAL LIFE EXPERIENCE OF COMBINED IMMUNOTHERAPY AND RADIATION (IRT). A SINGLE-INSTITUTION DATA ANALYSIS ON SAFETY AND LOCAL/DISTANT EFFECTIVENESS

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Aims: Combined Thoracic radiation therapy and immunotherapy (iRT) is an increasingly used strategy for NSCLC. However, there are concerns about the safety of a combined approach. Primary aim of our study was to evaluate the safety of the combined treatment in a mono-institutional cohort of NSCLC patients. Secondarily we tried to observe if any abscopal effect of iRT occurred.

Methods: We retrospectively evaluated IV stage NSCLC patients with confirmed histological diagnosis, undergoing radiation treatment and immunotherapy from 1st March 2015 to 28th February 2020 at our institution. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 was used to define acute and late toxicities. Follow-up time was calculated from the end of radiotherapy (RT).

Results: Fifty-one patients were evaluated. The majority of patients (74.5%, 38/51) underwent concurrent RT within immunotherapy, 21% (11/51) received at least once RT within 0 -3 months from last immunotherapy administration, 4% (2/51) underwent RT 0- 3 months before starting immunotherapy. EBRT was delivered in different settings: SBRT or long course RT to oligometastatic or oligoprogressive sites of disease (total 25 patients, 49.1%), VMAT (n=13) or 3DCRT (n=13) treatment for palliative intent in 26 patients (50.9%). The RT Planning Target Volume was localized in thorax in 12 patients (23.5%). Mean follow up was 10.1 Months (Range 1-24 M). 34/38 patients (89.4%) from the concomitant iRT group showed no/minimum adverse effects; 4/38 (10.6%) patients, all with thoracic PTVs, developed lung acute toxicity > G3; two of them died for G5 pneumonia after 21.6 Gy of radiotherapy and 6 months after the end of RT respectively. One patient discontinued treatment for bilateral G3 pneumo-

nia requiring hospitalization. Treatment details of patients experiencing grade > 3 lung toxicity are summarized in table 1.In a single patient treated with SBRT to a paraortic mediastinal node concurrently with IT a reduction in FDG uptake was detected also in a supraclavicular node not irradiated at the PET-CT scan performed after SBRT during first re-evaluation.

Conclusions: iRT should be administered with caution in patients undergoing treatment to PTVs localized in thorax due to the higher risk of lung toxicity. Abscopal effect is rare and difficult to detect. However it should be pursued during follow-up.

Table 1.

	Severity	Nr of patients
Neutrophil count decreased	Grade 1	2
	Grade 2	4
	Grade 3	3
	Garde 4	/
Lymphocyte count decreased	Grade 1	/
	Grade 2	6
	Grade 3	9
	Garde 4	2
Platelet count decreased	Grade 1	5
	Grade 2	/
	Grade 3	1
	Garde 4	/
Anemia	Grade 1	1
	Grade 2	1
	Grade 3	/
	Garde 4	/
Cough	Grade 1	2
	Grade 2	6
	Grade 3	/
	Garde 4	/
Pneumonitis	Grade 1	2
	Grade 2	3
	Grade 3	/
	Garde 4	/
Fatigue	Grade 1	2
	Grade 2	4
	Grade 3	/
	Garde 4	/
Esophagitis	Grade 1	2
	Grade 2	10
	Grade 3	/
	Garde 4	/
Nausea	Grade 1	3
	Grade 2	3
	Grade 3	/
	Garde 4	/
Sepsis	Grade 4	1
Neuropathy	Grade 2	1

**Adverse Events are defined according to Common Terminology Criteria for Adverse Events v4.0 (CTCAE)*

P106

IMPACT OF DOSE COVERAGE ON LOCAL CONTROL RATE IN ULTRA-CENTRAL LUNG OLIGOMETASTASES TREATED WITH STEREOTACTIC BODY RADIATION THERAPY.

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Aims: Ultra-Central (UC) lung tumors are a subset of lung tumors defined in the presence of planning target volume (PTV) overlap or direct tumor abutment to the central bronchial tree, esophagus, pulmonary artery or pulmonary vein. In this setting, the use of Stereotactic Body Radiotherapy (SBRT) is controversial, because of the high risk of severe adverse events concerning these critical mediastinal structures. This is of particular interest in oligometastatic patients, for whom an ablative dose coverage must be achieved in order to obtain a survival benefit. The aim of our study is to identify clinical and dosimetric predictors of local control and toxicity in a cohort of oligometastatic patients receiving SBRT for ultra-central lung metastases.

Methods: Clinical and dosimetric parameters have been retrospectively reviewed in a cohort of oligometastatic patients treated with SBRT for ultra-central lung metastases. Local control (LC) rate, incidence and grade of toxicities were evaluated. Statistical Analysis was carried out to assess the impact of those predictors on local recurrence and adverse events.

Results: One-hundred-nine consecutive patients were included. A median Biologic Effective Dose (BED10) of 105 (75-132) Gy was prescribed. At a median follow-up of 17 (range 3-78) months, LC rates were 88% at 1 year and 87% at 2 years. Improved LC was correlated to a V95% > 85% (HR 0.15, 95%CI 0.05-0.49, p=0.0017) and a GTV < 90cm^3 (HR 0.2, 95%CI 0.07-0.56, p=0.0021). Overall toxicity incidence and cumulative incidence of severe (grade ≥3) toxicities were 20% and 5%, respectively. Increased overall toxicity incidence was correlated to higher D1cm3 Esophagus and V5Gy Lung (p=0.016 and p=0.013, respectively). Increased severe toxicity incidence was correlated to higher D0.1cm3 Heart (p=0.036).

Conclusions: Dose coverage more than 85% to the 95% of the tumor volume and tumor size less than 90 cm3 are independent predictors of improved local control rates. SBRT for UC lung metastases is associated with acceptable overall rate of AEs, but dose exposure of esophagus, lung and heart should be carefully assessed in an effort to minimize treatment-related toxicities.

P107

RADIOMIC APPROACH FOR PREDICTION OF RESPONSE TO RADIOCHEMOTHERAPY IN STAGE III NON-SMALL CELL LUNG CANCER

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Aim: The aim of this study was to investigate whether the integration of radiomic signatures based on the Gross Tumor Volume (GTV), but also on Clinical Target Volume (CTV) and Planning Target Volume (PTV) can be identified for predicting the response to adaptive therapies.

Materials and Methods: 130 patients with stage IIIA-IIIB NSCLC who underwent concomitant radiochemotherapy (RCT) were enrolled. The characteristics analyzed were extracted from the CT simulation imagies by performing manual contouring and defining 3D ROI of GTV, CTV and the PTV. Through the pyradiomics system we performed the segmentation of the different targets GTV, CTV and PTV, the calculation, the extraction of the features and the subsequent division into groups. For each segmentation and feature we performed the Wilcoxon Test and analyzed the comparison between GTV-CTV; GTV-PTV; CTV-PTV.

Results: The analysis carried out between the various segmentations showed a higher p-value average for the GTV-CTV group, while CTV-PTV group had a lower p-value average (Figure 1). A machine learning process allowed to identify for all three segmentations radiomic signatures correlated significantly to the early response to treatment. ROC curves obtained showed an AUC of 0.77, 0.71 and 0.74, respectively (Figure 2).

Conclusions: These data support the hypothesis that a specific radiomic signature can be identified not only considering the CTV but also GTV and PTV, confirming the potential and feasibility of a radiomic approach in predicting the response in patients with stage III NSCLC.

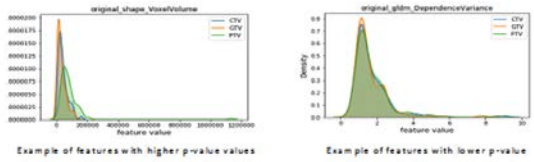

Figure 1.

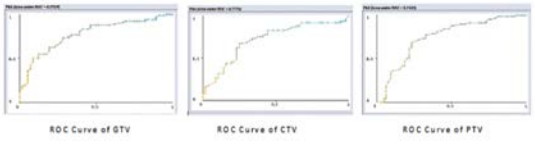

Figure 2.

P108

EXTREME HYPOFRACTIONATED STEREOTACTIC BODY RADIOTHERAPY IN LOCALLY-ADVANCED NON-SMALL-CELL LUNG CANCER: A PHASE II TRIAL

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Purpose: To assess local control (LC) and safety of extreme hypofractionated stereotactic body radiotherapy (SBRT) in unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients (pts) treated with radical intent.

Methods and materials: All patients were unfit for concurrent chemo-radiotherapy (ChT-RT). Neoadjuvant ChT was prescribed in fit patients. The tumor volume included primary tumor (T) and CT-PET positive node/s (N). A simultaneous integrated boost (SIB) was optimized to differentiate doses for T and N. Co-secondary endpoints were thoracic nodal-recurrence (tnR) free survival, distant-progression free survival (d-PFS) and overall survival (OS).

Results: 50 LA-NSCLC pts were recruited. Histology was squamous cell carcinoma (SCC) and adenocarcinoma (ADK) in 52% and 48%, respectively. 41(82%) had ultra-central tumor with PTV overlapping the major airways. 19 (38%) received neoadjuvant ChT and 5 (10%) adjuvant Durvalumab. In 24 (48%) cases T and N were separately treated using SIB technique to administer a higher dose to T. Median prescribed dose was 40 Gy (range, 35-55) and 40 Gy (35-45) in 5 fractions to T and N, respectively. At a median follow-up of 17 months (range, 4-59), 10 (20%) pts experienced local recurrence (LR) at a median time of 12 months (range, 9-28). The median LR-FS was not reached (95% CI ,28 to not reached). The 1-2- and 3-year LR-FS rates were 83%, 76% and 57%, respectively. Median tnR-FS was 34 months (95% CI, 34 to 34). The 1-, 2- and 3- year tnR-FS rates were 86%, 73% and 49%, respectively. Median d-PFS was not reached (95% CI, 24 months to not reached). The 1-2- and 3-year d-PFS rates were 85%, 65% and 57%, respectively. At last follow-up, 43 (86%) patients were alive, 27 (54%) without radiological evidence of disease. Median OS was not reached (95% CI, 42 months to not reached). The 1-2- and 3-year OS rates were 93%, 87% and 87%, respectively. No patients developed ≥ G3 acute and late toxicities. At multivariate analysis histology in favor of ADK (HR, 0.09;95% CI, 0.01-0.79), single nodal involvement (HR, 0.42; 95% CI, 0.04-0.88) and PTV (HR, 1.006;95% CI, 1.001-1.010) were predictors for LR-FS, distant progression and OS, respectively.

Conclusions: LA-NSCLC patients treated with extreme hypofractionated SBRT had optimal LC and promising OS in absence of ≥G3 toxicity. Our preliminary results provide an attraction to evaluate this approach in selected pts unfit to concurrent ChT-RT.

P109

LOCATION MATTERS: A NEW PREDICTIVE FACTOR FOR LOCAL CONTROL AFTER STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) FOR PRIMARY NON-SMALL CELL LUNG CANCER (NSCLC) AND LUNG METASTASES (LM)

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Aims: The use of stereotactic ablative radiotherapy (SABR) for the treatment of primary lung cancer and metastatic disease is rapidly increasing. The purpose of this study was to evaluate the correlation between tumor location and local control after SABR for primary non-small cell lung cancer (NSCLC) and lung metastases (LM).

Methods: Patients with lung tumors clinically staged, biopsy-confirmed NSCLC or lung metastases, treated with SABR between January 2017 and Jun 2019, were included. CT scan and 18F-FDG PET at 4 and 12 months after SABR were used for the response assessment. Retrospective analyses regarding patients' characteristics and local tumor control were performed. The RECIST Criteria ver 1.1 was used to evaluate morphological lesions response and the EORTC PET criteria (EORTC criteria) was used to assess metabolic tumor response.

Results: 435 lung lesions (186 NSCLC and 249 lung metastases) were treated with SABR, 234 parenchymal located tumors and 201 located to other sites in the lungs (76 central and 125 parietal lesions). The univariate analysis showed a correlation between tumor response and location. Four months after SABR, local control was 76.9% with no significant differences for tumor positions (p= 0.22). At 12 months, local control was 91.9% and parenchymal lesions showed a significant better response (p<0.001). SABR dose varied from 24 - 60 Gy (median 50 Gy) delivered in 3-8 fractions (median 5 fractions). No clinical acute or late toxicity was observed.

Conclusion: Tumor location is a predictive factor for local control after stereotactic ablative radiotherapy (SABR) for primary NSCLC and lung metastases. Parenchymal lesions showed a better response to SABR, probably due to lower doses received by central and parietal lesions, related to proximity of OARs.

P110

PROGNOSTIC ROLE OF PN STAGING, NODAL RATIO AND LOG ODDS OF POSITIVE LYMPH NODES IN BREAST CANCER PATIENTS

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Aims: Breast cancer (BC) is the first leading cause of cancer death in over 100 countries. Several prognostic factors are used in clinical practice but one of the most important has always been the lymph node status. Together to other predictors, it guide in the choice of adjuvant therapy. Nodal ratio (LNR) and more recently log odds of positive lymph nodes (LODDS) have been proposed as possible alternative to the traditional pN staging in several cancers. The aim of this study is to evaluate the prognostic power of pN, LNR and LODDS in BC patients.

Methods: All BC patients with positive nodes who underwent radiotherapy at the Radiation Oncology department of University "Federico II" from February 1999 to November 2012 were retrospectively analysed. Patients treated with neoadjuvant chemotherapy were excluded. The end points were breast cancer specific survival (BCSS) and disease free survival (DFS). LNR was calculated as the number of positive lymph node divided by the number of lymph node sampled, while LODDS was calculated as the log of the ratio between the number of positive and negative node; 0.5 was added to both numerator and denomination to avoid singularity. The univariate and multivariate analysis were performed using Kaplan-Meier and Cox Regression, respectively.

Results: 269 BC patients were analysed. The median follow-up was 88 months (12-213). According to Vinh-Hung et al patients were categorized into low (≤0.20), intermediate (>0.20 and ≤0.65), and high-risk (>0.65) LNR groups. LODDS was stratified using the ROC analysis while pN are defined according to AJCC TNM classification (8th edition). In Kaplan-Meier LNR, LODDS, pN and grading resulted significant for BCSS (p=0.001, p=0.009, p=0.004, p=0.03) instead the first three variables with T stage resulted significant for DFS (p≤0.001 for all four variables). In multivariate analysis, LNR has been confirmed as a better predictor than LODDS and pN for BCSS and DFS (p=0.004, p≤0.001), also T stage resulted an independent prognostic factor for DFS (p=0.012).

Conclusions: To date, there are no studies comparing at the same time LNR, LODDS and pN in patients with breast cancer. Although each factor has its own limitations, this study shows the prognostic value of LNR: It looks more powerful than LODDS and traditional pN staging in breast cancer patients, therefore it

should be taken into greater consideration in the management of these patients.

P111

THE ROLE OF HIGH SENSITIVITY CARDIAC TROPONIN T IN DETECTION OF CARDIAC TOXICITY DURING LEFT BREAST CANCER IRRADIATION: OUR EXPERIENCE AT TOR VERGATA UNIVERSITY

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Aims: The high sensitivity cardiac troponin T (Hs-cTnT) is a myocardial damage biomarker and could have a predictive value in patients who underwent radiotherapy for left sided breast cancer. The aim of this study is to evaluate the early effect of whole breast radiotherapy (WB-RT) on serum HscTnT levels and to correlate them to radiation dose to the whole heart, to its substructures and to patients' clinical features.

Methods: We conducted a prospective non-randomized study between December 2017 to May 2018. Forty-five patients with early stage left-sided breast cancer , who received adjuvant breast hypofractionated RT without prior chemotherapy, were included. Serum levels of Hs-cTnT were obtained before (T0), weekly during RT(T1-T2-T3) and within one week after the end of treatment (T4). Considering the physiological variations of serum levels, an increase of Hs-cTnT (ΔHs-cTnT) more than 30% from the baseline value was chosen as threshold. The patients were divided in two groups: group A (ΔHs-cTnT < 30%), group B (ΔHs-cTnT ≥ 30%) . The main cardiovascular risk factors were recorded. Dose volume histograms (DVHs) were used to provide a quantitative analysis. The maximum dose, the mean dose and a set of appropriate Vx (percent of organ at risk volume receiving the x dose) were evaluated for the whole heart, left ventricle and left anterior descending artery (LAD).

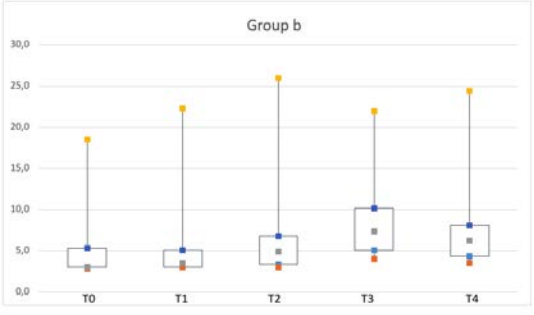

Figure 1. Box plot.

Results: 13 of 45 patients (group B, 28.9%) showed a ΔHs-cTnT ≥30% . In group B, the maximum Hs-cTnT level was recorded at T3 as shown in Figure1 (box plot). The univariate analysis (χ^2 test) was performed for the correlations between ΔHs-cTnT and clinical and dosimetric variables. The results show that ΔHs-cTnT is strongly associated to the heart V5 (p=0.05) and to the hypertension (p=0.05). Multivariate analysis confirmed the importance of the heart V5 correlating with ΔHs-cTnT (p<0.005, HR 3,75, CI 0,9- 14,8).

Conclusion: The increase in hscTnT serum levels during adjuvant WB-RT suggested a correlation with the cardiac radiation dose in chemotherapy –naive breast cancer patients. An eventual correlation with cardiac events needs a longer follow-up.

P112

EXCLUSIVE INTRAOPERATIVE RADIOTHERAPY (IORT) IN EARLY BREAST CANCER: LONG EXPERIENCE IN TREVISO HOSPITAL

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Aims: To evaluate our long-term experience on exclusive intraoperative radiotherapy (IORT) in early breast cancer, in terms of local recurrence and cosmetics outcomes.

Methods: Inclusion criteria were: menopause status, unifocal and unicentric disease, Luminal A phenotype based on biopsy data, not larger 2.5 cm disease, infiltrating ductal istological type, no evidence of pathological local nodes to axillary ultrasound and MRI, negative surgical macroscopical margins (≥2 mm), confirmed to extemporaneous histological examination. A mobile Novac7 Linac is used with single electron emission of 21 Gy (90% isodose, 9 MeV). From January 2004 to January 2020, 336 patients are treated. The primary endpoint was local ipsilateral recurrence rate; secondary endpoint were cosmetic results evaluated according to Harvard NSAPB-RTOG scoring scale and patients satisfaction.

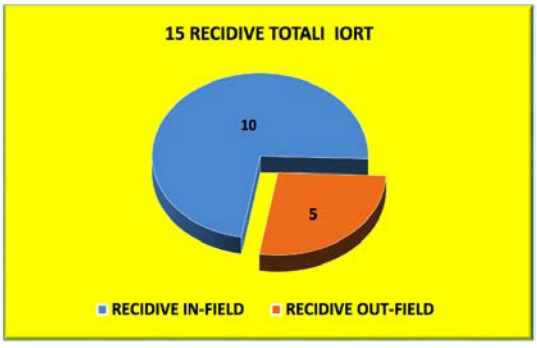

Figure 1.

Results: Median follow up was with a range of 3 - 192 months. 15 patients developed ipsilateral local

recurrence (4.46%); of these, 10 were “on filed” and 5 “out field” of planning treatment . Among these 15 patients, 4 patients developed distant metastasis (1.2%). 240 patients (71.4%) had good cosmetic outcomes and 10 excellent results (3%). 86 patients (25.6%) reported satisfactory results and only 10 patients presented poor outcomes/breast asymmetry (3%).

Conclusions: We think IORT could be a valid technique treatment in selected early breast cancer patients with similar local recurrence rate of whole breast irradiation women with same disease features. Cosmetic outcomes and patients satisfaction were encouraging.

P113

VMAT IN THE SUPRACLAVICULAR REGION IN LOCALLY ADVANCED BREAST CANCER

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Aims: The purpose of the study was to evaluate the acute side effects of skin and cosmetic result in patients, with locally advanced breast cancer, who received adjuvant radiotherapy on the breast or chest wall and on the supraclavicular lymph nodes.

Methods: From June 2019 to May 2020, in our center, were treated 17 women with locally advanced breast cancer. 13 patients underwent conservative surgery, 4 underwent mastectomy and all patients underwent axillary dissection. The median age was 61 (range 41-88). 9 patients were treated with technique field in field step and shoot on the breast or chest wall, 8 were treated with technique VMAT on the breast or chest wall. All women were treated with technique VMAT on the supraclavicular region. On the supraclavicular region the total radiotherapy dose was 50 Gy whit 2 Gy fraction dose. On the breast or chest wall the total radiotherapy dose was 50 Gy whit 2 Gy fraction dose. On the breast the integrated or concomitant boost was 0.33 Gy for fraction. 95% of the target dose was contained in 95% of the volume and all organ dose costrains have been respected.

Results: All women completed radiotherapy. 13 patients (76%) presented acute toxicity of skin of grade 1, mild erythema was observed in 12 patient and dry flaking was observed in 1 patient. 4 patients (24%) presented acute toxicity of skin of grade 2, moderate erythema was observed in 3 patients and wet flaking was observed in 1 patient.

Conclusions: In our study the VMAT technique, in particular on the supraclavicular region, allowed not to have high degrees of acute skin toxicity. The low degree of skin toxicity allowed a satisfactory cosmetic result. More patients are needed to confirm these results and follow up to also evaluate late skin toxicity.

P114

ELECTROCHEMOTHERAPY OF SKIN METASTASES FROM BREAST CANCER: A SYSTEMATIC REVIEW

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Aims: Skin metastases occur in 5-30% of breast cancer (BC) patients. Standard treatments include systemic therapies (chemotherapy, endocrine therapy, and immunotherapy) and local treatments (surgery and radiotherapy). Electrochemotherapy (ECT) could be another option in this setting based on preclinical and clinical studies. Aim of this review was to analyze the available evidence on ECT in skin metastases from BC.

Methods: Studies reporting on ECT in skin metastases from BC were included in this review. Studies not reporting toxicity or tumor response or not reporting results separately from other primary cancers were excluded. The search was based on Medline, Scopus, and The Cochrane Library databases.

Results: Eleven studies including 464 patients were analyzed. ECT was performed using intravenous/intratumoral bleomycin (10 studies) or intratumoral cisplatin (one study). Complete and overall pooled response rates were 46.2% (95%CI: 33.2-59.4 and 74.6% (95%CI: 60.6-86.4) in studies reporting results on a per patient basis and 61.9% (95%CI: 53.8-69.6) and 86.9% (95%CI: 80.0-92.6) in studies reporting results on a per lesion basis, respectively. Worse response rates in larger lesions were observed in 3 studies. The incidence of toxicity was heterogeneous but adverse events were mild and manageable in all studies. One- and 3-year local progression-free survival was 86.2% and 81.0% in two studies, respectively.

Conclusions: ECT is tolerable and effective in terms of response in BC skin metastases especially in less advanced lesions. Further studies are justified to compare ECT with other treatments in this setting.

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VOLUMETRIC MODULATED ARC THERAPY (VMAT) COMPARED TO CONVENTIONAL MODIFIED WIDE-TANGENT (MWT) TECHNIQUES FOR LEFT-SIDED BREAST CANCER

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Aims: Volumetric Modulated Arc Therapy (VMAT) is a novel extension of conventional intensity-modulated radiotherapy (cIMRT), in which an optimized three-dimensional dose distribution may be delivered. This study compared VMAT performed with RapidArc, against conventional modified wide-tangent (MWT) technique for locoregional radiotherapy for left-sided breast cancer.

Methods: 12 patients, mean age 54 years (range 45-64), previously treated in our Center between October 2019 and May 2020, were re-contoured by three trained physicians. Prescribed dose was 50 Gy in 25 fractions. Patients were re-planned comparing MWT and VMAT in each case. Comparative endpoints were dose homogeneity to planning target volume (PTV), and doses to adjacent structures, particularly left anterior descending coronary artery (LADCA) and left ventricle (LV). The heart was outlined according to the RTOG breast cancer contouring atlas. An Eclipse treatment planning system (TPS) was used (Varian Medical Systems; Palo Alto, CA, USA) with the Acuros XB model. We respected these constraints to the heart, according to RTOG recommendations: less than 5% of the heart volume should receive 40 Gy (V40Gy < 5%) and less than 10% of the volume should receive 25 Gy (V25Gy <10%). The constraints to the LADCA according to 'As Low As Reasonable Achievable' criteria were maximum dose (Dmax) < 25 Gy and mean dose (Dmean) < 10 Gy.

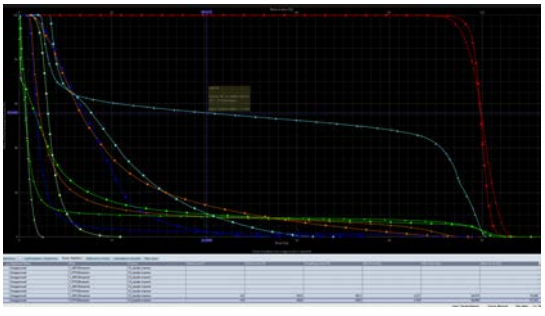

Figure 1.

Results: For VMAT, two at least 180° arcs were needed to optimize the dose on large treatment volumes. VMAT as compared with MWT obtained: LADCA Dmax respectively 25,5 Gy (range 18-38) and 44,5 Gy (range 27-54,4); LADCA Dmean 8,6 Gy (range 5,6-16,1) and 19,9 Gy (range 5,2-36,7); LV Dmax 25,7 (range 16,4-42,4) vs 36,4 (range 6,5-50,7). The heart V30Gy was respectively 0,09% (range 0-0,5) vs 5,3% (range 0-18,6) and ipsilateral lung V20Gy respectively 14,8% (range 9,8-19,8) and 15,3% (range 8,5-21,3). The Dmean to the contralateral breast was 3,7 Gy (range 1,4-5,6) for VMAT and 0,7 Gy (range 0,2-1,2) for MWT. The 5 Gy integral dose was significantly larger with VMAT (26,9% range 18,5%-37,7%) as compared with MWT (11,4% range 9,2%-14,6%)

Conclusions: Sparing of LADCA and left ventricle is feasible without compromising PTV coverage with VMAT technique in comparison of MWT technique. The advantage of VMAT appears in the treatment of left-sided breast cancer including breast and nodal volumes.

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ONCE-WEEKLY HYPOFRACTIONATED WHOLE-BREAST RADIOTHERAPY (WBRT) IN ELDERLY PATIENTS WITH BREAST CANCER: IS THE G8 SCREENING TEST AN ADDITIONAL SELECTION TOOL FOR RADIOTHERAPY? A PROSPECTIVE EVALUATION

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Aims: Hypofractionation, decreasing logistic issues, is helpful to older patients. Omission of WBRT after Breast Conserving Surgery is controversial. There is no subgroup of older patients in whom post-BCS WBRT can be sistematically omitted. The guidelines do not specifically recommend RT in low-risk patients. Literature suggests a detailed evaluation of the patient's status in order to detect the frail ones who whould poorly benefit from an adiuvant treatment. There is currently no standard method for identify cancer patients who require Comprehensive Geriatric Assessment (CGA). Abbreviated and international validated screening methods, like the G8, have been developed to facilitate a correct classification. The present study aimed to evaluate the applicability and compliance of the G8 questionnaire for our population of breast cancer elderly patients, enrolled in one of the "Rete Oncologica Piemonte e Valle d'Aosta" multidisciplinary groups.

Methods: We retrospectively reviewed 80 elderly (≥75 years) patients affected by breast cancer and treated with WBRT after surgery from 2016 to 2019. They were assessed by the G8 scale and classified according to their G8 score into two groups: high score group, G8 score > 14 ("fit" patients) and low score group, G8 score ≤ 14 ("unfit" patients). All the patients received 5.7 Gy in 5 weekly fractions (total dose, 28.5 Gy).

Results: Once-weekly hypofractionated WBRT produces good cosmetics results with a very low late toxi-

city rate and good outcomes. A multidisciplinary approach optimises management of elderly patients. G8 test has high sensitivity, it's a quick and easy-to-use screening tool that can be implemented by a nurse in less than ten minutes. It's useful for the prognostic evaluation and the treatment decision-making to prevent patients from receiving inappropriate treatments.

Conclusion: A short WBRT schedule leads to effective and safe results as the conventional schedule but it also reduces logistic issues facilitating radiation treatment for the elderly. It also permits to reduce treatments costs. The G8 test easily permits to identify vulnerable patients whom require CGA therefore it can guide the multidisciplinary team in the management of therapeutical decisions. Analysis of this cohort allows us to propose the G8 questionnaire as a daily practice screening tool for radiotherapy omission in all the "Rete Oncologica Piemonte e Valle d'Aosta" elderly patients affected by breast cancer.

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ROLE OF RADIOTHERAPY AFTER NEOADJUVANT CHEMOTHERAPY AND SURGERY IN BREAST CANCER PATIENTS: THE EXPERIENCE OF TOR VERGATA UNIVERSITY

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Aims: The aim of this study is to evaluate the efficacy of radiotherapy (RT) in local disease control in breast cancer patients treated with neoadjuvant chemotherapy (NAC) and surgery (S).

Methods: Clinical records from 46 patients with breast cancer treated at our institution with NAC, surgery and radiation therapy between October 2005 to November 2019 were retrospectively analyzed. These data were compared to those of 26 patients who received NAC+S but without RT. Primary outcome was locoregional control (LRC) and secondary outcomes were progression free survival (PFS) and overall survival (OS). Univariate analysis was performed using the Kaplan-Meier method, with the stratified long-rank method (Mantel-Cox) to assess for significance. Multivariate analysis was performed using Cox proportional hazards regression modelling.

Results: Of the entire 72 eligible patients, 46 (63.89%) received RT and 26 (36.11%) did not. Median age of patients at diagnosis was 51 years (34-77 years) and clinical stages at diagnosis were I in 1.39%, IIA in 16.67%, IIB 31.94%, IIIA in 6.94%, IIIB in 40.28%, IIIC 2.78% (American Joint Committee on Cancer 2017). Most chemotherapy was anthracycline based (68 patients, 94.44%). Three patients didn't complete NAC due to clinical progression disease during treatment. Fifty-six (77.78%) out of seventy-two patients have undergone mastectomy while the other (16 pts, 22.22%) were treated with breast conserving surgery (BCS). Fourteen pts (18.05%) achieved pathologic complete response (pCR) to NAC, twenty pts (27.78%) had negative nodal status after NAC (ypT+N0), thirty-seven pts (51.39%) remained positive on breast and lymph nodes (ypT+N+), only one pt presented breast pCR but was ypN positive after NAC (ypT0N+). The median follow-up was 62.97 months (range, 1.43-1390.87). The 5-years OS, 5-years PFS and 5-years LRC for the entire population were 93.5%, 78% and 90.5% respectively, while 10-years OS, PFS and LRC were 83.4%, 67.9% and 90.5%. Multivariate analysis showed an association between local control and adjuvant RT (RR: 0.10, 95%CI: 0.01-0.88, p=0.038), as well as with molecular pattern (RR for triple negative: 3.28, 95%CI: 1.03-10.42, p=0.04). No factor influenced both OS and PFS.

Conclusions: Adjuvant RT after NAC was found to improve LRC in breast cancer patients, as well as molecular pattern could help in this setting to select the best patient for adjuvant RT post NACT+S.

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DEEP INSPIRATION BREATH-HOLD (DIBH) HYPOFRACTIONATED RADIATION THERAPY IN LEFT-SIDED BREAST CANCER PATIENT: A SINGLE CENTER CLINICAL EXPERIENCE

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Aims: Adjuvant radiation therapy for left-sided breast cancer patients (pts) has been associated with an increased risk of potential adverse cardiovascular injury, particularly when associated with anthracycline-based chemotherapy regimens. The DIBH technique has been introduced into clinical practice in order to minimize the late cardiac toxicity. Our intent was to analyze the safety and feasibility in the clinical routine of the modulated intensity hypofractionated radiotherapy guided by the CatalystTM / SentinelTM system (C-RAD AB, Uppsala, Sweden).

Methods: Between May 2019 and May 2020 65 pts, median age 51 (38-69), candidates for adjuvant radiotherapy for left-sided breast cancer (T1-2 N0 M0) underwent a breath control assessment, of which 57 met the DIBH criteria (ability of BH for 30 s). The 8 excluded pts received the free breathing (FB) technique treatment. The prescription dose was 40.05 Gy / 15 fractions in 49 pts and 42.5 Gy / 16 fractions in 8 pts. Boost tumor bed, of 8.01 Gy / 2.67 fractions was used in 26 pts. We have analyzed retrospectively the mean and the maximum dose to the heart (MHD), the mean omolateral lung dose, controlateral breast and planning target volume coverage.

Results: The mean and the maximum dose to the heart (MHD) were 0.72 Gy (0.49-0.95) and 19.8 Gy (15.2-24.6) respectively; the mean ipsilateral lung dose was 4.86 Gy (3.6-5.4 Gy) and V20< 10.78 Gy (9.32-12.24). The maximum heart distance to the anterior car-

diac contour crossing over the posterior edge of the tangential fields was 1.32 cm (0.97-1.67). The mean PTV coverage of the 95% of the prescribed dose were 97.2% (96.8-97.6%).

Conclusions: DIBH and hypofractionated IMRT in clinical practice are safety and feasible, allowing adequate coverage of the target and a low level of irradiation of the organs at risk.

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TANGENTIAL FIELDS WHOLE BREAST RADIOTHERAPY IN CT1-2 CN0 BREAST CANCER PATIENTS WITH PATHOLOGICAL SENTINEL LYMPH NODE (PN1MIC, PN1A): PRELIMINARY RESULTS OF LISEN TRIAL, AN OBSERVATIONAL STUDY

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Aims: In breast cancer (BC) patients, the axillary management could be difficult when sentinel lymph node (SLN) results positive. The ACOSOG Z0011 trial led to a change and, despite several critics regarding also non-uniformity of radiation fields, ALND omission has been included in guidelines and clinical practice. Our observational study (LISEN trial), based on ACOSOG Z0011 trial, aims to analyze clinical outcomes, as regional recurrence (RR) and distant metastasis (DM), in cT1-2 cN0M0 patients undergoing conservative surgery with 1 or 2 positive SLN, omitting ALND, always followed by tangential fields whole breast radiotherapy (WBRT) without nodal irradiation.

Methods: Inclusion criteria were: female BC patients, histologically confirmed invasive BC at biopsy, cT1-2cN0, conservative surgery (BCS), no neoadjuvant treatment. Planned WBRT was mandatory. Patients were stratified in micrometastatic and macrometastatic lymph nodes groups. Adjuvant systemic therapy was administered according to staging and tumor biology. Time to RR and DM were measured from time of surgery until the first regional/distant recurrence.

Results: From May 2011 to June 2019, 195 BC patients joined LISEN trial: all patients underwent conservative surgery and SLN biopsy. One hundred-three of them were treated in our Radiotherapy Department. Patients and tumor characteristics are reported in Table 1. Seventy-eight patients (75.7%) had pN1a, whereas 25 (24.3%) had pN1mic. Negative prognostic factors, for example extra-capsular extension, required a change of surgical approach for 9 patients (8.7%): 6 (66.7%) underwent ALND while 3 (33.3%) had nodal sampling, so they were excluded from trial. The median total number of nodes removed in SLN was 2, with a median number of histologically positive nodes of 1. We analyzed data of 94 patients who underwent tangential WBRT; for 2 patients (2.1%) a change of prescription with high tangent irradiation was necessary. At a median follow-up of 45 months, only 3 patients (3.2%) developed DM (mainly bone sites): 2 Luminal-A and 1 Luminal-B. No RR was found in our trial, neither in basal-like patients.

Conclusions: Our preliminary results do not show RR in patients with pN1mic and pN1a, treated with BCS and SLN, WBRT and adjuvant systemic therapy, omitting ALND. A longer follow-up is necessary, in particular for underrepresented subgroups with not favorable prognostic factors. We aim to collect data about 92 patients treated in other Hospitals.

Table 1. Patients,tumorand treatment characteristics in 103breast cancer patients with micrometastatic and macrometastatic Sentinel Lymph Node.

Micrometastases	25 (24.3%)	Macrometastases	78 (75.7%)
	n (%)		n (%)
Age (years), mean (range)	54.7 (35-74)	Age (years), mean (range)	57 (38-83)
Pathological Stage		Pathological Stage	
T1b	6 (24.0)	T1b	15 (19.2)
T1c	12 (48.0)	T1c	49 (62.8)
T2	7 (28.0)	T2	14 (18.0)
Histological type		Histological type	
Ductal	22 (88.0)	Ductal	65 (83.3)
Lobular	1 (4.0)	Lobular	8 (10.3)
Other	2 (8.0)	Other	5 (6.4)
Grade		Grade	
1	12 (48.0)	1	41 (52.6)
2	9 (36.0)	2	34 (43.6)
3	4 (16.0)	3	3 (3.8)
Axillary dissection		Axillary dissection	
Yes	0 (0)	Yes	6 (7.7)
No	25 (100)	No	72 (92.3)
Lymph node sampling		Lymph node sampling	
Yes	0 (0)	Yes	3 (3.8)
No	25 (100)	No	75 (96.2)
Molecular subtypes		Molecular subtypes*	69/78
Luminal A	18 (72.0)	Luminal A	49 (71.1)
Luminal B (HER2 negative)	2 (8.0)	Luminal B (HER2 negative)	10 (14.5)
Luminal B (HER2 positive)	3 (12.0)	Luminal B (HER2 positive)	8 (11.6)
HER2+	0 (0)	HER2+	1 (1.4)
Basal like	2 (8.0)	Basal like	1 (1.4)
High tangent irradiation		High tangent irradiation*	69/78
Yes	0 (0)	Yes	2 (2.9)
No	25 (100)	No	67 (97.1)
Nodal ratio		Nodal ratio*	69/78
1/1=1	8 (32.0)	1/1= 1	12 (17.4)
1/2=0.5	6 (24.0)	1/2= 0.5	28 (40.6)
1/3= 0.33	5 (20.0)	1/3= 0.33	13 (18.8)
1/4= 0.25	4 (16.0)	1/4=0.25	3 (4.3)
2/2= 1	2 (8.0)	2/2= 1	6 (8.7)
		2/3= 0.7	6 (8.7)
		2/4= 0.5	1 (1.5)

*Patients who received axillary dissection or lymph node sampling were excluded

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COMPARING HELICAL AND DIRECT TOMOTHERAPY• IN POSTMASTECTOMY HYPOFRACTIONATED RADIOTHERAPY AFTER LEFT SIDE BREAST RECONSTRUCTION

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Aims: To compare the dosimetric outcome of two hypofractionated – post-mastectomy radiotherapy (PMRT) techniques for treating the chest wall and draining nodes after breast reconstruction. The aim is to assess the differences in dose distribution throughout the planning target volume (PTV) and the organs at risk (OARs) between Tomotherapy® in direct modality and Tomotherapy® in helical modality.

Methods: Left-sided breast cancer patients who underwent mastectomy, immediate breast reconstruction (IBR) with a temporary expander and PMRT with Tomotherapy® in direct modality were enrolled. All patients were treated with hypofractionated approach of 40.05 Gy in 15 fractions. For all patients an additional plan with Helical Tomotherapy® was elaborated. The two plans were compared in terms of dose to the PTV and to OARs. Data are reported as median value and the respective interquartile range. To determine statistical significance, ANOVA test was performed with $p < 0.05$ considered to be statistically significant. This study was part of research notified to our Ethical Committee (nr 725).

Results: The plans of 15 patients treated with Tomotherapy® in direct modality between May 2017 and September 2019 were considered in this study. The latter were compared with the plans of the same patients calculated with helical Tomotherapy®. Regarding chest wall PTV coverage, the only statistically relevant difference regarded the D0.03 cm3 with a dose reduction for the helical plans ($p < 0.001$). [Table 1] For the supraclavicular (SVC) PTV helical modality showed a better coverage for the V95% (97% vs 88%; $p < 0.001$) [Tab 1], even though the direct modality is still very close to the ideal value (90%). With regard to the OARs, the direct modality showed statistically relevant ($p < 0.05$) lower doses for OARs (specifically for heart, lungs, contralateral breast, spinal cord, liver and stomach). [Table 1].

Conclusions: Tomotherapy® in direct modality is a suitable modality for treating the chest wall and draining nodes offering a good PTV coverage and a optimized OARs exposure to lower doses. Although the planning is more "time-consuming", Tomotherapy® in direct modality might be a preferable option for women <40 years or BRCA mutation carriers due to lower OARs RT doses.

Tabella 1. Dosimetric parameters for organs at risk (OARs) and comparison of PTV coverage: Tomotherapy® direct modality vs Tomotherapy® helical modality.

OAR	Constraints	Tomo direct (%) (n = 15)	Tomo helical (%) (n = 15)	*p* value
Heart	$D_{15\%} < 8$ Gy	1.90 (1.55 - 2.12)	6.40 (6.00 - 6.75)	**< 0.001**
	$D_{20\%} < 6$ Gy	1.60 (1.33 - 1.77)	5.10 (4.80 - 5.30)	**< 0.001**
	$D_{mean} < 5$Gy	2.30 (1.75 - 2.85)	4.47 (4.05 - 4.56)	**< 0.001**
	$D_{35\%}$	9.30 (5.60 - 17.65)	13.90 (13.30 - 15.45)	0.07
Ipsilateral lung	$D_{15\%} < 31$ Gy	25.90 (23.60 - 27.95)	26.40 (26.10 - 26.90)	0.19
	$D_{20\%} < 26.4$ Gy	18.60 (15.60 - 22.75)	23.40 (23.10 - 23.70)	**0.001**
	$D_{25\%} < 17.6$ Gy	5.00 (4.00 - 9.35)	16.10 (16.00 - 16.50)	**< 0.001**
	$D_{50\%} < 13$ Gy	2.08 (1.90 - 2.80)	12.10 (11.75 - 12.20)	**< 0.001**
Controlateral lung	$D_{20\%} < 13$ Gy	0.39 (0.31 - 0.40)	7.80 (7.15 - 8.55)	**< 0.001**
	$D_{25\%} < 10.6$ Gy	0.30 (0.27 - 0.31)	6.00 (5.45 - 6.30)	**< 0.001**
	$D_{50\%} < 9$ Gy	0.26 (0.21 - 0.28)	4.40 (3.75 - 5.15)	**< 0.001**
Lungs	$D_{mean} < 10$Gy	4.10 (3.80 - 4.60)	9.50 (9.25 - 9.70)	**< 0.001**
Controlateral breast	$D_{15\%} < 17.6$ Gy	0.50 (0.43 - 0.58)	8.10 (7.95 - 8.20)	**< 0.001**
	$D_{20\%} < 9$ Gy	0.40 (0.37 - 0.49)	7.10 (6.95 - 7.20)	**< 0.001**
	$D_{25\%} < 6$ Gy	0.30 (0.27 - 0.37)	5.10 (5.00 - 5.35)	**< 0.001**
	$D_{50\%} < 4.4$ Gy	0.24 (0.21 - 0.305)	4.10 (4.05 -4.27)	**< 0.001**
	D_{mean}	0.30 (0.27 – 0.37)	5.10 (5.00 – 5.29)	**< 0.001**
	D_{max}	2.30 (1.93 – 2.55)	15.67 (14.50 – 18.40)	**< 0.001**
Spinal cord	$D_{0.03\ cm^3}$	3.50 (1.95 – 8.75)	14.80 (14.75 – 15.10)	
Liver	$V_{13Gy} < 10\%$	0.00	0.40 (0.00 - 2.60)	**0.007**
	$D_{mean} < 4.4$ Gy	0.20 (0.20 - 0.20)	1.47 (0.79 - 3.90)	**< 0.001**
Stomach	$D_{mean} < 2.4$ Gy	0.70 (0.46 - 0.80)	1.50 (1.18 - 1.85)	**0.003**
	$D_{max} < 8$ Gy	9.70 (1.5 - 20.15)	8.50 (8.05 - 9.25)	0.2
Thyroid gland	$D_{50\%} < 16.1$ Gy	0.80 (0.65 - 3.30)	14.50 (10.50 - 15.68)	0.08
Esophagus	$D_{max} < 15$ Gy	15.00 (13.75 - 17.52)	14.60 (14.21 - 14.75)	0.5
Humeral head	$D_{max} < 30$ Gy	29.90 (28.80 - 32.60)	28.50 (22.36 - 29.32)	0.13
Chest wall PTV				
$V_{95\%}$	$V_{95\%} \geq 90\%$	90.20 (86.25 - 95.05)	90.60 (87.15 - 92.35)	0.98
$V_{90\%}$	$V_{90\%} \geq 95\%$ (ideal) $V_{90\%} \geq 90\%$ (acceptable)	96.00 (94.60 - 98.70)	97.80 (94.85 - 98.3)	0.87
D_{mean}	$D_{mean} \geq 99\%$ (ideal) $D_{mean} \geq 95\%$ (acceptable)	99.50 (98.70 - 100)	99.00 (98.55 - 99.1)	0.11
$D_{0.03\ cm^3}$	$D_{0.03\ cm^3} \leq 110\%$ (ideal) $D_{0.03\ cm^3} \leq 115\%$ (acceptable)	110.30 (107.95 - 111.70)	107.10 (106.45 - 107.40)	**< 0.001**
$D_{50\%}$		100.00 (99.95 - 100.00)	99.70 (99.65 - 99.70)	**< 0.001**
D_{max}		110.80 (108.35 - 112.1)	107.30 (106.65 - 107.55)	**< 0.001**
PTV SVC				
$V_{95\%}$	$V_{95\%} \geq 90\%$	88.00 (81.80 - 93.25)	97.10 (95.4 - 97.95)	**< 0.001**
$V_{90\%}$	$V_{90\%} \geq 95\%$ (ideal) $V_{90\%} \geq 90\%$ (acceptable)	98.20 (97.30 - 99.05)	99.00 (97.80 - 99.50)	0.1
D_{mean}	$D_{mean} \geq 99\%$ (ideal) $D_{mean} \geq 95\%$ (acceptable)	98.00 (97.50 - 98.35)	98.50 (98.35 - 98.90)	**0.025**
$D_{0.03\ cm^3}$	$D_{0.03\ cm^3} \leq 110\%$ (ideal) $D_{0.03\ cm^3} \leq 115\%$ (acceptable)	106.80 (105.40 - 108.95)	106.20 (105.75 - 107.60)	0.3
$D_{50\%}$		98.20 (97.85 - 98.60)	98.70 (98.69 - 99.00)	0.05
D_{max}		107.30 (106.25 - 111.1)	107.20 (106.40 - 107.85)	0.32

List of abbreviations: *Dx*% = dose delivered to x% of OAR volume; *D*max = maximum dose *D*mean = mean dose; *V*xGy = OAR volume percentage receiving *x*Gy; PTV = planning target volume; SVC = supraclavicular

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USING THE BOLUS IN POST-MASTECTOMY RADIATION THERAPY (PMRT): A NATIONAL SURVEY ON BEHALF OF AIRO (ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY) BREAST ONCOLOGY GROUP

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Aims: According to literature, overall survival and loco-regional control were demonstrated to be improved by post-mastectomy radiotherapy (PMRT)in high risk breast cancer. Chest wall represents the area with the highest recurrence rate and bolus could be placed on it in the setting of PMRT to increase the surface radiation dose, although bolus practice and application remains still controversial. Aim of this study is to analyze bolus routine practice among Italian Radiation Oncology Departments

Methods: In 2018, an email survey was sent to the all members of Italian Association of Radiotherapy and Clinical Oncology without specific selection criteria for the respondents. The survey included a total of 21 questions about bolus application in PMRT, focused on clinical, target volume delineation, physical and treatment topics.

Results: The survey was initially joined by 102 Radiation Oncologists, but not all respondents answered every question. Regarding indications, bolus was used by 69.5% of 82 physicians in case of skin infiltration and 52 of 68 respondents (76.5%) affirmed to apply it every day during PMRT. Skin was included as part of chest wall Clinical Target Volume in PMRT both in case of absence of breast reconstruction and with breast reconstruction (52.2% of 69 respondents and 50.7% of 69, respectively) regardless clinical presentation and presence of high risk factors. About bolus thickness, 5 mm-bolus was found as the most shared choice regardless of breast reconstruction (50.7% of 67 participants in case of breast reconstruction and 58.8% of 68 without breast reconstruction). 3D-Conformal Radiotherapy resulted the most used technique in case of bolus application (73.5%, 50 of 73 respondents). Based on RTOG scale, acute G2 – G3 skin toxicity was recorded by a percentage of 93.9% (62 of 66 respondents) when bolus was applied.

Conclusions: There was wide heterogeneity in the use of bolus, though an agreement was found in some topics for its application. Compared to other International surveys, a limitation of this work was the relative small number of respondents but, at the same time, it seemed to be enough to understand the general trend for use of bolus in PMRT in the different Italian institutions. Future prospects could be an achievement of a National Consensus about bolus practice in PMRT starting from these results.

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FACTORS INFLUENCING ACUTE AND LATE SKIN TOXICITY OF WHOLE BREAST ADJUVANT HYPOFRACTIONATED FORWARD-PLANNED INTENSITY MODULATED RADIOTHERAPY WITHOUT BOOST IN 1325 CONSECUTIVE EARLY BREAST CANCER PATIENTS

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Aims: To report acute and late toxicities in a cohort of 1325 consecutive early-stage breast cancer (BCA) patients (pts) who underwent breast conservative surgery (BCS) and were treated with whole breast hypofractionated (WBH) adjuvant forward-planned intensity modulated radiotherapy (F-IMRT) de-escalated treatment, without boost.

Methods and Materials: From 02/2009-05/2017 1325 consecutive pts with pTis-pT2, pNx-N1a(≤ 3 positive lymph-nodes) cM0 BCA were treated with WBHF-IMRT, to a total dose of 40 Gy/15 fr delivered in 3 weeks, without boost. Median age was 62 (interquartile range-IR-:51.2-70.5) years. Right sided were 48.3% and left sided 51.7% (1.8% had bilateral tumor). Histology was in situ for 8% of pts and invasive in 92%. Chemotherapy was prescribed in 28% of pts, hormonal therapy in 80.3% and monoclonal antibodies in 8.3%. Acute toxicity was evaluated with RTOG scale, late toxicity with SOMA-LENT scale.

Results: Median follow up was 72.43 (IQR: 44.63-104.13) months. Acute toxicity was: 69.7% grading (G)1, 14.2% G2 and 1.5% G3. In 4% of pts maximal acute toxicity was postponed 7-10 days after the end of the treatment. Late toxicity was divided into edema-hyperpigmentation (which improved over time) and fibrosis-telangiectasia (due to their persistence over time), and are described in Table 1. Aesthetic result after surgery was evaluated on a 4-point scale and was excellent in 28.7%, good in 41.5%, acceptable in 20.3% and poor in 9.5% of pts. Change in breast appearance after radiotherapy was separately evaluated (clinically and with photographs) and was mild in 6.9%, moderate in 2.3% and marked in 1.3% of pts. Median target volume was 642.30 (445.50-916.61) cc and had a significant impact on acute G ≥2 toxicity [OR=2.05, 95% CI for OR: (1.61, 2.60), p<0.001], late edema and hyperpigmentation [OR=1.489, 95% CI for OR: (1.19,1.87), p<0.001] and telenagiectasia/fibrosis [OR= 1.55, 95% CI for OR: (1.17,2.05), p <0.001]. Patients treated with sequential or concomitant chemotherapy had an odd ratio 3.5 times higher of having acute G2/G3 toxicity.

(Late?)

Conclusion: WBHF-IMRT without boost after BCS demonstrated good acute and late toxicity in a large cohort of 1325 consecutive patients. Approximately 10% of pts presented changes in breast appearance after radiotherapy. Breast volume and chemotherapy had a significant impact on toxicity.

Table 1. Late toxicity.

Toxicity	G1	G2	G3	G4
Edema /hyperpigmentation	28.5%	4.3%	0.2%	0.1%
Fibrosis/teleangiectasia/pain	14.4%	3.2%	0.8%	0.1%

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OTHER PRIMARY CANCERS OBSERVED IN A COHORT OF 1325 CONSECUTIVE EARLY BREAST CANCER PATIENTS TREATED WITH WHOLE BREAST ADJUVANT HYPOFRACTIONATED RADIOTHERAPY

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Aims: A modified definition of second primary cancer was considered to include all primary cancers, regardless of the time of onset, observed in a large cohort of 1325 consecutive early-stage breast cancer (BCA) patients (pts) treated with whole breast hypofractionated adjuvant radiotherapy(WBHRT), where BCA was the reference (primary) cancer.

Methods and Materials: From 02/2009-05/2017 1325 consecutive BCA pts were treated with WBHRT, without boost. Our standard protocol included 66 months (mts) of follow up and all available information was recorded. Median age of pts was 62 (interquartile range-IR-:51.14-70.53) years. Chemotherapy was prescribed in 28%, hormonal therapy in 80.3% and monoclonal antibodies in 8.3% of pts. Genetic tests were not available.

Results: Median follow up was 72.43(IQR: 44.63-104.13) mts. More than half of pts had a follow up longer than 66 mts and were alive. During the observation period 81% of pts did not present any other primary tumor, 16.8% of pts one other primary tumor, 2% of pts two other primary tumors, and 0.2% of pts three other primary tumors. Of the 19% of pts with another primary tumor during the observation period the majority of pts presented a previous tumor (60.6%), 6.8% a concomitant tumor, 0.4% a previous and concomitant tumor, 3.2% a previous and successive tumor and 29% a successive tumor only. Of the pts presenting a previous tumor, 9.9% had two other primary tumors and 1.3% three other primary tumors, while of the pts presenting successive primary tumors 11.1% presented two primary successive tumors. Of the 285 other primary tumors 38.95% were BCA, 15.79% digestive tumors and 12.28% gynecologic tumors. Of all pts with other primary tumor 33.5% presented a family history of BCA. One breast angiosarcoma and one skin cancer of the irradiated breast were registered.

Conclusion: Radiotherapy is under special observation as it concerns secondary tumors, much more than other carcinogenic treatments as chemotherapy. Often successive primitive tumors are considered secondary cancers. A simple observation of a large cohort of 1325 consecutive BCA pts with a median age of 62 years shows that one of five pts presents another tumor during her life, but two thirds are registered previous or concomitantly to the (primary)BCA. A randomized treatment keeping into account genetic variability would not be possible, but maybe genetics will give the final response regarding the radiotherapy carcinogenicity.

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RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY CONCERNING QUALITY OF LIFE IN PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY FOR EARLY BREAST CANCER

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Aims: Advances in diagnosis and treatment of breast cancer (BC) have led to an increase in cancer survival, resulting in a greater remark on quality of life (QoL). Radiotherapy (RT) after conservative surgery is the standard of care in the most of breast cancer patients. However acute and late treatment-related side effects could influence QoL during and after RT. This study aims to evaluate the impact of RT, type of fractionation, Hormonotherapy (HT)and changes in Body mass Index (BMI)on the QoL and patient's satisfaction of care.

Methods: This study obtained ethical approval on 9th May 2018. We included: female >18 years, with early BC (stage I-II) treated with RT +\- HT after conservative surgery. Ninety-eight patients consented to participate and answered the questionnaire at the start and end of RT and during follow-up controls. Functional assessment of cancer therapy for BC (FACT-B 4.0 Italian version) questionnaire is composed by 37 items, divided into five subscales, namely physical (PWB), social (SWB), emotional (EWB), functional

well-beings (FWB), and the additional concerns for BC (BCS). BMI and acute or late toxicities (according to CTCAE 4.03) were recorded at each follow-up visit. Distribution of data for each subscale was assessed for normality using the Shapiro-Wilks test, while the Friedman test was used to detect differences in the variables for all questionnaires and the ANOVA one-way test to detect changes in the BMI.

Results: Mean age was 59 years and 74% of patients received HT combined with RT, 18 patients experienced acute skin toxicity of Grade ≥2. Th median trend of the QoL subscales was stable during all the five questionnaires. No difference was recorded between patients treated with Hypofractionated or Conventional RT. FACT-B Total score was not affected by radiation toxicity, dose, or BMI changes, while HT negatively impacted on FWB (p value 0,009) and Total FACT-B (p value0,011). With respect to skin toxicity no differences were found for any of the variables.

Conclusions: FACT-B resulted as a simple and quick questionnaire. Data from this study suggest that RT do not affects QoL of BC patients, neither in terms of fractionation regimen or RT-related side effects. On the other hand, these results demonstrated that women having systemic HT experienced a QoL worse than patients treated with only RT. As the sample size of this study is small, further and long-term protocols are needed to improve on the validity of the tool.

Table 1. Differenceon FACT-B variables

Variable	RT DOSE		p-value	HT		p-value
OVERALL	1	>1		0	1	
PWB	24.8 (22.9-26.6)	24.4 (22-26.8)	0.748	25.7 (23.8-27.4)	24.3 (22-26.5)	0.061
SWB	20.9 (18.8-24.5)	20.5 (17.2-23.7)	0.323	22 (18.2-25.5)	20.5 (17.7-23.7)	0.246
EWB	18.3 (17-20.1)	19 (16.7-20.8)	0.372	20 (17.9-21.7)	18.3 (16.3-20.3)	0.044
FWB	17 (14-20)	17.4 (14.3-20.8)	0.420	20.1 (16.8-23.2)	16.8 (14-19.3)	**0.009**
BCS	28.3 (26.2-31.1)	28.3 (25.2-31.6)	0.805	29 (26.4-31)	27.8 (25.3-31.6)	0.729
FACT-B-TOI	69 (65.1-74.3)	70.6 (60.5-76.7)	0.820	73 (67.1-80.5)	69.1 (61.6-74.5)	0.064
FACT-G-Total	81.2 (74.9-87.7)	82.3 (73-89.7)	0.955	86.1 (79.5-96)	79.3 (73.2-86.5)	0.051
FACT-B-Total	108.4 (100.9-115)	109.5 (95-119)	0.902	113.1 (104.4-124.5)	106.6 (97.9-115.2)	**0.011**

RT: Radiotherapy, p-value for Mann U Whitney test, HT: Hormonotherapy, PWB: physical well-beings, SWB: social well-beings, EWB: emotional well-beings, FWB: functional well-beings, BCS: breast cancer subscale.

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HYPOFRACTIONATED BREAST RADIOTHERAPY IN PTIS-2, N0-2, M0 BREAST CANCER PATIENTS AFTER CONSERVATIVE SURGERY: ACUTE SKIN TOXICITY AND EARLY AND LATE COSMESIS

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Aims: We aimed to evaluate safety, early and late toxicity and late cosmesis of a hypofractionated adjuvant radiotherapy (RT) after breast conservative surgery (CS).

Methods: From January 2015 to december 2017, 256 breast cancer patients (pts) received a hypofractionated RT after CS. They were aged between 43 to 93 (median 66), all with pTis-T2, N0-N2, M0 breast cancer diagnosis. Pts characteristics are reported in Table1. Eleven received neoadjuvant chemotherapy (5 plus Trastuzumab), 52 adjuvant chemotrerapy (16 plus Trastuzumab) and 225 adjuvant hormonal therapy (36 after chemotherapy). Both neoadjuvant and adjuvant treatment were taxans and/or anthracyclines based on. Hormonal therapy was Tamoxifene alone in 17.5% of cases, Tamoxifene plus LH-RH analogs in 6.6%, aromatase inhibitors in 72.4% and aromatase inhibitors plus LH-RH analogs in 3.5%. 3D RT schedule consisted in a total dose of 39Gy in 13 fractions (fx), 4 fx a week, with an additional concomitant boost of 3Gy/3 weekly fx on tumor bed. Boost dose rose to 4Gy/4 fx in case of close margins. Skin acute toxicity was estimated at RT completion according to RTOG classification. Global cosmesis was evaluated after 6 months and then once a year by the following visual scale: Excellent E=no RT sequelae; Good G=light permanent skin colour alteration and/or light subcutaneous oedema; Mediocre M=moderate severe skin colour alteration and/or oedema; Poor P=chronic flogosis with recurrent acute episodes and/or severe fibrosis and/or oedema.

Table 1.

Total	256	
pTis	27	(10.5%)
pT1a	20	(7.8%)
pT1b	61	(23.8%)
pT1c	112	(43.8%)
pT2	36	(14%)
pN0	215	(84.3%)
pN1	30	(11.7%)
pN2	2	(<1%)
pNx	9	(3.5%)
G1	65	(25.3%)
G2	132	(51.5%)
G3	51	(20%)
Gx	8	(3.2%)
Duttale	192	(75%)
Lobulare	25	(10%)
Misto	3	(1%)
Papillare	9	(3.5%)
NAS	9	(3.5%)
Altro	18	(7%)
Er+ PgR+	193	(75.3%)
Er+ PgR-	35	(13.7%)
Er- PgR-	28	(11%)
Margini negativi	212	(83%)
Margini close	44	(17%)
Her 2+	27	(10.5%)
Her 2 -	215	(84%)
Her 2 ND	14	(5.5%)
Premenopausa	215	(84%)
Postmenopausa	41	(16%)

Results: Among 256 pts acute toxicity after last RT fraction was G0 in 8% of pts, G1 in 62%, G2 in 23% and G3 in 7%. Cosmesis at 6 months among 229 pts was E in 66% of cases, G in 32%, M in 1.5% and P in 0.5%. At 1 year among 207 pts was E 77%, G 21.5, M 1% and P 0.5%. At 2 years among 193 pts was E 84%, G 14.5% and M 1.5%. At 3 years among 141 pts was E 90% and G 10%. At 4 years among 74 pts was E 90% and G 10%. Finally at 5 years among 21 pts was E 90% and G 10%. At a median follow-up of 37 months (range 6-65) no pts developed local recurrence and only 2 pts had systemic progression.

Conclusions: This hypofractionated adjuvant RT schedule provides an excellent local control combined with high rates of low grade acute toxicity (70% G0-G1). Cosmesis at 6 months is satisfactory (66% excellent, 32% good) and get better and better as the follow-up becomes longer. Imdeed at 3, 4 and 5 years we can observe the same rates of cosmetic outcome: E 90% and G 10%.

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ABSTRACT WITHDRAWN

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A FEASIBILITY STUDY OF SIMULTANEOUS INTEGRATED BOOST (SIB) ADVANCED TECHNIQUES IN THE TREATMENT OF BREAST CANCER

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Aims: We investigated the feasibility of a SIB on tumor bed in the treatment of left sided breast cancer and supraclavicular nodes by comparing a step and shoot intensity modulated radiotherapy (IMRT) technique with a Volumetric Arc Therapy (VMAT) method.

Methods: In this retrospective study, five patients with early-stage left-sided breast cancer after breast-conserving surgery and axillary node dissection were included and planned with a 7 fields IMRT and 2 partial dual arcs (angle span of 200°) VMAT. All patients were discussed in the Breast Unit of our center. The CTVs of the whole breast, tumor bed boost and levels III and IV lymph nodes were contoured by an experienced radiation oncologist, as well as the OARs (Lungs, Heart, Controlateral Breast, Spinal Cord, Humeral Head, Thyroid Gland, Esophagus and LAD). A prescribed dose of 64.4Gy to the PTVboost and 50.4Gy to the PTVbreast and PTVscv/icv in 28 fractions was planned. The planning objective was to deliver at least 95% of the prescribed dose to 95% of the target volume (D95%≥95%). All plans were generated using a 6MV photon Elekta VersaHD Linac. Plans coverage was evaluated according to ICRU 83 (D2, D98, D95, Heterogeneity Index (HI) and Conformity Index (CI)). In addition, the Chair Index (CHI) was introduced to evaluate the dose homogeneity for PTVbreast given the two levels of prescription dose. Furthermore, the dosimetric differences to the OARs between IMRT and VMAT plans were assessed.

Results: For both techniques, median D95% was higher than 96.3% on all targets. Dose distribution, evaluated through HI, CI and D2 for both PTVsvc/icv and PTVboost, were statistically the same for both techniques, while median IMRT ChI for PTVbreast was lower than in VMAT (8 vs 14). IMRT plans were more effective in containing the low dose bath to healthy tissues: median Dose to the controlateral Breast and Lung and V5 to the contralateral Lung and Heart were lower than VMAT. On the contrary, VMAT has proven its efficiency in the sparing of Esophagus, Humeral Head and Thyroid Gland and Heart mean dose.

Conclusions: In this retrospective study, targets and OARs dose distribution goals in all IMRT and VMAT plans were well achieved without a greater increasing of the whole radiation dose. These advanced techniques are an alternative to 3D-CRT to whole-breast irradiation, also thanks to an interesting reduction in delivery time for each session for VMAT technique.

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LYMPHEDEMA EVALUATION AFTER ADJUVANT HYPOFRACTIONATED RADIOTHERAPY FOR 1-2 MACROMETASTATIC SENTINEL LYMPH NODES WITHOUT AXILLARY DISSECTION IN BREAST CANCER CONSERVATIVE SURGERY: PRESENTATION OF AXILL-ART OBSERVATIONAL STUDY XXX 953

M.A. Zerella[1], F. Colombo[1, 4], S. Dicuonzo[1], M.A. Gerardi[1], A. Morra[1], D.P. Rojas[1], C. Fodor[1], F. Cattani[2], V. Galimberti[3], P. Veronesi[3,4], C. Morigi[3], R. Orecchia[5], M.C. Leonardi[1], B.A. Jereczek-Fossa[1,4]

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Aim: Breast cancer (BC) related lymphedema is one of the most common long-term complications, mainly due to axillary dissection. The recent trend in early stage BC aims at reducing surgical intervention on clinically negative axilla by performing sentinel node biopsy alone or by substituting dissection with nodal irradiation. In this context the Intensity modulated radiation therapy (IMRT) technique ensures better dose homogeneity and conformity to the planning target vol-

umes. We designed a prospective protocol to evaluate the incidence of ipsilateral arm lymphedema after adjuvant irradiation given with IMRT, exploring potential association between the risk of lymphedema and the extention of radiotherapy (RT).

Methods: Patients to be enrolled in the protocol must present: 1) Invasive BC, staged T1-T2, 2) Breast conserving surgery with no axillary dissection, 3) ≤ 2 positive sentinel node biopsy . Hypofractionated whole breast RT (WBRT) with simultaneous integrated boost to the tumor bed is planned. The axillary radiotherapy (ART) volume is defined according to the tumor molecular classification: Luminal B HER2- and HER-2+ receive WBRT and axillary level I-II irradiation. HER2+ and basal-like or Triple Negative receive WBRT with axillary level I-II-III irradiation, including supraclavicular fossa (level IV). Nodal contouring flows the ESTRO guidelines for early stage. Primary endpoint is the incidence of arm lymphedema 1 year after RT; based on the rate detected by the Amaros trial it is expected ≤15%. Follow-up is set at 1, 2 and 3 years. The assessment consists of arm circumference measures as well as joint mobility. Acute and chronic toxicity and locoregional relapses are secondary endpoints. The protocol has been recruiting since February 2020; nevertheless at our institution ART was prescribed following the above mentioned classification since 2016.

Results: Between February and May 2020, 5 patients were considered eligible for accrual. Four patients received WBRT and axillary level I-II; one patient received WBRT with axillary level I-II-III-IV. No acute toxicity events >G2 were reported. From 2016 to 2019 a total of 217 patients was treated with ART following volume extension according to the patient category of risk, who are being analyzed.

Conclusions: The protocol has been based on our previous experience, confirming compliance and feasibility. Further trials, in order to achieve consensus on axillary treatment in early stage BC are warranted.

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CUP-SYNDROME, BREAST-CANCER METASTASIS OR LOBULAR CARCINOMA IN MAMMARY ECTOPIA? MULTIDISCIPLINARY CLINICAL ASSESSMENT AND THERAPEUTIC PATHWAY: A CASE REPORT

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Aims: to present the multidisciplinary diagnostic, therapeutic and follow-up pathway in a woman with skin lesion of the right axilla.

Methods: In January 2018, a 59-year-old female patient was subjected to the excision of a cutaneous lump at a Surgical Dermatology clinic, insurgent on the skin of the right axilla for a few years, but recently increased in size. Histological findings demonstrated infiltrating lobular carcinoma of about 2 cm in diameter, no skin involvement, with resection margin positive and perineural invasion, ER score 5, PgR score 5, Mib-1 40%, HER-2/neu negative (0). Then, the patient was taken over by our Breast Unit for diagnostic completion and subsequent therapeutic pathway. We decided to perform diagnostic completion by bilateral eco-mammography, came back negative, bilateral mammary MRI, also negative, and standard staging imaging (chest X-rays and abdominal ultrasound), which did not detect secondary lesions. Because of the unusual clinical presentation and the resection positive margin, the core-team decided to perform the radicalization of surgical margins on axillary pillar and axillary lymphadenectomy. The histological examination showed no residual disease at the site of the previous surgery, nor any ectopic breast tissue; the 31 axillary lymph nodes taken were all negatives. Thus, after further discussion within the Breast Unit, it was agreed to consider the lesion as lobular neoplasm in mammary ectopia in pT2 pN0 M0 stage (IIA), and proposed to the patient a Letrozole-based hormonotherapy and adjuvant Radiotherapy to the near-scar region, prescribing a dose of 50 Gy at standard fractionation. After expressing informed consent, she was subjected to CT scan virtual simulation by CT equipment Toshiba Aquilion LB 64 slices, using RADIUS chest immobilization system, finding the scar with a metal thread. In addition to the standard OAR and the ipsilateral mammary gland, a CTV was delineated, comprising the tissue area around the surgical scar with an isotropic margin of 1 cm, wich in turn expanded to PTV for an additional 1 cm margin. Then a 3D treatment plan was developed by TPS Oncentra Master-plan (calculation algorithm Collapsed Cone): the coverage of the PTV was obtained by 4 photons beams narrow-X shaped (gantry at 165°,180°, 345°, 0°) in order to preserve the right mammary gland as much as possible; OAR doses were found to be well below the dose-constraints in use at our Institution. The treatment was performed using Versa HD Elekta Medical System LINAC, by 6-10 MV photon beams, performing setup verification daily by CBCT (XVI). On the first day of therapy, once the correspondence of the setup had been verified, the upper and antero-lower vertices of the treatment field at 0° were tattooed, in order to carry out the daily verification of the reproducibility in field-light after CBCT; in addition, it was considered useful to reconstruct the treatment field in the event of future breast irradiation. Treatment was completed without interruption, and without any cutaneous or hematological toxicity. Subsequently, the patient was regularly assessed in the joint multidisciplinary BU

practice, carrying out the examinations required by follow-up protocols.

Results: at 19 months from the end of the Radiation Therapy, the patient is free from breast disease (carried out 2 mammographies, negative for neoplasia). A re-assessment with CT-scan performed at 1 year from the end of treatment showed no secondary lesions. The patient presents an excellent cosmetic response of the irradiated region and continues hormone therapy with good tolerance.

Conclusions: 2 years after the patient has been taken over by the multidisciplinary unit, the evaluation of the excised lesion as breast cancer in mammary ectopia can be con-sidered correct, although histological examination of the radicalization intervention of the scar region did not reveal glandular residue. The Radiation Therapy, planned and conducted with accuracy, proved to be effective and well tolerated.

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TAILORED CLINICAL PATHWAY IN A PATIENT WITH FRAILTY AFFECTED BY LOCALLY ADVANCED BREAST CANCER AND AXILLARY LYMPHOADENOPATIES

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Aims: Present the shared clinical pathway in a woman with frailty affected by a left breast inflammatory carcinoma with axillary lymphadenopathy, subjected to radiation therapy alone after neoadjuvant chemotherapy, for his categorical refusal to undergo surgery.

Methods: In November 2016, a 76-year-old woman, alone, who had already undergone QUART and right axillary lymphadenectomy in 1991, went to surgical evaluation for the appearance of orange-peel, erythematous, warm left breast skin, over a large area of increased consistency. Therefore, she was undergone to clinical assessment: mammography revealed a large oval area of distortion and calcifications at the outer quadrants of the left breast, confimed by the whole-body CT scan (about 91 x 47 mm and edema of the perilesional and subcutaneous soft tissues), with axillary lymphadenopathies of 32 x 14 mm, excluding the presence of repetitive lesions (cT4d cN+ M0 stage). The biopsy revealed Infiltrating Ductal Carcinoma G3, ER negative, PgR negative, Mib-1 30%, HER-2/neu negative (0). Due to the age, the poor general conditions (moderate/severe obesity, COPD, bilateral total hips joint replacement, bilateral deafness), the patient has been prescribed a Paclitaxel-based chemotherapy dd. 1-8-15 q28, but, owing to personal reasons (loneliness, mobility impairments), it started about 10 months after. After two cycles of chemotherapy there was an objective cutaneous response, confirmed at the end of the fourth cycle; thus, the patient was expected to be re-assessed prior to radical surgery, but she opposed firm and lively rejection to this option, due to her loneliness. After new discussion at Breast Unit, which has now been set up, in view of the comorbidities and the condition of social frailty, exclusive radiotherapy option was proposed to the patient; she, due to the opportunity of transfer to our institution by dedicated vehicle, has agreed. The clinical examination documented no skin alterations, the presence of gross left central-equatorial swelling, and axillary lymph node swelling. After cardiological assessment, Radiation therapy to left whole breast and axillary homolateral region, site of macroscopic disease for a dose of 59.4 Gy (fr. 1.8 Gy/die), and supra-infraclavicularnodal drainages for a dose of 50.4 Gy (fr. 1.8 Gy/die) was indicated. Therefore, a CT scan simulation by CT equipment Toshiba Aquilion LB 64 slices was performed, using custom RADIUS chest immobilization system. Then, contouring of the standard OARs, left breast, and homolateral axillary region, both fused into a single PTV, and left supra-infraclavicular lymph nodes was performed. The 3D treatment plan has been developed with TPS Oncentra Masterplan v. 4.5.3 (Collapsed Cone calculation algorithm), with single isocenter technique, tangential beams on the mammary gland and axilla, and opposing beams on the supra-infraclavicular region; all OARs dose constraints provided at our Institution have been widely respected. The treatment was performed using a Versa HD Elekta Medical System LINAC, by 6-10 MV photon beams, performing setup verifications by portal imaging (i-View) daily in the first week and twice a week thereafter. In view of his frailties, the patient was evaluated with bi-weekly clinical examination and CBC.

Results: The treatment was completed without interruptions to the prescribed dose. The patient showed G2 cutaneous toxicity to the inframammary fold at a dose of 45 Gy and G3 to the su-praclavicular skin 2 days after the end of treatment on the supraclavicular region), completely regressed within 10 days of the end of treatment with topical therapy only. There was no hematological toxicity. The re-assessment CT scan, performed 3 months after the end of treatment, documented the disappearance of axillary lymphadenopathies and the presence of generic thickening of soft mammary tissues. This finding remained unchanged even in subsequent CT scans, until the last one in May 2020. A CT-PET scan performed 6 months after the end of the Radiation Therapy, has evidenced a weak uptake (SUV 4.3) only, and another at 15 months from the end of the Radiotherapy has showed further reduction of SUV (3.7) of the mammary region, without others uptake area. The patient was first treated with oral Capecitabine-based chemotherapy dd. 1-14 q21 for 9

cycles, and then at a treatment with liposomal, still in course. Currently, 22 months after the end of the Radiotherapy, the patient maintains the partial response to the breast and the complete response on the axillary lymphadenopathies, in stable clinical status, without any significant radio- or chemotherapy-related toxicities.

Conclusions: The tailored clinical pathway based on the patient's frailties, has been accepted and well tolerated. In particular, Radiation Therapy has proved effective for local disease control, determining a good response, even if partial, that has been maintained so far thanks to the pharmacological treatments followed by the patient.

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COMPARISON BETWEEN ACCELERATED PARTIAL BREAST IRRADIATION AND WHOLE BREAST IRRADIATION: APBI-IMRT TRIAL RETROSPECTIVE ANALYSIS OF SUBJECTIVE, OBJECTIVE AND PATIENT-REPORTED COSMETIC OUTCOMES (NCT02104895)

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Aims: In selected low risk patients with early stage breast cancer, accelerated partial breast irradiation (APBI) is a valid alternative to whole breast irradiation (WBI). The long-term analysis of the randomised phase 3 trial of APBI using Intensity Modulated Radiotherapy (IMRT) versus WBI (NCT02104895) showed no significant difference in terms of both local and distant disease control and survival outcomes. Acute/late toxicity and cosmesis evaluations were significantly in favor of the APBI arm. The aim of this analysis is to compare the agreement between objective and subjective patient-reported outcome measures (PROMs) of cosmesis assessment.

Methods: From June 2019 to January 2020, 95 women previously enrolled in our trial accepted to undergo this analysis. Late skin toxicity was assessed following the RTOG/EORTC late Radiation Morbidity Scoring questionnaire. Digital photographs were assessed (objective method) using the BCCT.core software v.31 (Breast Cancer Conservative Treatment. Cosmetic Results). Breast cosmetic outcomes scored both by physician and patient (subjective methods) were recorded using the Harvard Breast Cosmesis Grading Scale.

Results: At median follow up of 11 years (IQR 10.5-11.6 years), we evaluated 95 patients (51 APBI, 44 WBI). Late skin toxicity rates (any grade) were significantly in favor of the APBI group of patients (36.4% vs 6%; p=0.0003). Also, cosmetic assessment was significantly in favor of the APBI group both evaluated by physician (excellent-good [EG] 98% vs 90%, p<0.0001; fair-poor [FP] 2% vs 10%, p=0.0455) and patient (EG 86% vs 70%, p<0.0001; FP 14% vs30%, p<0.0001). The BCCT.core cosmetic assessment showed significantly improved outcomes in the APBI group (EG 65% vs FP 35%) as compared to WBI group (EG 52% vs FP 48%; p=0.0001). We observed a good agreement between BCCT.core objective evaluation and both patients (p=0.19) and physicians PROMs (p=0.17).

Conclusions: APBI patients showed significant improved late toxicity and cosmetic outcomes. There is a significative agreement between patients/physician PROMs and BCCT.core. This score has proven to be a feasible tool in breast cancer clinical practice.

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RADIOLOGICAL SCREENING AND GLANDULAR RESIDUE IN NIPPLE/SKIN-SPARING MASTECTOMY: WHAT PERSPECTIVES FOR ADJUVANT RADIOTHERAPY IN EARLY BREAST CANCER PATIENTS?

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Aims: To evaluate the role of radiological screening in early breast cancer patients submitted to nipple/skin-sparing mastectomy (NSM/SSM) for making a decision adjuvant approach with external beam radiation therapy.

Methods: We retrospectively evaluated all patients who underwent NSM and/or SSM followed by radiation therapy from October 2011 to June 2020.

Results: 57 patients who underwent mastectomy were retrospectively screened from our recordings. Among these, we selected 22 early breast cancer patients who performed the NSM and/or SSM followed by radiation therapy. At the time of primary diagnosis, the staging was T1-2 N0-1 (M0), all patients had Karnofsky index ≥ 80, and nobody presented postoperative complications. 18/22 had expander breast reconstructions and 2/22 had implants breasts positioned. The patients underwent surgery in different hospitals and with different surgical operators. Before radiotherapy, we chose to perform ultrasound or mammography evaluation on 22/22 patients to evaluate the possible persistence of glandular residue behind the NAC or the skin flap. After the radiological evaluation of the chest wall, we found residuals of mammary tissue in 22/22 patients. Of these, 20/22 were treated with radiation therapy while 2/22 patients refused the treatment. We also evaluate the loco-regional acute and late toxicities: 10/20 patients had erythema G1-G2 related to burning and pruritus (NRS> 5). None had vascular or cutaneous urgencies by the NAC or skin flap's necrosis. None of the patients interrupted the treatment course. To date, all

treated patients are disease-free. One of two patients who refused radiotherapy showed local recurrence and metastatic disease.

Conclusions: Waiting to accrue more patients and sufficient time to better analyze the oncological outcomes, we can advise in the meantime to submit patients operated with NSM and/or SSM to ultrasound or mammographic investigation after the surgery, for a positive percentage of glandular residue (>60% was described in literature data). This choice could be used in daily clinical practice to better define whether or not to submit early breast cancer patients to adjuvant RT after NSM and SSM.

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ADJUVANT HYPOFRACTIONATED BREAST IRRADIATION WITH VMAT-SIB TECHNIQUE: A PHASE II TRIAL ON TOXICITY AND EFFICACY AFTER 5 YEARS OF FOLLOW-UP

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Aims: Breast-conserving surgery followed by adjuvant radiotherapy is a standard of treatment for patients affected by early-stage breast cancer. Conventional 3D Radiation Therapy has been historically estabilished as the traditional RT technique in this setting. A phase II institutional trial was opened in 2010 in order to evaluate, in terms of toxicity and clinical outcomes, the role of Hypofractionated Volumetric-Modulated Arc Therapy with simultaneous integrated boost scheduling as adjuvant treatment. In this study we present results of this trial after a minimum 5-years follow-up.

Materials and methods: Patients affected by early-stage breast cancer, treated with breast conserving-surgery, have been enrolled in this phase II trial. Any systemic therapy was allowed either in neoadjuvant or adjuvant setting. All patients underwent VMAT-SIB technique to irradiate the whole breast with concomitant boost irradiation on tumor bed. Doses to whole breast and surgical bed were 40.5 Gy and 48 Gy respectively, delivered in 15 daily fractions over 3 weeks. Acute skin toxicities were recorded according to RTOG scoring criteria, while chronic skin toxicities according to CTCAE v4.0. Cosmetic outcomes were assessed as excellent/good or fair/poor according to the Harvard scale.

Results: Between August 2010 and August 2014, 450 patients were enrolled, with a median age of 60 years (range 27-88). The median follow-up was 77 months (range 23-116). Acute skin toxicity profile was G0 in 40.1%, G1 in 47.9%, G2 in 12.0% of patients, respectively; no higher toxicities have been recorded. After 5 years, chronic skin toxicity was G1 in 3.2% and G2 in 1.3% of patients; no G3 or higher toxicities were reported. Cosmetic outcome was good/excellent in 98.4% of patients. Breast pain was declared by 12.7% of patients. The evaluation of the clinical outcome showed 21 cases of recurrence (4.7%). Only 8 (1.7%) patients recurred in the homolateral breast; 6 (1.3%) patients presented contralateral recurrence, while 10 (2.2%) patients had distant metastases.

Conclusion: Hypofractionated Radiation Therapy with VMAT-SIB technique is a safe and effective option for adjuvant treatment in patients affected by early stage breast cancer, assuring low recurrence rate, excellent toxicity profile and good cosmetic outcome.

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ADJUVANT RADIOTHERAPY IN LEFT BREAST CANCER WITH REAL-TIME SURFACE IMAGE GUIDED SYSTEM: PRELIMINARY DOSIMETRIC RESULTS

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Aims: Adjuvant radiotherapy in breast cancer treatment still represents a staple to increase disease local control; however, in long-term surviving patients, late toxicity appearance has often been observed in the last decades, mainly in left breast treatment due to heart proximity. Although probability of cardiac toxicity occurrence is relatively low respecting QUANTEC doses constraints (<15% risk of pericarditis with mean dose and V30 <26 Gy and <46% respectively; <1% risk of long term cardiac mortality with V25 <10%), the use of low accurate techniques led to higher average heart doses, without considering respiratory movements. Our aim is report preliminary data using a body surface image-guided system that, detecting real-time respiratory movements, allows target treatment when it is in the most distant position from heart, reducing doses when compared to standard rival treatment plans.

Methods: From January 2019 to December 2019, we enrolled 13 consecutive female patients with left breast cancer (median age 63y, range 47-78). 2 patients have a DCIS, 11 DCI, with stage range Ib-IIIc. 11 patients were treated with 3D-Conformational technique, while 2 patients with VMAT (II, III and IV axillar nodal levels were included). Two treatments were planned for all patients: standard and using the Real-time surface image-guided system. Prescription dose range was 42,56 – 60 Gy in 16-30 fractions.

Results: A total of 26 treatment plans have been developed; for each patient was calculated standard and body surface image-guided treatment plan dosimetry. DVH comparison showed how the organs at risk dose constraints were respected in both treatment modalities and in all fractionation proposed (16, 20 and 30 fractions). However, in surface image-guided planning, mean and maximum doses at cardiac structures is clear-

ly lower than standard plans. All enrolled patients underwent surface image-guided treatment, that was well tolerated and no breathing control difficulty was reported. Max, mean and min heart doses were 4,13 Gy, 3,22 Gy and 0,47 Gy respectively lower in surface image-guided plans. Current mean follow-up is 11 months, and all patients have disease control and no cardiac toxicity has been reported.

Conclusions: The use of body surface image-guided system increases treatment accuracy, guaranteeing lower organ at risk doses in dosimetric evaluation. Clinical data on reduced cardiac toxicities must be assessed over a longer period.

P135

ONCE-WEEKLY HYPOFRACTIONATED RADIOTHERAPY FOR BREAST CANCER IN ELDERLY PATIENTS: EFFICACY, TOXICITY AND COSMETIC RESULTS.

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Aims. Adjuvant Radiation after breast conservative surgery is a standard of care. At present time hypofractionation is widely adopted, with regimen up to 15-16 fractions. In elderly patients, weekly schedules could eventually ameliorate patients' compliance. The aim of this clinical study is to analyze 5-years results of once-weekly hypofractionated radiotherapy in terms of efficacy, toxicity and cosmesis in these patients.

Methods. All patients who underwent breast-conserving surgery (BCS) for American Joint Committee on Cancer stage 0, I, or II breast cancer with negative surgical margins received adjuvant hypofractionated irradiation, administering 5.7 Gy in 5 fractions once weekly, over 5 weeks (total dose 28.50 Gy). The eligibility criteria were the same as for UK FAST Trial (CRUKE/04/015) and there were no restriction on breast size, tumor grade, receptor status. The primary endpoint was acute and late toxicity (Common Terminology Criteria for Adverse Event version 5.0) and cosmesis (Harris scale scoring system). Patients were evaluated for ipsilater breast tumour recurrence too. All patients gave their informed consent and the trial was approved by local Ethical Committee.

Results. Between 2015 and 2020, 49 elderly patients with median age of 73 years (range, 58-88 years) were enrolled and treated. At present time, three patients are on treatment. All but one patients completed treatment as planned; in this patient, a cerebrovascular event occurred and RT was ended after 1 fraction. Forty-five patients have completed treatment and are evaluable for acute toxicity. Acute skin toxicity was as follows: G0 19/45 (42.2%), G1 21/45 (46.7%), G2 5/45 (11.1%). Thirty-five patients, with at least 6 months of follow-up, are evaluable for late toxicity and cosmesis: late toxicity G0 25/35 (71.5%), G1 10/35 (28,5%), while cosmesis was evaluated by patients as good in 21/35 (60%), excellent in 14/35 (40%). Ipsilateral breast tumor recurrence developed in 2/35 patient (5.7%).

Conclusions. The once-weekly hypofractionated radiotherapy for elderly patients is a valid and suitable therapeutic option with satisfying side effects. These results are consistent with similar hypofractionation trials as UK FAST and FAST Forward.

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PRELIMINARY RESULTS OF HYPOFRACTIONATED REGIONAL LYMPH NODES RADIATION THERAPY IN LOCALLY ADVANCED BREAST CANCER: LOCO-REGIONAL CONTROL AND TOXICITY

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Aims: Hypofractionated radiation therapy to regional lymph node (LN) for locally advanced breast cancer patients (pts) is not a standard of care yet. Data supporting hypofractionated regional LN is limited. This study aims to determine whether an hypofractionated schedule in 15-16 fractions is safe and effective.

Methods and Matrials. Eligible patients with stage IIA to IIIC primary breast cancer received hypofractionated radiation therapy (RT) with 3DCRT technique to the chest wall (CW) or breast and supra-infraclavicular LN. Prescription dose was 40.05Gy in 15 fractions (frs) and 42.5Gy in 16 frs daily. The primary endpoint was loco-regional recurrence free survival (LRRFS); secondary endpoints were acute and late skin and thyroid toxicity, brachial plexophaty and lymphedema, distant metastasis free survival (DMFS) and overall survival (OS).

Results: Between 2010 and 2018, 57 patients with a median age of 60 years old were retrospectively analysed. The majority of pts (96%) had stage III breast cancer at diagnosis. All patients received axillary dissection and adjuvant hypofractionated radiation therapy to supra and infraclavicular LN: 59,6% to the breast and regional LN and 40.4% to the CW and regional LN. Prescription dose was 40,05Gy/15 frs /2.67Gy per fraction in 47 pts (82.4%) and 42,56Gy/16 frs /2,66Gy in 10 pts (17.6%). At a median follow-up of 80 months (min 30-max 113), 4 patients developed loco-regional recurrence (locally, 2 in the scar and 2 in-field regional lymph node). 14 patients developed distant metastatic disease, including 2 patients with loco-regional relapses. The 7-year actuarial LRRFS and DMFS were 93% and 76%, respectively. The hypofractionated regimen was well tolerated with 19.3% (11/57) G2 acute skin toxicity. No cases of G2 and G3 late skin toxicity have been observed. Only 5 patients developed late radiation-induced hypothyroidism. Lymphedema was observed in 14 patients (24.6%) and no patients experienced brachial plexopathy. The 7-year actuarial OS was 67%.

Conclusions. Hypofractionated regimen is well tolerated. Our experience suggests local control rates and toxicity outcomes aligned with those already reported in literature with conventional fractionation schedules.

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BREAST CANCER LOCAL RELAPSE AFTER INTRAOPERATIVE RADIATION THERAPY (IORT) IN ELDERLY WOMEN

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Aims: To evaluate the oncological outcomes of early breast cancer patients treated with breast conservative surgery and electron intraoperative radiotherapy (IORT).

Table 1. Patients' characteristics.

Patients Characteristics	N° (%)
Age	
Median (range)	77
Lesion size	
<10mm	73 (27,1%)
10-20	161 (59,9%)
>20 mm	26 (9,7%)
Unknow	9 (3,3%)
N stage	
Negative	218 (81%)
Positive	37 (13,8%)
Unknow	14 (5,2%)
ER+	237 (88,1%)
ER-	11 (4,1%)
Unknow	21 (7,8%)
PGR+	227 (84,4%)
PGR-	27 (10%)
Unknow	15 (5,6%)
KI67>20%	116 (43,1%)
KI67<20%	138 (51,3%)
Unknow	15 (5,6%)
RT dose	
21 Gy	203 (75,5%)
18 Gy	48 (17,8%)
10 Gy	18 (6,7%)
Grading	
1	36 (13,4%)
2	187 (69,5%)
3	35 (13%)
Unknow	11 (4,1%)
Margins	
Positive	7 (2,6%)
Negative	250 (93%)
Close	4 (1,4%)
Unknow	8 (3%)
Hystology	
Ductal	209 (77,7%)
Lobular	29 (10,8%)
Intraductal	2 (0,7%)
Other	22 (8,2%)
Unknow	7 (2,6%)
Breast	
Left	139
Right	130
Median prescription isodose	90%
Electron energy	
Median (range)	8MeV (4-10)

Methods: We analyzed all elderly patients over 70 years treated with IORT during breast conservative surgery between April 2009 and September 2016 . Patients received a dose of 18 Gy or 21 Gy according to T size (less or more than 1 cm, respectively) or a dose of 10 Gy (as boost) followed by whole breast external beam radiotherapy (40Gy in 16 fractions) if intraoperative pathological features were not considered suitable. Primary endpoint was locoregional control rate.

Results: A total of 269 patients with a median age of 77 years (range: 70-89) were evaluated. Table 1 shows patients characteristics . The median follow up was 61 months (range: 0-126). 48 (17,8%), 203 (75,5%) and 18 (6,7%) of patients received 18, 21 and 10 Gy, respectively. Locoregional recurrence was observed in 16 (5.9%) patients: 14 (5.2%) pts recurred on breast, 1 (0.37%) on breast and lymphnode and one (0.37%) on regional nodes. All these patients presented one or more high risk features: 12 had high proliferation index, 3 had grade 3 tumour and 1 had negative hormone receptors. Nine of the sixteen patients underwent to mastectomy and one to axillary node dissection; two patients have been started chemotherapy, while there are no data of the remaining two patients. A total of 24 pts developed distant metastases (10 bone metastases; 5 lung; 4 node; 3 liver; 3 brain; 3 large bowel; 1 skin). There are 71 (26%) deaths: 17 due to cancer progression while 54 patients for non-cancer related causes.

Conclusions: In selected elderly patients intraoperative Radiation Therapy can be a valid therapeutic option compared to standard whole breast irradiation.

P138

USE OF OPERA® (AN -LIPOIC ACID, BOSWELLIA SERRATA, METHYLSULFONYLMETHANE AND BROMELAIN DIETARY SUPPLEMENT) IN AROMATASE INHIBITORS-RELATED ARTHRALGIA MANAGEMENT, A PROSPECTIVE PHASE II TRIAL (NCT04161833)

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Aims: Aromatase Inhibitors (AIs) are recommended for adjuvant treatment of hormone-receptor-positive breast cancer in postmenopausal setting. To date, arthralgia is the main cause of discontinuation of therapy in 25% patients. However, data on drugs efficacy to reduce this side effect are still needed. OPERA® (GAMFARMA srl, Milan, Italy) is dietary supplement combining α-Lipoic acid, Boswellia serrata, Methylsulfonylmethane and Bromelain in a single hard-gelatin capsule. To evaluate the efficacy of OPERA ® for AIs related arthralgia management, a phase II, monocenter, self-controlled clinical trial was designed and carried out in our Radiation Oncology Unit.

Methods: We enrolled patients with arthralgia (NCI-CTCAE v4.0 grade ≥ 1) occurring during AIs therapy. OPERA® was administered once daily from enrollment (T0) up to sixth months (T3). Patients' AI-related arthralgia was evaluated every two months with VAS Scale, PRAI questionnaire and CTCAE scale. Primary endpoint was rate of symptoms resolution at T3 compared to baseline.

Results: Between November 2018 and April 2019, 53 patients were recruited in our institution, seven

(13.2%) were lost to follow-up; 46 patients were eligible for final analysis. A significant reduction of VAS score between T3 time and T0 was observed (p=0.02). Analysis of PRAI score and CTCAE scale, showed a significant reduction in arthralgia-related pain perceived (p=0.0001 and p=0.0009, respectively). Treatment with OPERA® was well tolerated; no grade 3-5 adverse event was reported.

Conclusions: Supplementation with OPERA® in patients affected by arthralgia during AI treatment is feasible and reduced the intensity of AIs-related arthralgia. Randomized, double-blind studies are warranted to confirm the effectiveness of this dietary supplement. Furthermore, it is necessary to investigate the impact of arthralgia reduction in terms of quality of life and compliance with AIs treatment.

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LONG-TERM OUTCOME OF ADJUVANT RADIOTHERAPY IN EARLY BREAST CANCER STAGES WITH INTRAOPERATIVE ELECTRON BOOST AND HYPOFRACTIONATION TO THE WHOLE BREAST IN A LARGE MONOINSTITUTIONAL SERIES OF PREMENOPAUSAL WOMEN

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Aim: To evaluate the efficacy and tolerance of an anticipated boost with intraoperative tumor electron radiation therapy (IOERT) during breast-conserving surgery followed by hypofractionated whole breast irradiation (WBI) in breast cancer (BC).

Methods: The study population included premenopausal women treated with breast conserving surgery for early BC who received 12- Gy IOERT boost to the tumor bed with mobile dedicated linear accelerator and subsequent WBI. The WBI schedule consists of 13 fractions of 2.85 Gy over 2.5 weeks. If axillary radiotherapy (RT) was needed, it was delivered after the planned chemotherapy with conventional fractionation (50 Gy/25 fractions). Patients were analyzed to assess locoregional control, distant metastases and survival outcome. This study was part of research notified to our Ethical Committee (nr N98/11)

Results: From 6/2004 to 12/2014 582 consecutive BC patients with a median age of 43 (range, 24-48) were retrospectively reviewed. Very young patients (<35) were 50. Median tumor size was 1.7 cm (range, 0.08-4.5 cm). On the axillary investigation, nodal positive patients were 163 (pN1, 136 and pN2-3, 27). LVI invasion was present in 170 cases and extensive intraductal component (EIC) in 359 cases. Both hormonal receptors were negative in 104 patients. Regarding 12 Gy-IOERT boost, median collimator size was 4 cm (range, 4-6) and median electron energy was 8 MeV (range 5-10 MeV). After a median gap of 23 days (range, 15-123 days), hypofractionated WBI was delivered with 3-dimensional conformal RT (6-MV photons). All patients completed RT as scheduled. Chemotherapy, when planned, started at the end of RT. Very few patients (n. 18) had neoadjuvant chemotherapy. After a median follow-up of 118 months (range, 9-182 months), locoregional relapses occurred in 35 patients (6%), while 49 patients developed distant metastases. The median time to the occurrence of the first event was 59.6 months (range, 5.5-177.3 months). Second malignancies included 31 contralateral breast and 17 tumors to other primary sites. At the last follow-up available, 522 patients were alive without disease, 28 were alive with disease and 31 had died. Data on acute and late toxicities were also collected.

Conclusions: After 10 years, boost IOERT and hypofractionated WBI showed to be effective and safe in this premenopausal population.

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RETROSPECTIVE ANALYSIS OF ANAL CANAL CANCER TREATED WITH RADIO-CHEMOTHERAPY: ASSESSMENT OF INFLAMMATORY PROFILE

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Aims: Inflammatory profile has been widely evaluated in many solid tumors. Here we assessed the prognostic value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in anal cancer patients treated with definitive chemoradiation.

Methods: Clinical records from patients with squamous cell carcinoma (SCC) of the anus treated with curative intent between January 2007 to May 2020 were retrospectively analyzed. Data about pre-treatment blood tests and radiological staging from multidisciplinary meeting records were collected. Receiver Operating Characteristic curves was constructed to determine the cut-off values for NLR and PLR to dichotomize the data. The measured cut-off was 4 and 250 for NLR and PLR respectively. NLR and PLR were correlated with PFS and OS.

Results: Forty patients were identified. Twenty-one out of twenty-nine patients with NLR<4 (72%) presented pCR while only four out of eleven patients with NLR>4 (36%) presented pCR (OR 4.63). The same was observed in patients with PLR < or > 250 respectively. In the whole population, 5-years PFS and 5-years OS were 74% (95% CI: 56%-85%) and 86% (95% CI: 70%-94%), respectively, while median PFS was 83

months and median OS 95 months. Patients with low-NLR recorded better PFS (5 years PFS High 41% vs 59% Low NLR, p=0.3) and OS (5 years PFS High 41% vs 81.5% Low NLR, p=0.05), even if OS only reached a statistical significant value. High-and low PLR influenced PFS (5 years PFS High 35.8% vs 63.8% Low PLR, p=0.05).

Conclusion: Our findings suggest that elevated pretreatment NLR and PLR are associated with poor complete response and survival outcome in patients with anal cancer who undergo to definitive chemoradiation.

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VMAT FOR NEOADJUVANT RADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER IN A DOSE-ESCALATION PROTOCOL AND SIMULTANEOUS INTEGRATED BOOST (SIB) APPROACH: THE EXPERIENCE OF OUR INSTITUTION

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Aims: To report the feasibility of volumetric modulated arc therapy (VMAT) for neoadjuvant radiotherapy in locally advanced rectal cancer in a dose-escalation protocol and simultaneous integrated boost (SIB) approach. Moreover, the VMAT technique was compared with three-dimensional conformal radiotherapy (3D-CRT) and fixed-field intensity modulated radiotherapy (IMRT), in terms of target coverage and irradiation of organs at risk.

Methods: Eight patients with locally advanced rectal cancer were treated with the SIB-VMAT technique. The VMAT plans were compared with 3D-CRT and IMRT techniques in terms of several clinically dosimetric parameters. The number of monitor units and the delivery time were analysed to score the treatment efficiency. All plans were verified in a dedicated solid water phantom using a two-dimensional array of ionisation chambers.

Results: All techniques meet the prescription goal for planning target volume coverage, with VMAT showing the highest level of conformality. VMAT is associated with 40, 53 and 58% reduction in the percentage of volume of small bowel irradiated to 30, 40 and 50 Gy, compared with 3D-CRT. No significant differences were found with respect to SIB-IMRT. VMAT plans showed a significant reduction of monitor units by nearly 20% with respect to IMRT and reduced treatment time from 14 to 5 min for a single fraction.

Conclusions: SIB-VMAT plans can be planned and carried out with high quality and efficiency for rectal cancer, providing similar sparing of organs at risk to SIB-IMRT and resulting in the most efficient treatment option. SIB-VMAT is currently our standard approach for radiotherapy of locally advanced rectal cancer.

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NEOADJUVANT CHEMOTHERAPY AND RADIOTHERPY FOR LOCALLY ADVANCED RECTAL CANCER. OUR EXPERIENCE

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Aims: To evaluate feasibility, tolerance and impact on local control in neoadjuvant chemotherapy and radiotherapy for locally advanced rectal cancer.

Methods: From January 2011 to December 2019, 170 Patients (pts) affected by locally advanced rectal cancer were treated with Neoadjuvant Chemotherapy (capecitabine) followed by radical surgery in our center. All patients had rectal adenocarcinomas, 70 G2 and 60 G3 at pretreatment biopsy. All patients had endoscopy and RM. The majority of patients had also an Endoscopic Ultrasound. At staging 42 patients had T3N0, 58 T3N1, 36 T3N2 and 34 T4aN1. All patients received 50.4 Gy in 28 fraction on whole pelvis, 1,8 GY for fraction, All patients had radical surgery after a median of 79 days (range 68– 118 days). 139 patients had radical anterior rectal resection, 31 pts a “Miles” surgery.

Results: After neoadjuvant treatment 131 pts had G0-1 rectal toxicity, 37 pts G2. In 2 cases treatment was interrupted. In one case per G3 local toxicity in a frail patient, In one case we founded lung progression during treatment. No genitourinary toxicity was recorded. At surgery 38 pts had a T0N0 (22%), 43 T1N0 (25%) 53 T2N0 (33%), 28 patient T2N1 (14%). 162/170 (94%) patients had a complete response on nodal site initially N+. During follow up one patient ad a gastric cancer (primary, total gastrectomy, NED after a total of 16 month). One patient T3N1 had a T1N0 at surgery but a local recurrence after 14 month. The patient with lung progression during treatment had also liver metastasis 6 month after initial treatment, and died after 17 month. No patients had post treatment permanent toxicity.

Conclusions: Our data suggests the feasibility of the treatment, because it results in a nonaggressive management, with good results in desease local control.

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THE PROGNOSTIC VALUE OF TUMOUR REGRESSION GRADE IN RECTAL CANCER PATIENTS TREATED WITH LONG-COURSE PREOPERATIVE CHEMORADIOTHERAPY

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Aim: Mandard's tumor regression grade (TRG) is widely used to evaluate the pathological response to preoperative concurrent chemoradiotherapy in locally advanced rectal cancer. The aim of this study was to evaluate the prognostic significance and clinical applicability of TRG.

Methods: from January 2015 to December 2019, 108 patients with rectal cancer in the upper, middle or lower third of the rectum clinically staged with endorectal ultrasound (ERUS) or magnetic resonance imaging (MRI) as cT3/cT4 N0 or cT(any) cN1/2, in line with NCCN guidelines, were treated with preoperative 3-dimensional conformal radiotherapy (3-D CRT) or intensity-modulated radiotherapy (IMRT) receiving 45 Gy in 1.8 Gy daily fractions to the pelvis with a 5.4 Gy boost to the tumor, concomitantly with oral capecitabine or infusional 5-fluorouracil. Surgery was attempted 4-8 weeks after completing preoperative CCRT. In all patients surgery was carried out under the rule of total mesorectal excision technique. The neoadjuvant treatment response was evaluated by Mandard's TRG.

Results: complete regression (TRG1), good regression (TRG2), moderate regression (TRG3), minor regression (TRG4) and no regression (TRG5) were seen in 17 (15.7%), 24 (22.3%), 51 (47.2%), 9 (8.3%) and 7 (6.5%) patients, respectively. Disease free survival decreased with the increase in TRG class in node-negative patients ($p < 0.001$), while in N+ patients it was worse, indipendently of TRG class ($p= 0.241$).

Conclusions: Mandard's TRG is therefore useful for staging patients undergoing preoperative chemoradiotherapy, because it displays high prognostic significance. In our exeprience, however, N was the main prognostic factor and for this reason it is mandatory to consider nodal status along with TRG.

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NEOADJUVANT RADIO-CHEMOTHERAPY IN RECTAL CANCER: COMPARISON OF TOXICITY AND CLINICAL RESULTS BETWEEN 3DCRT AND VMAT TECHNIQUE

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Aims: Neoadjuvant radio-chemotherapy is the standard treatment for loco-regional advanced rectal cancer patients. Currently, 3DCRT and IMRT are the recommended radiation techniques, even though IMRT has advantages compared to 3D-radiation regarding dose sparing to organs at risk like small bowel and urinary bladder. The primary objective of our study is the evaluation and comparison of acute gastro-intestinal and genitourinary toxicity between neo-adjuvant chemo-radiotherapy treatment performed with VMAT technique and 3DCRT, in rectal neoplasms treated in our Department. The secondary objective is the comparison of downstaging in the two groups of patients, comparing the clinical stage and the subsequent pathological stage of disease after surgery.

Methods: Since 2018, at Oncological Radiotherapy Department of Treviso Hospital, the standard of radiotherapy treatment for loco-regional advanced rectal cancer patients, has been intensity-modulated radiotherapy with VMAT technique. We compared 35 patients undergoing VMAT treatment from 2018 to 2019 with a group of 35 patients irradiated with 3DCRT technique in the two years prior. Patients in both groups received 50.4 Gy in a chemoradiation protocol (28 x 1.8, 5 d/week, capecitabine chemotherapy). The CTCAE scale (version 5.0 2017) and the total duration of treatment were used respectively for the assessment of toxicity and as an indicator of any interruptions related to acute toxicity. The two groups of patients were homogeneous for gender, age and distribution by clinical stage.

Results: Grade 0-1-2 acute small bowel and urinary bladder radio-induced toxicities were equivalent in the two groups of patients undergoing radiotherapy with VMAT and 3DCRT techniques; no patient developed G3 toxicity and no one required treatment discontinuation or hospitalization; the mean time of radiotherapy was 39.4 days. Regarding the evaluation of down-staging, we observed decreasing from the III-IV clinical stage to a lower one in 68% of the patients treated with VMAT technique compared to 53% of the patients treated with 3DCRT; complete pathological remission was achieved in 17% of the VMAT group and in 11.5% of patients undergoing 3DCRT.

Conclusions: The results of this study suggest that there are no substantial differences in toxicity between the two treatment techniques. The group of patients undergoing radiotherapy with the VMAT technique obtained a greater share of down-staging.

Table 1. Clinical Features of Patients.

	VMAT	3D
MALE GENDER	26 PATIENTS	23 PATIENTS
FEMALE GENDER	9 PATIENTS	12 PATIENTS
AVERAGE AGE	68,1 YEARS OLD	68,8 YEARS OLD
PREOPERATIVE CLINICAL STAGE	STAGE II = 6	STAGE II = 5
	STAGE III = 1	STADIO III = 3
	STAGE IV = 28	STADIO IV =27

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TREATMENT INTENSIFICATION FOR RECTAL CANCER PATIENTS: PATHOLOGICAL COMPLETE RESPONSE AND OUTCOMES

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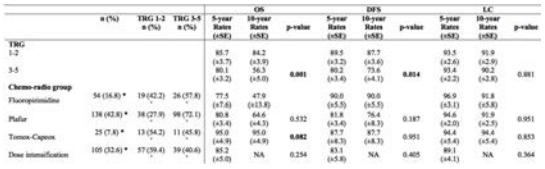
Aims: Neoadjuvant long-course chemoradiotherapy (CRT) followed by total mesorectal excision (TME) is a standard of care for locally advanced rectal cancer (LARC) patients. With the aim of increase pathological complete response (pCR) and clinical outcomes we retrospectively evaluated the effects of different intensification strategies, as dose escalation and/or drug combination.

Methods: We retrospectively analyzed 322 LARC patients (M: 209; W: 113), divided in sub-groups according to the different CRT schedules used. RT was delivered with a total dose of 4500 cGy followed by a sequential boost of 540 cGy (total dose 5040 cGy), or a concomitant boost of 1000 cGy (total dose 5500 cGy) with a 3D-CRT technique or with a simultaneous integrated boost with intensity modulated radiotherapy (SIB-IMRT) (total dose 5500 cGy). Patients were divided in four groups: fluoropirimidine chemotherapy plus 50 Gy (Fluoropirimidine group), Fluoropirimidine plus Cisplatin plus 50 Gy (Plafur group), Fluoropirimidine plus Oxaliplatin plus Raltitrexed plus 50 Gy (Tomox-Capox group) and capecitabine with dose escalation up to 55 Gy (Dose intensification group). pCR was evaluated according to Mandard tumor regression grade (TRG). The Kaplan-Meier method was used to estimate overall survival (OS), disease-free survival (DFS) and local control (LC).

Results: The majority of patients (80.8%) had cT3 tumors and 303 (94.1%) underwent surgery. The primary endpoint was tumor regression grade rate: TRG1 was obtained in 81 (26.7%) patients, TGR2 in 46 (15.1%), TRG3 in 100 (33.0%), TRG4 in 69 (22.8%) and TRG5 in 5 (1.7%) patients. Data were missing for 2 patients (0.7%). The major pathological response (TRG1-2) rate was 41.8%. The proportion of patients with a TRG 1-2 was higher in the Dose intensification group compared to the remaining groups (p= 0.046) (Table 1). The 5- and 10-year OS, DFS and LC rates were 82.5%±2.5% and 65.5%±3.8%, 81.2%±2.4% and 79.3%±2.9%, 93.1%±1.7% and 90.5%±2.1%, respectively. Table 1 reported the percentage of patients in each sub-group and the different rates of 5- and 10-year OS, DFS and LC for patients with TRG1-2 and TRG3-5 and the outcomes for the different sub-groups.

Conclusions: Neoadjuvant CRT in LARC patients resulted in favorable long-term oncologic outcomes with high pCR rate (TRG1-2: 41.8%). Dose intensification strategy seems to obtain a major pathological response higher respect to drugs combination.

Table 1. Tumor regression grade (TRG) in chemo-radiation groups and clinical outcomes at 5 and 10 years according to tumor regression grade (TRG) and different sub-groups.



	n (%)	TRG 1-2 n (%)	TRG 3-5 n (%)	OS 5-year Rates (±SE)	OS 10-year Rates (±SE)	OS p-value	DFS 5-year Rates (±SE)	DFS 10-year Rates (±SE)	DFS p-value	LC 5-year Rates (±SE)	LC 10-year Rates (±SE)	LC p-value
TRG												
1-2				85.7 (±3.7)	84.2 (±3.9)		89.5 (±3.2)	87.7 (±3.6)		93.5 (±2.6)	91.9 (±2.9)	
3-5				80.1 (±3.2)	56.3 (±5.0)	**0.001**	80.2 (±3.4)	73.6 (±4.1)	**0.014**	93.4 (±2.2)	90.2 (±2.8)	0.881
Chemo-radio group												
Fluoropirimidine	56 (16.8) *	19 (42.2) ^	26 (57.8) ^	77.5 (±7.6)	47.9 (±13.8)		90.6 (±5.5)	90.6 (±5.5)		96.9 (±3.1)	91.8 (±5.8)	
Plafur	136 (42.8) *	38 (27.9) ^	98 (72.1) ^	80.8 (±3.4)	64.6 (±4.3)	0.532	81.8 (±3.4)	76.4 (±4.3)	0.187	94.6 (±2.0)	91.9 (±2.5)	0.951
Tomox-Capox	25 (7.8) *	13 (34.2) ^	11 (45.8) ^	95.0 (±4.9)	95.0 (±4.9)	**0.002**	87.7 (±8.3)	87.7 (±8.3)	0.951	94.4 (±5.4)	94.4 (±5.4)	0.853
Dose intensification	105 (32.6) *	57 (59.4) ^	39 (40.6) ^	85.2 (±5.0)	NA	0.254	83.1 (±5.8)	NA	0.405	89.1 (±4.1)	NA	0.364

TRG: tumor resection grade; *: Total patients retrospectively analysed. ^: patients evaluable for TRG; OS: Overall Survival; DFS: Disease Free Survival; LC: Loco-regional Control; Plafur: cisplatin and 5-FU; Tomox: raltitrexed and oxaliplatin; Xelox: capecitabine and oxaliplatin. A p value of 0.05 or less was considered statistically significant

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STEREOTACTIC BODY RADIATION THERAPY IN UNRESECTABLE INTRAHEPATIC CHOLANGIOCARCINOMA: A SYSTEMATIC REVIEW

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Aim: The role of stereotactic radiotherapy (SBRT) in the treatment of unresectable intrahepatic cholangiocarcinoma (ICC) is unclear. Randomized trials and systematic reviews on this topic are lacking. Therefore, the aim of this study was to present a systematic review on efficacy and safety of SBRT in the treatment of unresectable ICC.

Methods: A systematic review based on Prisma methodology was performed. Only articles reporting outcomes in terms of Overall Survival (OS) related to SBRT treatment for unresectable ICC were included. Secondary aim was to report outcomes in terms of Progression Free Survival (PFS), Local Control (LC) and Toxicity.

Results: Six papers (145 patients) were included in this analysis. Median SBRT dose was 45 Gy (range: 24-60) delivered in 3-5 fractions. Median follow-up ranged

between 9 and 18 months (median: 16 months). Median OS ranged between 10 and 48 months (median: 14 months). In one study, 1-year and 2-year LC was 85% and 71%, respectively. One–year PFS was 50% and 68% in two studies. Toxicity was not reported in 3 studies. Only one fatal adverse event was recorded in the other two papers.

Conclusions: SBRT is an effective treatment option in unresectable ICC. Only little evidence is available on the efficacy of SBRT in the treatment of ICC. Therefore prospective studies on larger series or pooled analyses are needed. Based on the available data, there are no clear differences compared to the results of systemic treatments or of other ablative therapies.

Table 1. Treatment outcomes.

Authors, Year	LC % 1-y	OS % 1-y	Median OS (month s)	PSF % 1-y	Median PFS (months)	Toxicity scale	Acute toxicity G≥3 % (no of pts)	Late toxicity G≥3 % (no of pts)	Tumour response %
Shen et al., 2017	NR	57.1 2-y: 32.1	15.0	1-y: 50.0 2-y: 21.4	11.0	CTCAE v.4.0	Nausea: 3.6 (1) Anorexia: 7.1 (2) Vomiting: 3.6 (1) Gastric ulcer: 3.6 (1) Altered hepatic values: 25.0 (7) Altered bone marrow values: 10.8 (3)	NR	(RECIST criteria) CR: 10.7 PR: 35.7 SD: 42.9 PD: 10.7
Weiner et al. 2016	NRS	51.0	13.2	68.0	24.7	CTCAE v.4.0	Hepatic failure (G5): 1	NRS	(EASL criteria) Radiographic response: 33.3 Complete radiographic response: 8.3
Klein et al. 2015	NR	NR	12.1	NR	NR	NR	NR	NR	NR
Jung et al., 2014	85.0 2-y: 71.0	39.0 2-y: 18.0	10.0	NR	NR	CTCAE v.4.0	NRS	NRS	NR
Sebastian et al, 2019	NR	NR	48	NR	NR	NR	NR	NR	NR
Kozak et al, 2020	NR	NR	23	NR	NT	NR	Hepatobiliary 42.5 (17)* Non hepatobiliary 2.5 (1)*	Hepatobiliary 42.5 (17)* Non hepatobiliary 2.5 (1)*	40.0 % local-failure 8.0 % regional-failure

Legend: CR: Complete response; CTCAE: Common Terminology Criteria for Adverse Events; EASL: European Association for the Study of the Liver; G: grade;; LC: local control; no: number; NR: not reported; NRS: not reported separately; OS: overall survival; PD: progression disease; PFS: progression free survival; PR: Partial response; pts: patients; RECIST: Response Evaluation Criteria In Solid Tumours; SD: Stable disease; y: year; *data related to all group of population.

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PROTON BEAM RADIOTHERAPY IN PANCREATIC CANCER: A SYSTEMATIC REVIEW

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Introduction: The role of proton beam radiotherapy (PBRT) in pancreatic cancer (PC) is still uncertain due to lack of clinical evidence. Aim of this review was to analyse the available evidence on this topic.

Material and methods: A bibliographic search was performed using PubMed, Scopus, and Cochrane databases. All studies in English language reporting toxicities and/or outcomes data after PBRT were included.

Results: Ten studies were analysed: 5 retrospective, 2 prospective phase I/II, one prospective phase II, and 2 simply defined as prospective. Total number of included subjects was 362 patients. Median follow-up ranged between 10 and 38 months (median: 15 months). PBRT was performed with concurrent chemotherapy in all studies, with doses ranging between 25.0 and 70.2 GyE (median: 67.5 GyE). Overall acute or late gastrointestinal (GI) toxicity G ≥3 was observed almost in every study, ranging from 3.0% to 20.0%, and from 1.1% to 20.0%, respectively. The highest toxicity rate (20.0%) was reported in the study where PBRT was delivered with the highest dose (70.2 GyE). In two studies same cases of G5 late GI toxicity were recorded (2.2% and 2.5%, respectively). Overall survival ranged between 16.7 and 26.1 months (median: 20.8 months) in 7 studies. Progression-free survival ranged between 10.4 and 15.4 months (median: 12.7 months) in 3 studies.

Conclusions: PBRT is an emerging therapy but with unclear role in PC. In fact, our analysis showed a not negligible G≥3 rates, and some lethal toxicities. Overall survival, and progression-free survival rates were similar to other radiotherapy techniques. Therefore, further investigation on this treatment modality in PC are needed.

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ABLATIVE STEREOTACTIC RADIOTHERAPY FOR EARLY STAGE PANCREATIC CANCER IN ELDERLY PATIENTS: A SINGLE CENTER EXPERIENCE

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Aims: Pancreatic tumors still represent poor prognosis diseases with 8% 5-year overall survival. Better results are obtained when the disease is diagnosed in the early stages; however, many elderly patients have comorbidities that do not allow surgery, therefore the only available locoregional treatment is offered by radiation therapy. We report our experience with inoperable elderly patients undergoing stereotactic radiation therapy for early stage pancreatic cancers.

Methods: From January 2009 to January 2019, we enrolled 6 patients (2 M, 4 F, median age 77,3 years) with early stage pancreatic head cancer (5 pancreatic adenocarcinoma, 1 neuroendocrinal cancer; all patients have a Ib stage); 4 patients had advanced COPD, 2 patients had II-III stage NYHA heart failure that contraindicated surgery. 2 patients received neoadjuvant gemcitabine treatment, while neuroendocrine cancer patient underwent to fluorouracil regimen. All patients received body Stereotactic Radiotherapy (SBRT) treatment with image fusion 4DCT-MRI planning : 4 patients underwent to SBRT with no-coplanar arches and couch body frames (CT localizer) with 30-42 Gy doses range in 4-6 fractions (30 Gy in 2 patients, 40 Gy

in 4 and 42 Gy in 6 in other two patients respectively); the last 2 patients received SBRT with VMAT technique and respiratory motion monitoring by 4D IGRT with 23,55 Gy in 3 fractions dose.

Results: All patients completed treatment. Mean follow-up was 10 months and mean survival was 13 months for five pancreatic adenocarcinoma patients, while mean follow-up and survival were 52 and 60 months respectively for the neuroendocrine cancer patient. No G3-4 toxicities were observed. In planning observation, mean PTV volume and mean dose at organ at risk were smaller and higher respectively in no-coplanar arches planning and VMAT planning patients group (PTV mean volume: 75,6 cc in no-coplanar planning vs 57,8 cc in VMAT patients; Mean dose at pancreas and duodenum: 27 and 19,1 Gy in no-coplanar patients vs 17,4 and 10,2 Gy in VMAT patients respectively).

Conclusions: SBRT can considered an effective and safe treatment in early stage pancreatic cancer for elderly and no-fit surgery patients, using advanced technique such as VMAT. Larger studies are needed for optimal fractionations identification.

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IS HYPOFRACTIONATED SEQUENTIAL RADIOTHERAPY BOOST (HRB) A PROMISING STRATEGY IN UNRESECTABLE, NON-METASTATIC LOCALLY ADVANCED PANCREATIC CANCER PATIENTS?

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Aims: To investigate the feasibility and potential benefits of hypofractionated radiotherapy boost (HRB), following chemotherapy (CT) and concomitant chemoradiotherapy (CRT), in patients (pts) with unresectable, non-metastatic, locally advanced pancreatic adenocarcinoma (LAPC). Primary endpoints were early and late toxicity, local control (LC) and pain-free progression (PFP). Secondary endpoints were overall survival (OS) and metastases-free survival (MFS).

Methods: Patients affected by unresectable, non-metastatic LAPC already treated with concomitant CRT (50.4 Gy in 28 fractions to primary and 39.6 Gy in 22 fractions to nodal drainage area with concurrent gemcitabine) and CT (Gemcitabine or Folfirinox), were selected for a HRB on the primary lesion. The pain assessment was defined by Kersh-Hazra scale; early and late toxicity were assessed according to CTCAE v.4.0 classification.

Results: From November 2004 to October 2019, 31 pts affected by unresectable non-metastatic LAPC were consecutively enrolled. All pts completed the planned HRB. HRB was delivered to primary lesion with a total delivered dose varying according to duodenal dose constraints (maximum dose to the duodenum 90Gy in EQD2 alfa/beta 2 summing the dose received during CRT and HRB): 20Gy in 5 fr (N: 6; 19.4%), 20Gy in 4 fr (N: 5; 16.2%), 25Gy in 5 fr (N: 18; 58.0%) and 30Gy in 6 fr (N: 2; 6.4%). At restaging imaging after CT/CRT, partial response to treatment was documented in 13 pts (41.9%). No Grade 3 or 4 acute gastrointestinal toxicity (nausea, vomiting, diarrhea) and no late gastrointestinal complications occurred. Median follow-up was 11 months (range 2-156). Median LC from the completion of HRB was 19 months (range: 1-156) and 1- and 2-years PFP following HRB were 85% and 62.7% respectively (median: 28 months; range: 2-139). According to the Kersh-Hazra scale, four pts had a Grade 3 and four pts had a Grade 1 abdominal pain before HRB. At last follow-up only 3/31 pts (9.7%) had residual Grade 1 abdominal pain; while Grade 3 residual abdominal pain was observed in 2 patients (6.4%). The 2-years OS after HRB was 57.4%, while the 2-years OS from diagnosis was 77.3. Median MFS was 18 months (range 1 – 139).

Conclusions: Treatment intensification with HRB is feasible and well tolerated in pts affected by unresectable non-metastatic LAPC previously treated with CT and concomitant CRT.

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PRETREATMENT ANEMIA PORTEND POOR PROGNOSIS IN PATIENTS WITH RECTAL CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY

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Aims: To retrospectively assess the relationship between pretreatment anemia and clinical outcomes in patients who underwent neoadjuvant chemoradiotherapy for locally advanced rectal cancer (LARC)

Methods: Pre-treatment blood hemoglobin (Hb) levels were measured in a cohort of 140 LARC patients, and their correlation with local control (LC), overall survival (OS), and disease-free survival (DFS) were analyzed. Anemia was defined as the lowest quartile for both males and females. Survival rates were estimated with Kaplan-Meier analysis, and univariable and multivariate Cox proportional hazard ratios were used to assist in risk stratification.

Results: Median follow up was 39 months (range 18-60 months). The average pre-treatment Hb level was 134 g/L (128 g/L in women , 137 g/L in man). Of 140 patients, 14 females and 16 males were found anemic. Overall, 2-y OS was decreased in anemic patients (64%

vs 91%; p= 0.021), who also reported higher positive margins and local recurrence rates (36% vs 15%; p=0.021 and 38% vs 7%; p= 0.003), respectively. After adjusting for age, gender, stage, comorbidities, pre-treatmemt anemia in female patients was significantly associated with lower rates of OS (69,2% vs 91,7%; p=0.022); DFS (64,2% vs 91,1 p= 0.021) and local control (19,4% vs 30,8%; p=0,011).

Conclusions: Our findings have demonstrated that pre-treatment anemia was associated with worse clinical outcomes, especially in female patients. Correcting blood Hb levels might improve tumor response and survival in LARC patients who are candidates for neoadjuvant chemo-radiotherapy. A prospective evaluation is warranted to confirm these results.

P151

LOCALLY ADVANCED ESOPHAGEAL CANCER: A 5 YEARS MONOINSTITUTIONAL TUMOR BOARD EXPERIENCE

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Aims: Neoadjuvant chemoradiotherapy (CRT) plus oesophagectomy is considered the standard treatment for locally advanced oesophageal cancer (LAOC). Radio +/- chemotherapy is the main treatment modality for patients (pts) who cannot undergo surgery. There is no strong evidence in literature for the best CRT schedule, considering different histologic subtypes and different sites of disease; this leads to a wide heterogeneity in the treatment of LAOC both in preoperative and definitive setting. We aimed to retrospectively analyse our cohort of LAOC.

Methods: Inclusion criteria were the following: 1-histological diagnosis of both squamous cell carcinoma (SCC) and adenocarcinoma (ADC) LAOC; 2-radiological diagnosis of non-metastatic LAOC; 3-neoadjuvant or definitive CTR; 4-multidisciplinary board approval; 5-written informed consent for treatment and research data use. This study was part of research notified to our Ethical Committee (nr N87/11).

Results: From 2015 and 2020, 24 pts matched the inclusion criteria: half experienced neoadjuvant CRT and oesophagectomy (group A) and half definitive CRT (group B). In group A, 8 pts were diagnosed with SCC, 9 had a distal thoracic LAOC. The most frequent schedules of RT treatment were 41.4 Gy in 23 fractions (8/12) and 50.4 Gy in 28 fractions (4/12). The most frequent CT scheme was carboplatin/paclitaxel every 8 days (8/12). Four pts did not complete CRT for G3/4 toxicities. Before surgery, 6 pts experienced a radiological partial response. After surgery, only 4 pts still had lymph nodes involvement. At last follow up, 5 pts had not evidence of disease (NED), 4 pts died and 1 pt was alive with disease (AWD). Group B comprehended 12 pts who underwent a definitive CRT. The majority (10/12) had a SCC LAOC. The most frequent RT schedule was 54 Gy in 27 fractions (10/12) with different schemes of concomitant CT. Ten patients completed prescribed CRT. A G3/4 toxicity event was described in 4 cases. At last follow up, we registered 4 deaths, 2 pts with NED and 2 pts AWD; 1 pt had just completed the whole treatment. A total of 5 pts in both groups were lost in follow up.

Conclusions: Our data, inconsistent to draw conclusions, reflect the big heterogeneity in neoadjuvant and definitive CRT for LAOC treatment; due to the low incidence and high variety of oesophageal cancer presentation and pts, treatments are challenging and multicentric studies are mandatory to define the best strategy in the management of this disease.

P152

INTENSITY MODULATED RADIOTHERAPY (IMRT) IN THE TREATMENT OF SQUAMOUS CELL ANAL CANAL CANCER: LATE TOXICITY AND TUMOR OUTCOME

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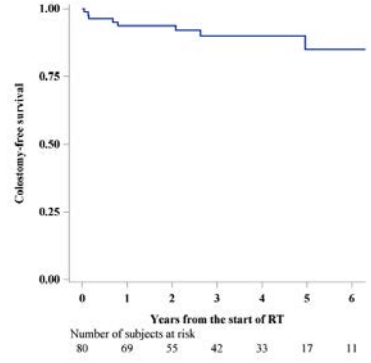
Aims: To retrospectively review our experience on 83 patients (pts) with squamous cell anal canal cancer (SCAC) after curative IMRT concomitant to chemotherapy, in terms of late toxicity, colostomy-free survival (CFS), disease-free survival (DFS) and overall survival (OS).

Methods: Inclusion criteria were the following: 1-histological diagnosis of SCAC (cT1-T4, cN0-N3, cM0); 2- IMRT concomitant to chemotherapy with a curative intent; 3- written informed consent for treatment and research data use. Late gastrointestinal (GI), genitourinary (GU), cutaneous (CU), vulvo-vaginal toxicities and sexual disfunction were assessed according to Common Toxicity Criteria for Adverse Events (CTCAE) v.4.03 and the Radiation Therapy Oncology Group (RTOG) late radiation morbidity scoring system. Clinical and radiological examinations were managed every 4 months for the first 2 years after treatment and every 6 months for the next 3 years (to a total of 5 years). This study was part of research notified to our

Ethical Committee (nr. N87/11).

Results: The median follow-up was 3.7 years (range 2-4.9). Late toxicity was collected for 79 pts (95%): severe (≥ G3) GI and vulvo-vaginal toxicity was observed in 5 (6%) and 2 pts (3%), respectively. No other ≥ G3 late toxicity was collected. At the univariate analysis, there was no statistically significant correlation between pts and treatment characteristics and severe late toxicity. One pt died within 6 months after the completion of the chemoradiotherapy (CRT) and 3 pts had a follow-up < 6 months, so they could not be considered for this analysis. The CFS was analysed in 80 pts, as 3 pts had colostomy before the start of CRT [see Figure 1]. The DFS was 85%, 77%, 73%, at 1 yr, at 3 yr, at 5 yr, respectively. Sixteen pts showed a progressive disease and 4 pts died as first observed event. The 1-yr, 3-yr and 5-yr OS was 98%, 93% and 93%, respectively.

Conclusions: Our study showed a mild late toxicity and excellent tumor outcome results, confirming the IMRT as standard of care for curative treatment of anal cancer pts.



Colostomy	Median (Q1-Q3) Follow-up (years)	1-yr CFS (95% CI)	3-yr CFS (95% CI)	5-yr CFS (95% CI)
8/80 (10%)	3.4 (1.7-4.9)	94 (85-97)	90 (80-95)	85 (68-93)

Figure 1. Colostomy-free survival (CFS) (N=80).

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STEREOTACTIC BODY RADIATION THERAPY IN PATIENTS WITH EXCLUSIVE LIVER DISEASE: OUTCOME AND PROPENSITY SCORE MATCHING ANALYSIS IN SINGLE CENTER INSTITUTION

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Aim: The aim of this study was to evaluate long-term efficacy and outcomes of stereotactic body radiation therapy (SBRT) for patients with both primaries and secondaries liver lesions.

Materials and methods: Fifty-two patients and 67 liver lesions were addressed to SBRT from December 2007 up-to August 2017. Most of patients received either one or multiple fractions (59.5 and 40.5%, respectively), with 23-30 Gy/1-fraction and 45-54Gy/3-fractions (31.5%) and sere were matched together, via propensity score (PSM).

Results: The median age at time of enrolment was 68 years (range=43-88 years). The median follow-up time for all surviving patients was 55 months (range 24 -138 months). Metastatic tumors comprised the majority of lesions (87.8%), with pancreatic, CRC, breast, lung, gastric primaries and gastrointestinal stromal tumor (GIST) as the predominant histologies. Hepatocellular carcinoma represented 3% and intrahepatic cholangio-carcinoma 8% of all lesions. Forty-five out of 52 (86.5%) patients received one or more chemotherapy cycles before SBRT. Median LPFS was 17 months (range 1-138 months), 1- and 2-year LPFS rates of 81.1% and 59.6%, respectively (Figure 1), for overall cohort, median LPFS was 16 months (range 1-75 months), 1- and 2-year LPFS rates of 83.4% and 68.8%, respectively for PSM cohort. Median, 1- and 2-year OS rates were 22 months (range 2-138 months), 75.0% and 48.1%, respectively for overall cohort, despite were 20 months (range 2-75 months), 78.6% and 50.0%, respectively, for PSM cohort. PSM analysis confirmed the results evidenced on baseline cohort except for metastases free survival (MFS).

Conclusion: Our study confirms SBRT as valid option in primary or oligo-metastatic hepatic malignancies. We report a very convincing local control rates, encouraging results concerning survival and a low rate of high-grade toxicity. Single fraction schedule presented the same results of multi-fractions schedule. Prospective data are helpful to select patients potentially beneficiating a loco-regional treatment.

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RADIOCHEMOTHERAPY IN ANAL CANCER, WHAT IS THE OPTIMAL DOSE? A SINGLE ISTITUTIONAL EXPERIENCE

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Aims: Radiation therapy(RT) plus concurrent 5-fluorouracil(5-FU) and mitomycin(MMC) represents the preferred standard of care for squamous cell carcinoma of the anus.To date remains unclear what RT doses are commonly prescribed in the treatment of this cancer.Our aim was to evaluate how the dose influenced local control (LC) and overall survival(OS) of patients with anal carcinoma.

Methods: Between September 2010 and July 2019, 54 patients with pathologically proven anal canal carci-

noma were treated with Radiochemotherapy(RT-CT) at Pisa University Hospital. Stage distribution was as follows: I,19(35%); II-III 35(65%). The median age was 65.5 years (range, 42-90 years), M:F=19:35.RT was performed with IMRT technique.Regarding CT, patients were treated with capecitabine 825 mg/mq BID 1-28 or continuous infusion of 5-FU (1000 mg/m^2) and MMC (10 mg/m^2). Median overall treatment time (OTT) was 46 days (range, 34-115 days).Patients were stratified by RT dose at primary tumor: <56 Gy, 56Gy, > 56Gy. Patient's age, HIV status, stage, OTT, and RT dose were variables analyzed for OS and LC.

Results: Median follow-up time was 47.5 months(range, 9-114 months).Complete response after 6 months was observed in 43 patients (79%). Local recurrence occurred in 9 (16%) patients, and of these, 7 were rescued by surgery. Distant metastasis was observed in 11 patients (20%). Interruption of RT-CT higher than 5 days as a result of acute toxicity was necessary in 7 patients (12%). When the treatment is suspended for more than 10 days (occurred in 15 patients,27%) there is a reduction in LC, although it is not statistically significant (p=0,192). The most commonly prescribed RT dose was 56 Gy (median RT dose 56 Gy). According to the RT dose, LC was lower among patients who received less than 56 Gy at primary tumor(HR=0.44, p=0.088). There was no significant difference in OS for patients who received <56 Gy or 56 Gy compared with >56 Gy. This results is also confirmed in the analysis by subgroups. RT dose >56 Gy was associated with greater gastrointestinal toxicity, although it was not statistically significant(p=0.0092).

Conclusions: In clinical practice, it remains to be determined what is the optimal RT dose in anal cancer. In our study, we found that RT dose <56 Gy was associated with less LC but in absence of significance. This could be linked to the small number of patients. Prospective randomized studies designed with the aim of defining the appropriate dose are required.

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DOSE-ESCALATED RADIOCHEMOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER PATIENS (LARC). MID-TERM FEASIBILITY, EFFICACY AND SURVIVAL ANALYSIS.

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Aim: To evaluate feasibility efficacy and survival of a Neoadjuvant Dose Escalated Radiotherapy and concomitant Capecitabine, for locally advanced rectal cancer (LARC).

Methods: From January 2011 to December 2019, 74 patients with LARC stage IIA, IIIB, IIIC underwent neoadjuvant dose-escalated, chemoradiation. Staging included: clinical history, colonoscopy, digital rectal examination (DRE), endorectal ultrasound (EUS), multiparametric MRI, and 18FDG PET/CT scan. CTV segmentation included rectum, the entire mesorectum and lateral nodes (external iliac if cT4 or sphyncterial involvement). Nodal PTV was obtained with isotropic 0.5 cm CTV expansion, while rectal CTV-PTV expansion was 1 cm in all-directions, with respect to anatomic boundaries. SIB was outlined as 40% of PET/CT SUV max with corresponding mesorectum. A 1 cm isotropic CTV-PTV was given. pCR was defined as no residual disease in both tumour and lymph-nodes (ypT0 pN0) or as no residual tumor (TRG 1 according to Mandard) in patients who underwent local excision.

Results: Median age was 64 years (42-80), 25 patients were stage IIA, 3 stage IIIA, 34 stage IIIB and 12 stage IIIC. Thirty-seven patients had tumor located in the lower rectum while 37 patients in the middle or middle-upper rectum. Mesorectal Fascia (MRF) involvement was found in 23/74, (32%) of patients. 37 patients underwent VMAT with simultaneous integrated boost, while 37 patients 3D conformal RT with sequential boost. Boost dose was 54 Gy in 15 patients, 55 Gy in 3 patients and 56 Gy in 56 patients. Boost EQD2 was 54-55Gy in 9 patients, 56Gy in 24 patients and 59Gy in 41 patients. Abdomino-perineal resection APR was performed in 16 patients, anterior resection (RAR) in 45 and TEM in 9 while 4 patients underwent WW. Pathologic complete response (pCR) was achieved in 23/70 patients (33%) while major response (TRG2) was obtained in 25 patients. Median follow-up time was 33 months (6-104). 2-years and 5-Years survival probability were as follows: OS 97% and 77%, LRFS 97% and 87%, MFS 88% and 77% respectively. No G3-G4 toxicity were documented. For operated patients, bivariate analysis showed that only boost EQD2 was significantly related to pCr (p=0.025) and LRR (P=0.011). At the end of the analysis organ preservation rate was 74% (55/74).

Conclusions: A neoadjuvant dose escalated radiochemotherapy appears to be effective and feasible. Further prospective studies, with larger cohort and longer follow-up are needed to confirm this data.

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RADIATION DOSE INTENSIFICATION IN NEOADJUVANT LOCALLY ADVANCED RECTAL CANCER TREATMENT: A MONOCENTRIC EXPERIENCE

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Aims: The aim of this study was to analyze the role of RT dose-intensification in the neoadjuvant treatment of LARC in terms of pathological complete response(pCR), acute toxicity, OS and DFS.

Methods: We retrospectively analyzed 89 patients (pts) with LARC treated from 2008 to 2019 with 3D

conformal radiation therapy or volumetric modulated arc therapy (VMAT) and simultaneos integrated boost (SIB) in our institution. Concurrent Capecitabine was administered in all patients. Treatment response was evaluated in terms of pCR and acute toxicity was evaluated according to the CTC-AE 4.02 scale. The gross target volume (GTV) encompassed the primary lesions and the positive lymph nodes: The clinical target volume (CTV) was defined as the GTV plus mesorectal space, the presacral region, the mesorectal limphnode and the perirectal and internal iliac lymph node. A dose of 50.4 Gy was prescribed to CTV and a dose of 56 Gy was prescribed to GTV.

Results: The patients population consisted of 58 males (65.1%) and 31 female (34.9%) with mean age 66.7 years (range 37-85 years). Overall, 9 pts (10.1%) had stage I, 11 pts (11.4%) stage II,60 pts (67.4%) stage III and ,6 pts (6.7%) stage IV. Seventy-eight pts underwent to surgery after the neoadjuvant therapy; pCR rate was 19.1%. The median interval between Chemoradiotherapy and surgery was 9.4 weeks (range 7-11.5). The most frequently reported toxicity was grade 1 and grade 2 perianal erythema in 45 pts (50.5%); grade 1 and 2 tenesmus was reported in 24 pts (26.9%) No toxicity over grade 2 was reported. Median follow up was 56 months. Overall survival (OS) at 5 years was 73.7 % and Disease Free Survival (DFS) at 5 years was 65.8%.

Conclusions: Radiation dose intensification appears well tolerated, feasible and effective in terms of pathological complete response with a good DFS and OS. It might be interesting to intensify treatment in patients with major risk factors (N2, distance to MRF ≤ 1 mm, disease located in the lower rectum) and to make a risk stratification in order to personalize the treatment.

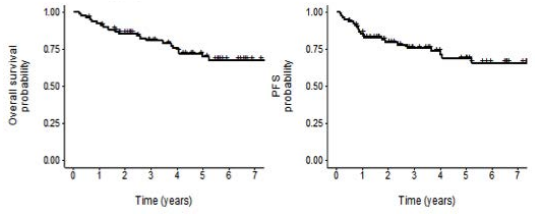

Figure 1. Overall survival and progression free survival.

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SIMULTANEOUS INTEGRATED BOOST WITH DOSE-ESCALATION AND CONCURRENT CHEMOTHERAPY FOR LOCALLY ADVANCED MID-LOW RECTAL CANCER: REPORT OF TOXICITY BETWEEN IMAGE-GUIDED VMAT VS 3DCRT

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Aims: to compare the GI and GU toxicities of patients with locally advanced mid-low rectal cancer (LARC) and treated with preoperative concurrent chemotherapy and image-guided (IG) 3DCRT or VMAT. A dose escalated simultaneous integrated boost was used.

Materials and methods: The records of patients with LARC were retrospectively analyzed. A dose of 45Gy in 25/27 fractions was delivered to the pelvis, and 54 Gy was prescribed for the primary tumor with a simultaneous, integrated boost. All radiation treatments were delivered with concurrent chemotherapy. Radiation treatments include both 3DCRT or VMAT. The acute GI and GU toxicities were assessed during the treatment, two weeks after the end of the radiation therapy and before surgery according to Radiation Therapy Oncology Group (RTOG) scale for early side effects. The incidence of toxicity between the two groups were evaluated by the Fisher's exact test. A p-value <0.05 was defined as statistically significant.

Results: A total of 55 patients were selected. Twenty-seven were treated by VMAT and 28 by 3DCRT, respectively. Twenty-three patients (85,2%) in the VMAT group and 25 (89,3%) in the 3DCRT group had stage cT3 or cT4. In the VMAT and 3DCRT groups tumor was in the lower rectum in 14 (52%) and 17 (61%) patients, respectively. A no significant trend toward a lower incidence in any grade of GI toxicity was observed in VMAT (66.7%) with respect to 3DCRT (85,7%). Grade 2 GI toxicity was observed in 22,2% and in 39,3% of patients treated by VMAT and 3DCRT, respectively. A significant increase in the any grade of GU toxicity was observe in the group treated by 3DCRT (67,9%) when compared with patients treated by VMAT (26%) p=0.0028. The incidence of G2 GU toxicity was 11% and 24,4% in the group treated by VMAT and 3DCRT, respectively. No G3 or greater acute GU and GI toxicity was observed. Grades 3 leukopenia, anemia, and thrombocytopenia were observed in 1 (3,5%) patients, 2 (7%) patients, and 2 (7%) patients treated by 3DCRT. The same toxicity was observed in 0 (0%) patients, 1 (3,7%) patients, and 2 (7,4%) patients treated by VMAT.

Conclusions: This retrospective analysis indicates that neoadjuvant, image-guided VMAT and 3DCRT with 54 Gy boosted to the primary tumor was well tolerated. A lower acute GU toxicity was reported after more conformal techniques. Further studies are needed to better define the role of dose-escalated VMAT radiotherapy for rectal cancer treatment in a neoadjuvant setting.

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NEOADJUVANT SHORT-COURSE RADIOTHERAPY (5 × 5 GY)FOR RECTAL CANCER: IMMEDIATE OR DELAYED SURGERY?

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Aims: Preoperative short-course radiotherapy (SCRT) is an important treatment option for rectal cancer. The length of time between completing SCRT and surgery can influence postoperative outcomes, but the evidence available to determine the optimal interval is limited and often conflicting. We retrospectively evaluated the optimal timing of surgery after SCRT in a monoinstitutional series.

Methods: Between January 2006 and December 2019, a total of 24 patients with stage II-III histologically confirmed rectal adenocarcinoma underwent SCRT with a total dose of 25 Gy in 5 consecutive daily fractions by means of 3D conformal technique. Acute and late toxicities were graded according to the CTCAE v.3 scale. Survival probability analysis was performed using the Kaplan-Meier method.

Results: Median age was 80,25 years (range 63-93), with 11 females and 13 males. According to common recommendations, preoperative SCRT was followed by immediate surgery (6-10 days) in 7 patients. In 12 and 4 patients, surgery was offered within 6 weeks and after 8 weeks, respectively. One patient did not receive surgery. The most common procedures were low anterior resection 9 patients (39%) and Miles resection in 9 patients (39%). Three patients underwent proctosigmoidectomy (Hartmann's), 1 had a transanal excision and 1 explorative laparotomy. There was no postoperative mortality and none of the patients experienced major postoperative complications. One patient had a pathologic complete response, and 18 (78%) achieved downstaging (TRG Mandard 2-3). Four patients showed stable disease (TRG Mandard 4-5). After a median follow-up of 32 months (range 2,67-62,27) the overall survival rate was 79%, disease-free survival 83%, locoregional relapse-free survival 92%, with no statistically significant difference between SCRT with early surgery and SCRT with delayed surgery. No toxicity was detected in patients with delayed surgery, while 3 patients who received early surgery reported a mild gastrointestinal toxicity (2 proctitis G2,1 abdominal pain G1).

Conclusions: Our findings show that delayed surgery following SCRT does not compromise clinical outcomes compared to immediate surgery. Postponing the intervention might be helpful in case of emergency and inability to operate. Prospective data are needed to confirm this strategy.

P159

STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR INOPERABLE HEPATOCELLULAR CARCINOMA (HCC): OUTCOME AND TOXICITY FROM A LARGE MONOCENTRIC EXPERIENCE

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Introduction: Stereotactic Body Radiotherapy (SBRT) emerged as a valuable option in early to advanced-stage Hepatocellular Carcinoma (HCC) as defined by Barcelona Clinic Liver Cancer (BCLC) system. The aim of our study is to evaluate SBRT in HCC patients and to identify predictors of outcome and toxicity.

Material and Methods A retrospective review of HCC patients treated at our Institution between November 2011 and December 2018 was carried out. SBRT was delivered in 3-10 fractions to a median Biologically Effective Dose (BED10) of 103 Gy10.

Results: SBRT was performed in 128 patients to 217 HCC localizations, accounting for 142 treatment courses. BCLC stage was A, B, C in respectively 40 (31%), 72 (56%) and 16 (13%) patients. Median follow-up interval was 19 (range 3-49) months. Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS) at 2 years were respectively: 78%, 15% and 58%. LC was influenced by BED10>120 Gy10 (Hazard Ratio, HR: 0.08, 95%CI 0.01-0.59; p=0.013) and size >3cm (HR: 2.71, 95%CI 1.10 -6.66; p=0.03). BCLC stage was correlated to PFS (median 14 versus 12 versus 5 months, p=0.012). In BCLC stage A-B disease (n=112), LC was associated with improved survival (median 30 months versus not reached, p=0.036). Acute and late toxicity rate was 26%(n=37) and 8% (n=11). Patients with BCLC B-C stage disease showed increased acute toxicity (HR: 2.9, 95%CI 1.10-7.65; p=0.032).

Conclusion Delivery of ablative doses >120 Gy10 and tumor size are determinants of LC. Prolonged PFS and improved OS can be obtained in BCLC A-B patients. Grade 3 liver dysfunction is infrequent.

P160

PREOPERATIVE RADIO-CHEMOTHERAPY (RT-CT) IN LOCALLY ADVANCED RECTAL CANCER (LARC) USING TWO DIFFERENT DOSES; OUTCOMES OF A MONOISTITUTIONAL EXPERIENCE

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Aims: The aim of this study was to evaluate pathological response, survival rate and toxicities in pts affected by LARC underwent neoadjuvant RT-CT (Capecitabin 1650 mg/mq/day) using two different RT doses.

Methods: From January 2014 to January 2020, 47 patients were analyzed; of them twenty-four pts were male (51%) and twenty-three female (49%). The median age was 68 years old with a range wide from 27 to 80 years old. Thirty-five pts (Group 1) received 55 Gy in 25 FF (45 Gy to the pelvis and 55 Gy to T, N+ and mesorectum in SIB-VMAT technique) and 12 pts (Group 2) received 50.4 Gy to the pelvis in 28 FF and VMAT technique. We evaluated survival rates and clinical pathological characteristics of Tumor (T), Nodal (N), grading, margins, N-down-staging and T-down-staging, tumor. According to CTCAE vs 5 scale acute and late toxicity was evaluated.

Results: After a median follow-up of 32 months (range 3-61 months) the progression free survival (PFS) was 80%. Local control was reached in 92,3% of pts with similar rate and no statistically differences between two groups. The distant PFS was 83%; 93% in patients receiving 55 Gy/25 and 66% in patients receiving standard treatment 50,4 Gy/28 fractions with a trend in favor of patients receiving 55 Gy/25 ff (p-value 0,12). At histological examination 13 (27,7%) pts (31,4% Group 1 and 16,6% Goup2) had a T- complete response (CR), 33 (71.2%) pts (80% Group 1 and 66% Group 2) had N-CR and 11 (23,4%) pts (25,7 Group 1 and 16,6 Group 2) had both T and N-CR. Tumor down-staging was observed in 32 (76,61%) of pts with no statistically differences between two groups. Nodal down-staging was reached in 85% of pts (86% in Group 1 and 77% in Group 2). GI and GU G3 acute toxicity was observed in 3 pts (6,4%) with no statistically differences between two groups. Finally, late toxicity/ post-surgical complications were observed in 10 (21%) patients (20% group 1 and 23% group 2). The majority consisted in post-surgical complications such as wound dehiscence in two pts, fluid collection in 3 patients and fistula in two pts.

Conclusions: Neoadjuvant RT-CT with SIB technique and TD of 55 Gy/25ff showed an advantage regarding T and N-down-staging improving PFS compared to standard RT treatment (50.4 Gy/28ff) with a acceptable acute and late toxicity. Randomized trials with higher number of pts and longer follow-up are needed to confirm our results.

P161

SELECTING PATIENTS FOR CHEMORADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER: A SINGLE-ISTITUTIONAL COHORT OF 104 PATIENTS

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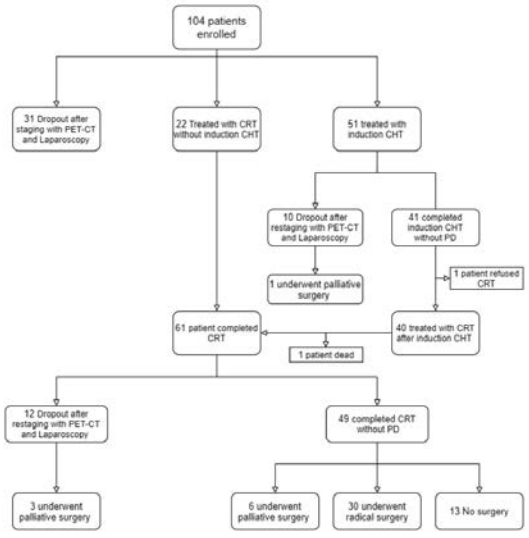
Aim: To report clinical outcomes in patients with locally advanced pancreatic cancer (LAPC) selected for chemoradiotherapy (CRT).

Methods: From 2008 through 2019, 104 patients LAPC were accrued in three consecutive prospective studies of CRT with or without induction chemotherapy (IC). In all cases an accurate pre-treatment staging including CT scan, FDG-PET/CT and laparoscopy with peritoneal washing was performed. After IC and approximately 4 weeks after the completion of CRT, a re-evaluation was performed regarding cancer response and resectability with clinical examination, CT scan, FDG-PET/CT scan and laparoscopy.

Table 1. Flowchart of the study. Abbreviations: CRT, chemoradiotherapy; CHT, chemotherapy; PD, progression of disease.



Results: 104 patients were evaluated (Table 1). According to the results of the pre-treatment workup, 31 patients (29.8%) had metastatic disease and were therefore excluded from the protocols. Ten patients experienced disease progression after IC. Sixty-one patients completed CRT. After the combined therapy 13 patients had a disease progression, 49 patients were evaluated for surgery. Of these, 30 patients (61.2%) underwent surgical radical resection. The median follow-up was 17.2 months (range, 4.6 to 105.8 months). The median PFS was 13 months. Two-year and three-year LC were 72% and 66%, respectively. Two-year

and three-year MFS were 35% and 28%, respectively. Median OS was 17.2 months. One-year OS, two-year OS and three-year OS were 75%, 38% and 29%, respectively. Patients who underwent resection had a significantly longer median OS compared with non resected patients (38.1 months vs 12.9 months, p<0.001). The median PFS for resected patients was 22.5 months compared with 6.5 months for non resected patients (p<0.001).

Conclusions: In the management of LAPC, CRT plays a crucial role to improve resectability and clinical outcomes after an accurate selection of patients.

P162

MESORECTUM MOTION EVALUATION DURING CHEMORADIOTHERAPY FOR RECTAL CANCER USING MR-GUIDED RADIOTHERAPY: AN EXPLORATORY STUDY TO QUANTIFY PTV MARGINS

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Aims: Data related to the quantification of mesorectal motion (MM) have been previously published using cone-beam computed tomography (CBCT) imaging, during neoadjuvant chemoradiotherapy (nCRT) for locally advanced rectal cancer (LARC). The aim of this preliminary analysis is to assess the inter-fraction MM using the higher tissue contrast provided by daily magnetic resonance imaging (MRI) obtained on a 0.35 Tesla MR hybrid accelerator.

Methods: Our study includes patients (pts) undergoing nCRT with a total dose of 55Gy/2.2Gy/die on gross tumor volume plus the corresponding mesorectum and 45Gy/1.8Gy/die on total mesorectum and nodal volumes at risk. On the day of simulation and each day of the MRgRT treatment, a true fast imaging with steady state precession sequence (TRUFI) was acquired for each patient. An expert radiation oncologist contoured the mesorectum on all the volumetric MRI (17-175 seconds) obtained. The total mesorectum and the lower mesorectum were considered for the analysis. The lower mesorectum was defined as the section below the recto-uterine pouch for female and the recto-vesical pouch for male. Six PTVs were obtained adding a 0.5cm, 0.7cm, 1cm, 1.3cm, 1.5cm and 2 cm margin to the total and lower mesorectum CTVs respectively, starting from the simulation MRI. The inter-fractional MM was studied considering the mean displacement of the mesorectum in all the 6 spatial directions. The margins including 95% of the mesorectal structures during the whole treatment in 95% of pts were considered adequate. The correlation between the MM and treatment time was performed using Pearson's Correlation Coefficient

Results: A total number of 3000 fractions of 12 consecutive pts (10 male, 2 female) was retrospectively analyzed. The disease was localized above, below and in correspondence of the recto-uterine/recto-vesical pouch, for 5, 2 and 5 pts, respectively. The ideal PTV margins taking into account the motion both of the total and lower mesorectum are summarized in the table. No correlation between MM and mesorectal volume with the delivered fractions number was found. Only in one case, the anterior MM was correlated with the mesorectal volume reduction during treatment.

Conclusions: This study confirms that MM occurs mainly in the anterior direction, and this finding appears to be applicable also for lower mesorectum. The results of this exploratory study recommend that the PTV margin should be defined taking into account tumor's location and using asymmetric margins.

Table 1.

	All	Douglas
Left	1.5 cm	1.3 cm
Right	1.5 cm	1 cm
Anterior	2 cm	1.5 cm
Posterior	1.3 cm	1.3 cm

P163

PREDICTION OF RESECTION MARGIN STATUS AFTER INDUCTION CHEMOTHERAPY AND SBRT IN PATIENTS WITH UNRESECTABLE PANCREATIC CANCER USING CT TEXTURE ANALYSIS

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Aims: To evaluate the ability of texture analysis of computed tomography (CT) images to predict the resection margin status after induction chemotherapy and stereotactic body radiation therapy (SBRT) in patients with unresectable pancreatic adenocarcinoma (PDAC).

Methods: Between January 2017 and May 2019, 84 patients with histologically proven unresectable PDAC underwent induction chemotherapy (FOLFIRINOX or Gemcitabine+Nab-Paclitaxel) followed by SBRT. Patients who received surgery after SBRT were included in this retrospective study. Forty-seven texture features were extracted from 3D ROIs (region of interest) based on pre-SBRT contrast-enhanced CT images. Stepwise logistic regression analysis was used to build a radiomic-based predictive model for R0 resection; area under the curve (AUC), sensitivity, specificity, positive and negative predictive values (PPV, NPV), and accuracy of the model were assessed.

Results: SBRT was delivered over 5 consecutive daily fractions by administering 30 Gy to the tumor

while simultaneously delivering 50 Gy to the tumor-vessel interface (SIB TVI). After SBRT, 43 (51.2%) patients (27 males and 16 females; mean age, 65 years; age range, 48-81 years) underwent surgery and were available for the analysis. A vascular resection was required in 12 (27.9%) patients. Twelve patients (27.9%) had an R0 resection, while 31 (72.1%) had positive resection margins. A model based on arterial phase skewness and portal phase 50th percentile had an AUC of .743, with sensitivity of 70%, specificity of 84.8%, PPV of 58.3%, NPV of 90.3%, and accuracy of 81.4% for the prediction of R0 resection.

Conclusions: Radiomics features derived from texture analysis of CT images may predict R0 resection after induction chemotherapy and SBRT in patients with PDAC. The results of the present study may add further data for the planning of a complex surgery in the setting of unresectable PDAC after total neoadjuvant/conversion strategy.

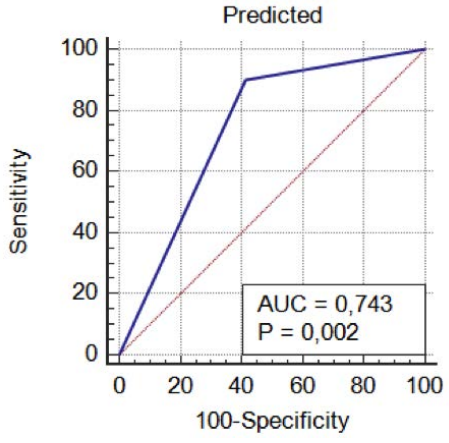

Figure 1. ROC curve of the R-status prediction model.

P164

VALUE OF 18F-FDG/PET FOR PREDICTING RESPONSE TO INTENSIVE NEOADJUVANT CHEMORADIATION PROTOCOL IN ESOPHAGEAL CANCER

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Aims: To assess the capability of Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) to provide functional information for predicting response to a single intensive neoadjuvant chemoradiotherapy protocol (nCRT) for either esophageal squamous cell carcinoma (SCC) and adenocarcinoma (ADC).

Methods: Fifty-four patients treated at our Center between 2014 and 2018 were retrospectively reviewed. The nCRT protocol schedule consists of an induction phase of weekly administered docetaxel, cisplatin, and 5-fluorouracil (TCF) for 3 weeks, followed by a concomitant phase of weekly TCF for 5 weeks concurrent with radiotherapy (50-50.4 Gy in 25-28 fractions). Three consecutive 18F-FDG PET/CTs were performed: before (PET1) and after (PET2) induction chemotherapy (before concomitant phase), and before surgery (PET3, 5-6 weeks after the end of nCRT). To evaluate PET parameters [maximum and mean standardized uptake values (SUVmax and SUVmean), metabolic tumor volume (MTV), and total lesion glycolysis (TLG)], tumoral regions of interest (ROIs) were delineated using "PET Edge" (MIM software, Mim Software Inc., US). Correlation with tumor regression grade (TGR) and complete pathologic response to nCRT (pCR or ypT0N0) was performed.

Results: At pathological evaluation patients were classified according to TRG class as poor (TRG 3-4, 13/54, 24.1%) or good (TRG 1-2, 41/54, 75.9%) responders to nCRT and 27 (50%) patients achieved a pCR. MTV and TLG measured at baseline (PET1) were predictive for TRG response (p=0.0017 and p=0.0068, respectively). After induction chemotherapy (PET2) good responders experienced a greater reduction in SUVmax versus poor responder patients (p=0.0308). In addition, change in TLG at PET2 was predictive for TRG 1-2 (p=0.0281). Also, MTV at PET1 appeared predictive for pCR (p=0.0117).

Conclusions: 18F-FDG PET/CT parameters (SUVmax, MTV and TLG) appear able to predict pathologic response (TRG class and pCR) to intensive neoadjuvant chemoradiation in esophageal cancer. These prognostic biomarkers might be useful for the design and development of future trials or the selection of personalized therapeutic options, possibly changing the management and improving prognosis of esophageal cancer.

P165

SBRT FOR LOCALLY ADVANCED PANCREATIC CANCER: WE ARE RAISING THE BAR

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Aims: Stereotactic body radiation therapy (SBRT) has demonstrated promising results in locally advanced unresectable pancreatic cancer (LAPC). However, long lasting local control (LC) remains challenging, and higher biologically effective doses (BED) are advocated to achieve tumor ablation. Advances in radiation technique delivery, image-guidance (IGRT) and treatment planning may allow for dose escalation to doses not previously feasible, potentially improving LC and

survival. In preparation for a Phase I/II adaptive dose escalation trial, we realized a dosimetric study to determine the maximum possible dose escalation while maintaining safe organs at risk (OARs) constraints.

Methods: Twenty patients treated at our institution with 5 consecutive daily fractions SBRT were re-planned. Original prescribed dose was 50/30/25 Gy to tumor-vessel interface (TVI)/planning target volume (PTV)/overlap area between the PTV and PRV OARs, respectively, using a simultaneous integrated boost (SIB) and simultaneous integrated protection (SIP) approach. Dose was escalated up to 60/40/33 Gy/5 fractions. All the plans were realized with inspiration breath hold (IBH) technique and planned with volumetric modulated arc therapy (VMAT). Well-established OARs dose constraints were used (D0.5cc < 33 Gy for luminal OARs and D0.5cc < 38 Gy for corresponding PRV). Descriptive plan statistics were generated for PTVs, homogeneity, conformality, and OARs.

Results: PTV60Gy median dose/D95/conformity index were 60.54 Gy (SD 0.85)/58.96 Gy (SD 0.86)/0.99 (SD 0.01), respectively, while PTV40Gy median dose/D95 were 44.51 Gy (SD 2.69)/38.44 Gy (SD 0.82), respectively. With regard to OARs, median maximum dose (D0.5cc) to duodenum/stomach/bowel was 29.31 Gy (SD 5.72)/25.29 Gy (SD 6.90)/27.03 Gy (SD 5.67), respectively. A minor acceptable deviation was found for a single plan (bowel D0.5cc 34.8 Gy). V38 < 0.5 cc was achieved for all PRV OARs.

Conclusions: A SBRT dose escalation protocol with SIB/SIP approach for LAPC up to 60/40/33 Gy/5 fractions is dosimetrically feasible with adequate PTVs coverage and respect for OARs constraints. A Phase I/II adaptive dose escalation trial is ongoing at our Institution.

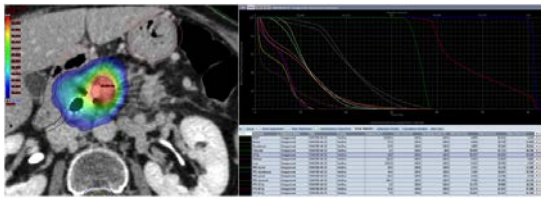

Figure 1. Sample plan of dose-escalated stereotactic body radiation therapy for LAPC. These example demonstrate excellent coverage of target volumes and respect of OARs (duodenum – black, and stomach - pink). The PTV_{40Gy} (red) was created by adding 3 mm to the integrated gross target volume (iGTV) structure. The PTV_{60Gy} (blue) was generated to cover the tumor vessel interface (TVI) inside the iGTV, while the PTV_{33Gy} (green) corresponded to the overlap area between the PTV_{40Gy} and PRV OARs (luminal OARs + 3 mm).

P166

RESULTS OF MONO-INSTITUTIONAL CLINICAL EXPERIENCE IN PATIENTS WITH ESOPHAGEAL OR ESOPHAGEAL GASTRIC JUNCTION CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY AND IG-IMRT PET BASED

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Aim: To report our experience in patients (pts) with esophageal (EC) and esophageal gastric junction (EGJ) cancer treated with neoadjuvant chemoradiotherapy (CRT) and IG-IMRT PET based.

Methods: From April 2014 to February 2020, 80 pts (F: 14; M: 66), with histologically proven EC or EGJ were treated according to CROSS study. Median age at diagnosis: 63 years (29-80), median KPS: 90 (80-100). Forty-eight pts had adenocarcinoma (60%), 31 pts had squamous cell carcinoma (38.7%), 1 pt had adeno-squamous carcinoma (1.3%). All pts underwent c-e CT and PET simulation, repeated for restaging. Radiotherapy (RT) consisted in 41.4 Gy in 23 fractions (1.8 Gy/fr) concomitant to chemotherapy (ChT) with carboplatin and paclitaxel.

Results: Clinical stage was: T1 (3pt), T2 (19 pts), T3 (55 pts), T4 (3 pts), N0 (19 pts), N+ (61 pts). The site of tumor was proximal in 6 pts, middle third in 20 pts, distal third in 34 pts and EGJ in 20 pts. Median tumor length was 5 cm (1-15). RT was delivered by Tomotherapy in 54 pts and by VMAT in 26 pts. All pts completed RT. Median cycles of ChT was 4 (2-6 cycles), 68% pts received a full dose of ChT. G3 acute haemathological toxicity was: neutropenia in 5% (4pts), lymphopenia in 65% (52pts), anemia in 1% (1pt). G3 gastrointestinal toxicity occurred in 11% (9 pts). Three consecutive pts (4%) had bacterial pneumonia, 1 pt had aorto-esofageal fistula and underwent surgery 15 days after CRT. Responses: 78/80 pts were evaluable (2 pts early lost). Median time to restaging was 42 days (14-87). CT/PET showed local PR in 40 pts, SD in 12 pts, RC in 24 pts, PD in 2pts. Median time from CT/RT to surgery was 70 days (15-148). Sixty-two pts (79%) underwent surgery, 16 pts were excluded from surgery (PD: 8 pts. Worsening clinical condition: 4 pts. Died: 1pt. Lost: 2 pts. cCR: 1 pt) and 1 pt underwent early surgery. Post-surgery stage was T0: 11 pts, T1: 12 pts, T2: 14 pts, T3: 24 pts, T4: 1 pt; N0: 37 pts, N+: 25 pts. R0 was shown in 59/ 62 pts (97%). Mandard TRG was: TRG1: 11 pts (18%), TRG2: 13 pts (21%), TRG3: 30 pts (48%), TRG4: 8 pts (13%). 32/62 (52%) had a PD, median time to progression was 9.3 months (1.9-43). With a minimum FUP of 24 months, the median OS of alive pts was 42 months. OS at 1, 2 and 3 years was

respectively 84%, 61% and 52%.

Conclusions: Our data seem to be comparable to those of the CROSS study data in term of R0 and toxicity profile. Differently from CROSS study only 68% of our pts received the full dose of ChT due to the high rate of G3 lymphopenia. This data could explain the lower TRG responses in comparison with CROSS study.

P167

CORRELATION OF ACUTE HEMATOLOGIC TOXICITY AND IRRADIATION OF PELVIC BONE MARROW AFTER CONCURRENT CHEMORADIATION FOR ANAL CANCER PATIENTS

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Aims: Hematologic toxicity (HT) in patients (pts) undergoing chemoradiation (RCT) for anal cancer still represents one of the major causes of treatment interruption, increasing the overall treatment time. The aim of this work is to evaluate a dosimetric correlation between the dose received by specific pelvic bone marrow subsites and the HT.

Methods: We retrospectively selected 50 pts treated with concurrent RCT for anal cancer from 2011 to 2019. Pts underwent pelvic intensity-modulate radiotherapy (IMRT) or volumetric-modulated-arc radiotherapy (VMAT) with total dose of 45 Gy to prophylactic nodes and 50.4 Gy to intermediate risk volume with a boost to gross tumor volume up to 59.4 Gy. We prescribed concomitant chemotherapy (5-fluorouracil 1000 mg/m2 day 1-4 + mitomycin bolus 10 mg/m2 day 1, q28) for 2 or 3 cycles. To assess a correlation between dosimetric parameters (mean dose, V5, V10, V15, V20, V30, V40, V45) of bone marrow (BM) and HT, we identified 4 subsite volumes in the pelvic bones: iliac crests, lumbar sacral BM (LSBM), lower pelvis (bilateral pube+ischia+acetabula+femur heads) and their sum, defined as total pelvic bone marrow. HT was evaluated according to RTOG scoring scale; endpoints included white blood-cells-count (WBC), neutrophil-count (NC), hemoglobin (Hb) and platelet (PTL) nadirs.

Results: 76% of pts were women; 3/50 were HIV positive and 21/43 HPV positive. Clinical stage was 32% T2, 38% T3 and 24% T4; 64% of pts had positive nodes. RCT was interrupted for more than 3 days in 10 pts due to HT. 32.8% of pts showed G3 HT toxicity: 26% WBC, 20,9% NC and 9% PTL, 44,7% Hb. The preliminary variance analysis performed on the first 32 pts demonstrated no statistically significant correlation between the evaluated dosimetric parameters and the HT for each identified subsite (see figure 1). Further investigation will be performed on the whole sample.

Conclusions: The introduction of more conformational techniques - IMRT and VMAT – could reduce the radiation dose to the pelvic bone structure, sparing BM and reducing HT. With further statistical analysis on all the available cases on our database, we might identify dosimetric parameters able to predict HT and to improve the safety profile of the integrated treatment.

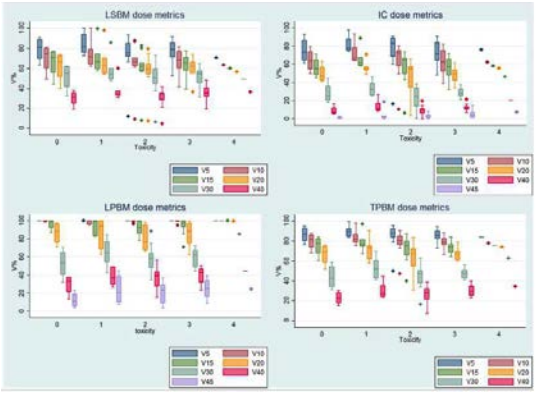

Figure 1. Correlation between hematologic toxicity and dosimetric parameters (V5, V10, V15, V20, V30,V40, V45) for each analyzed pelvic bone subsite: lumbar-sacral bone marrow (LSBM), iliac crests (IC),lower-pelvis bone marrow (LPBM), total pelvic bone marrow (TPBM).

P168

STEREOTACTIC BODY RADIOTHERAPY (SBRT) VS. CONVENTIONAL FRACTIONATED RADIOTHERAPY FOR UNRESECTABLE PANCREATIC CANCER IN ELDERLY PATIENTS

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Aims: Patients ≥65 years with unresectable pancreatic cancer (UPC) due to clinical stage, comorbidities or surgical-associated risks are considered for chemotherapy (CT) ± chemoradiotherapy (CRT). In this setting SBRT is an option but evidence of tolerability and efficacy in older patients' population is lacking. Aim of this study is to assess toxicity and outcomes of patients ≥65 years treated with SBRT or conventional fractionated CRT in several Italian centres.

Methods: A retrospective multicentric study was performed. 174 patients ≥65 years with non-metastatic UPC treated with SBRT or conventional fractionated CRT ± CT from 10 different Italian centres were enrolled. Patient' characteristics between the two groups were compared using Chi-square test and univariate and multivariate analysis were performed using log-rank test and Cox-proportional hazard model, respectively.

Results: 35 patients were treated with SBRT ± neoadjuvant or adjuvant CT with a median total dose of 30 Gy (18-37.5) with 6 Gy (5-10) per fraction and 139 patients underwent conventional fractionated CRT ± neoadjuvant or adjuvant CT with a median total dose of 50.4 Gy (45-60). Median BED10 (48 Gy and 59.5 Gy) were significantly different between the two groups (p .000). In SBRT group no G3 acute gastrointestinal toxicity was experienced while in conventional CRT group 3 G3 toxicities were registered, with similar G0 to G2 toxicity in both treatment settings (p .117). At univariate analysis no statistically significant differences in local control (LC), distant metastasis-free survival (DMFS) and overall survival (OS) between SBRT and conventional RT were seen. 1 and 2-years OS in SBRT group were 76.6% and 15% while in the conventional CRT group were 58.8% and 19.8%, respectively.

Conclusions: In patients ≥ 65 years with UPC a safe radiation treatment option may be offered with SBRT instead of traditionally-used conventional CRT with no relevant differences in terms of toxicity and outcomes between the two groups. In this setting further prospective studies with a larger sample size are needed.

P169

CONSERVATIVE APPROACHES AS A SAFE STRATEGY IN THE TREATMENT OF LOCALLY ADVANCED RECTAL CANCER: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: The conservative approach (CA) could be considered in locally advanced rectal cancer (LARC) patients (pts) with a complete response (CR) or near-complete response (nCR) after neoadjuvant chemoradiotherapy (nCRT). We conducted a retrospective mono-institutional analysis with the aim to assess the impact of a CA on survival outcomes and quality of life (QoL), compared with surgical approach.

Methods: The analyses included LARC pts who reached a nCR or CR after nCRT. All pts underwent re-evaluation with digital rectal examination (DRE) and T2 and DWI magnetic resonance imaging (MRI) 7-8 weeks after nCRT; rectoscopy was not mandatory. Surgery was performed 10-12 weeks after the end of nCRT. Surgery included anterior resection or abdominal-perineal resection. CA included local excision (LE) or watch and wait (WW). In case of tumor regrowth, Total Mesorectal Excision was mandatory. QoL was assessed through EORTC QLQ-30, QLQ29 and FIQL questionnaires within 12 months from the end of the treatment. The follow-up (FUP) was at least of 2 years. The examined survival outcomes were overall survival (OS), disease free survival (DFS) and Local recurrence (LR). The statistical analysis was done in Python. OS and DFS were calculated through Kaplan-Meier curves and the impact on the QoL was evaluated through specific surveys that were then compared through two-tailed t-tests. All evaluations kept a confidence level of 95%.

Results: From January 2010 to September 2019, 105 nCR e CR pts were collected. 54(51.4%) and 51(48.5.4%) pts obtained nCR and CR, respectively. For nCR pts, 39(72.2%) underwent surgery and 15(27.7%) CA. For CR pts,17 (33.3%) underwent surgery and 34 (66.6%) CA. The LR events occurred in 8 pts (7.61%), mainly in CA pts (75%); all pts underwent TME and were alive at the time of the analyses. At a median FUP of 51 months (mts)(range 43-59 mts),the median OS was 53 mts and 51 mts for surgical and CA pts(p: 0.67),respectively. The median DFS was 52 mts and 51 mts for surgical and CA pts (p: 0.81), respective-

ly. In terms of QoL, there was a statistical advantage for CA group (Table 1).

Conclusions: The obtained results support a CA in a subset of LARC pts with a MR or CR after nCRT. Pts underwent CA seem to benefit in terms of QoL with a not substantial differences in survival outcomes if compared to pts undergoing surgery.

Table 1. Differences have been highlighted between the two groups.

EORTC 30	Media Surgical	Media CA	p-Value T-test
Emoctional Funcioning (tension, depression, irritability)	1700	1394	<0.02
Global Health Status	4775	5697	<0.01
EORTC 29			
Abdominal pain	1250	1030	<0.01
Body image	1900	1516	<0.01
Defecation and incontinence	3265	4240	<0.01
FIQL			
Changes in life habits	3125	3636	<0.02
Limitation of free time and travel	3250	3758	<0.04

P170

FACTORS PREDICTING PATHOLOGICAL RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY IN RECTAL CANCER

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Aims: The aim of this study was to evaluate pathological complete response rate (pCR) and downstaging rate after neoadjuvant chemoradiotherapy (CRT) in relation to chemotherapy intensification, time interval to surgery and specific relevant clinical factors in patients affected by locally advanced rectal cancer (LARC).

Methods: We retrospectively analyzed patients with LARC treated with CRT followed by surgery. pCR was defined as the absence of tumor cells in the surgical specimen both at the primary tumor site and at regional lymph nodes. Downstaging was defined as lower pathologic T stage compared with the pre-treatment clinical T stage. Patients were divided according to chemotherapy regimens concurrent to radiation therapy (one-drug vs two-drugs) and according to the time interval between neoadjuvant CRT and surgery (≤8 weeks vs >8 weeks), such as in relation to gender, age (≤70 years vs >70 years), clinical stage (II vs III) and distance of tumor from anal verge (≤5 cm vs > 5). Logistic regression was used to estimate the independent factors for pCR and downstaging.

Results: Among 564 patients with diagnosis of rectal cancer treated at our institution from July 2007 through July 2018, 269 patients resulted eligible for this analysis. Overall, pCR and downstaging rate were 26% (70 patients) and 75% (203 patients), respectively. Univariate analysis indicated that gender male (p=0.016) and time to surgery > 8 weeks (p=0.04) were associated with pCR; age >70 years (p=0.05) and time to surgery > 8 weeks (p=0.002) were correlated to downstaging after neoadjuvant CRT. At multivariate analysis, interval time to surgery > 8 weeks was the only independent factor for both pCR and downstaging (p=0.02; OR: 0.5, CI: 0.27-0.93 and p=0.003; OR: 0.42, CI: 0.24-0.75, respectively). Moreover, logistic regression analysis showed that other variables such as a double drugs chemotherapy schedule were not significantly associated with pCR and downstaging.

Conclusions: This study indicates that, in our population, interval time from CRT to surgery >8 weeks is an independent significant factor for pCR and downstaging. Further prospective studies are needed. Randomized trials are warranted to define the best interval time.

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ADJUVANT CHEMORADIATION IN AMPULLARY CARCINOMA: A RETROSPECTIVE MONO-INSTITUTIONAL ANALYSIS

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Aim: To retrospectively analyze the outcome of patients affected by ampullary carcinoma in adjuvant setting.

Materials and Methods: We retrospectively analyzed twenty-three patients with ampullary carcinoma treated with definitive surgery followed by adjuvant radiochemotherapy +/- chemotherapy between May 2008 and October 2017. The outcome of patients was evaluated in terms of local control (LC), overall survival (OS) and metastasis free survival (MFS).

Results: 23 patients were analyzed. 13 males and 10 females. The median age was 67 years (range = 22-81

years). Pathological staging was IB in 2 patients, IIB in 4 patients and 8 patients were in stage III. Patients underwent concurrent chemoradiation after duodenocephalopancreasectomy; seventeen of them also received upfront adjuvant chemotherapy with platinum, gemcitabine- or 5-fluorouracil-based regimens. In all patients 3D-conformational radiotherapy was administrated (50.4 Gy to the tumor bed and 39.6 Gy to the nodes). Concurrent chemotherapy was administered in all patients with a good compliance. With a median follow-up of 47 months (range = 9-122 months), for the entire group, 1-year and 3-years LC were 95% and 90% respectively with a median LC of 49 months (range 6-134). 1-year and 3-years MFS were 94% and 83% respectively. One-year and three-years OS were 93% with a median of 49 months (range 21-134). Toxicities were acceptable.

Conclusion: Our data confirm the role of adjuvant chemoradiotherapy in patients with ampulla of Vater cancer after curative resection to improve locoregional control and overall survival.

P172

CONCURRENT RADIOCHEMOTHERAPY AND TECHNOLOGICAL IMPROVEMENT IN THE MANAGEMENT OF ANAL CANCER

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Purpose: Concurrent radiochemotherapy has been accepted as the standard treatment for anal cancer. From 2010 onwards, we performed FDG PET/CT and integrated the metabolic and morphologic imaging to obtain a biological conformation of the dose of radiation delivered to the tumor volume by the definition of the Biological Target Volume (BTV). We report our experience at Santa Maria Goretti Hospital in these last years.

Materials and Methods: From March 2010 to September 2019, 25 patients diagnosed with anal cancer referred to Radiatiotherapy Dpt of the S.M. Goretti Hospital. 21 patients were females and four were males. Clinical stage, as assessed by clinical examination, RM. They were all submitted to whole body PET/CT scan (GE Discovery ST). PET images were evaluated and then processed with a dadicated software (PET-VCAR, GE). BTV was calculated on the primitive site and the node localizations by using a threshold of segmentation set on the 42% of the SUV max. 19 patients performed FDG PET/TC before and after the treatment. We performed a schedule of 150 cGy b.i.d or 2Gy/die, up to a dose of 30-45 Gy to cover the pelvic area, followed by a boost to the tumor volume as assessed by FDG PET - CT with 1.2 cm margin up to the total dose of 45 Gy to the inguinal lymph nodes and 60 Gy to the tumoral lesion of the anal canal. Concomitant chemotherapy was based on protracted venous infusion 5 FU (225 mg/mq/day) or capecitabine per os. Patients were treated by a 3D-CRT or VMAT. Results: PET/CT showed focal and intense FDG uptake corresponding to anal lesion in each patient. FDG PET/CT was performed in 19 patients showing partial or complete metabolic response three months after the treatment. We observed two relapses of disease locally at a distance. Starting from the use of FDG CT-PET we have reduced the margin around the GTV of 45% (from 2cm to 1.2), this has resulted in a reduction of toxicity in terms of fewer side effects, both acute and delayed The main acute toxicity represented by skin erithema and disepithelization localized at the perineum, was reduced grade from G3 to G2 (according to RTOG scale), transitory rectal tenesmus decreased duration (from 45 days to 30).

Conclusion: FDG PET/CT proved useful tool for the radiation therapy treatment planning by the definition of the Biological Target Volume (BTV), for the contouring of the tumor lesion of the anal canal and the identification of lymph node metastases. The reduction of the margin around the tumor lesion has made it possible to reduce the side effects of treatment without entailing recurrent disease.

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ACUTE AND LATE TOXICITY IN THE RADIOTHERAPY TREATMENT OF PROSTATE CANCER, COMPARISON BETWEEN HYPOFRACTIONATED AND CONVENTIONALLY FRACTIONATED RADIATION THERAPY: THE CLINICAL EXPERIENCE OF PIACENZA HOSPITAL.

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Aims: Radiation therapy is a well-established treatment for localized and locally advanced prostate cancer (PCa). Our aim is to evaluate the patients (Pt) treated with PCA in order to highlight the differences between acute and late toxicity in conventional (CF) and hypofractionated (Hypo) treatment.

Methods: From January 2014 to December 2019 we treated 212 patients affected by PCa, treated with CF or Hypo RT. 3 risk classes have been identified (Table 1). 80 Pt received CF , out of which 55 Pt were treated on the prostate (dose 66-80 Gy, 1.8-2 Gy / fr.) and 25 Pt were treated on the prostate (P) and pelvic lymph nodes (N) with a total dose respectively between of 67-80 Gy (1.8-2 Gy / fr.) and 45-50 Gy (1.8-2 Gy /fr.). 132 Pt underwent hypo RT: 128 pt received on the P 70 Gy in 28 fr. and 4 Pt received 70 Gy in 28 fr. on the P, 63 Gy in 28 fr. on the seminal vesicles and 50 Gy in 28 fr. on the N. (Table 2). All patients were treated with VMAT technique. A clinical evaluation of the patients was performed: weekly during treatment, at the end of RT and every 3 months from the end RT for the first year and every 6 months thereafter. Toxicity was scored according to RTOG/EORTC.

Table 1. Patient and Disease Characteristics.

		Total patients 212	
N		80 CF-RT	132 Hypo-RT
Age, years	Average	73	74
	Median	75	74
	Interval	50-97	60-81
Gleason	≤6	30 (37%)	75 (57%)
	7	23 (29%)	41 (31%)
	≥8	27 (34%)	16 (12%)
PSA ng/ml	Average	12.0	9.0
	Median	9.0	7.4
	Interval	2.0-50.0	2.3-32.0
	<10	43 (54%)	88 (67%)
	10-20	28 (35%)	37 (28%)
	>20	9 (11%)	7 (5%)
T Classification	T1a	6 (7%)	0 (0%)
	T1b	1 (1%)	0 (0%)
	T2a	35 (44%)	90 (68%)
	T2b	32 (40%)	42 (32%)
	T2b	1 (1%)	0 (0%)
	T3a	1 (1%)	0 (0%)
	T3b	2 (3%)	0 (0%)
	T3c	2 (3%)	0 (0%)
N Classification	N0	77 (96%)	132 (100%)
	N1	3 (4%)	0 (0%)
ADT		38 (48%)	22 (17%)
Risk group	**Low** ≤ cT2a e Gleason score ≤ 6 e PSA <10 ng/ml	21 (26%)	41 (31%)
	Intermediate cT2b e/o Gleason score 7 e/o PSA 10-20 ng/ml	26 (33%)	68 (52%)
	High ≥cT2 e/o Gleason >20 ng/ml or positive lymph-node	33 (41%)	23 (17%)

Table 2. Dose and target volume.

	CF RT	Hypo RT
Prostate+vescicle seminal (P)		
Patients (N)	55	128
Dose (Gy)	66- 80	70
Prostate + pelvic lymph-node (P+N)		
Patients (N)	25	4
Dose (Gy)	45-50 N + 67-80 P	50 N + 63-70 P

Tab.le 3. Acute and late toxicity.

		Grade	CF N =80	Hypo N=128
Acute Toxicity	GI	0	57	67
		1	28	32
		2	15	1
		3	0	0
	GU	0	43	43
		1	42	47
		2	11	7
		3	4	3
Late Toxicity	GI	0	78	84
		1	21	2
		2	1	14
		3	0	0
	GU	0	91	94
		1	2	2
		2	7	4
		3	0	0

Table 4. Response of treatment.

		CF N (%)	Hypo N (%)
Follow up (months)	*median*	22(2-60)	23(2-50)
Local control		78 (98%)	127 (96%)
Local recurrence		2 (2%)	1 (1%)
Progression disease		0 (0%)	4 (3%)

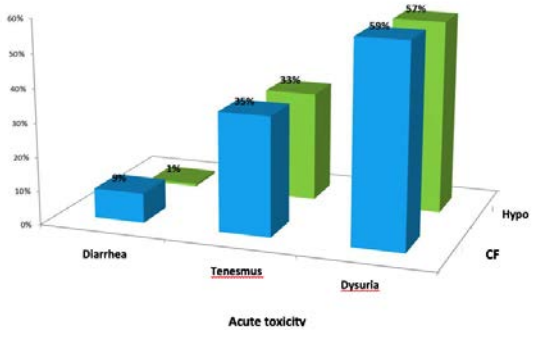

Figure 1.

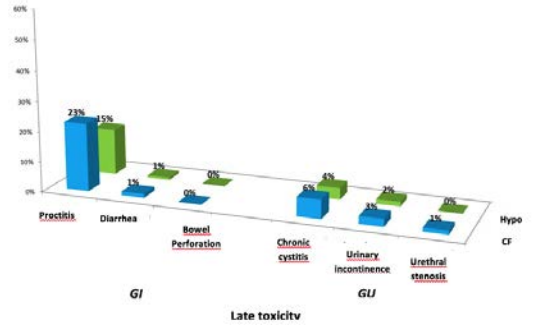

Figure 2.

Results: Baseline characteristics of all 212 patients are reported in Table 1.The median of follow-up was of 22 months (2-60) in the CF and 23 months (2-50) in the hypo-RT. Grade 2 acute GI and GU toxicity in CF treatment was 15% and 11% respectively, while in the Pt treated with Hypo-RT was 1% and 7% . 15% of GI toxicity in CF treatment was mainly related to the fact that the Pt had received WPRT. No grade 3 GI toxicity was detected in both treatments. Grade 3 GU toxicity was 4% in the CF and 3% in the hypo-RT. Late grade 2 GI and GU toxicity in the two CF and hypo treatment groups was 1% and 14% and 7% and 4% respectively. No chronic grade 3 toxicity was shown in both group (Table 3). Local control was 98% in the CF group and 96% in the hypo group, 2 LR (2%) were found in the FC group, 1 LC in the hypo group (Table 4).

Conclusions: The use of hypo-RT in the radical

treatment of PCa does not increase rates of severe GI or GU toxicity. We can conclude that the hypo-RT seems safe and tolerable by patients with acceptable rates of acute and late toxicity.

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RECTAL SPACER HYDROGEL IN 1.5T MR-GUIDED AND DAILY ADAPTED SBRT FOR PROSTATE CANCER: DOSIMETRIC ANALYSIS AND PRELIMINARY PATIENT-REPORTED OUTCOMES (PROMS)

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Aims: The main aim of the current analysis was to explore the hypothetical advantages using rectal spacer during 1.5T MR-guided and daily adapted SBRT for low and intermediate risk prostate cancer compared to a no-rectal spacer hydrogel cohort of patients.

Methods: The SBRT protocol consisted of a 35 Gy schedule delivered in 5 fractions to prostate volume (for low risk PC) and prostate + seminal vesicles (for intermediate risk PC) by means of 1.5T MR-guided adaptive therapy ("Adapte-To-Shape" strategy). The primary endpoint was dosimetric analysis between spacer and no-spacer groups. Secondary endpoints were: the clinicians-reported outcomes at the end of treatment and patient-reported outcomes measures (PROMs) in both arms. Toxicity and quality of life (QoL) were assessed at baseline and after treatment using the Common Terminology Criteria for Adverse Events v5.0, International Prostatic Symptoms Score (IPSS), ICIQ-SF, IIEF-5, and EORTC-QLQ-C30 and PR-25 questionnaires.

Results: 120 plans (pre- and daily adaptive SBRT planning) were analyzed in 20 patients (10 patients in "Spacer"-Group and 10 patients in "No-spacer"-Group) treated by means of 1.5T MR-guided adaptive SBRT. Statistically significant dosimetric advantages were observed in favor of the spacer insertion, improving the PTV coverage, in terms of V33.2Gy >95% and PTV 37.5 Gy <2%, and significantly improving the rectum dose constraints in both phases of planning. Concerning the PROMS, all questionnaires showed no difference between the pre- and post-SBRT evaluation in both arms, excepting the physical functioning item of EORTC QLQ-C30 questionnaire that was declined in the no spacer group. Regarding the clinician-reported outcome measurements, no grade 3 or higher acute toxicity measured at any study time point was observed. In the "spacer" arm, two patients (20%) and one patient (10%) suffered grade 2 and 1 acute genitourinary toxicity respectively; only one patient (10%) experienced acute grade 1 GI at the last session of radiotherapy. In the "no spacer" arm, one patient (10%) suffered grade 1 acute GI toxicity, only one patient (10%) and four patients (40%) experienced acute grade 2 and 1 GU respectively.

Conclusions: These preliminary results strongly suggest the adoption of peri-rectal spacer due to dosimetric advantages not only for rectal sparing but also for target coverage. Longer follow-up is required to validate the clinical impact in terms of Clinicians-reported toxicity and PROMs.

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CURATIVE RADIOTHERAPY OF PROSTATE CANCER: ANALYSIS OF PROGNOSTIC FACTORS AND DEVELOPMENT OF A RISK STRATIFICATION SYSTEM

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Background: The aim of this study was to analyze the prognostic impact on the outcome of patients with prostate cancer (PCa) treated with curative radiotherapy (RT) based on a comprehensive analysis of parameters related to tumor, patients, and treatment characteristics. Furthermore, we aimed to develop a simple risk stratification system based on real life data from a large patient population

Material and methods: A retrospective analysis of 1074 patients enrolled in an observational study was performed. Endpoints of the study in terms of outcome were biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS). Variables with P value less than 0.05 or with a trend ($p < 0.1$) at univariate analysis (log-rank) were entered into a multivariate Cox's regression model.

Results: At multivariate analysis a worse bRFS was observed in patients with higher PSA levels, in patients with higher Gleason Score values, and in patients with wider margins between CTV and PTV. A lower LC rate was observed in patients with higher Gleason score and with a larger CTV to PTV margin while higher values were recorded in patients treated with adjuvant ADT or with a Charlson's comorbidity index > 1. A worse MFS was recorded in patients with higher Gleason score values. Similarly, DFS was worse in patients with higher Gleason score values. DFS was lower also in patients with larger margins between CTV and PTV while a

higher DFS was recorded in patients undergoing TURP or adjuvant ADT. OS correlated only with the presence of a GTV to CTV margin. In fact, patients planned with this margin showed an improved OS. We designed a prognostic model of 5-year bRFS using three PSA categories and 5 Gleason score categories to define 15 different groups of patients. We arranged these 15 group in only 4 categories based on the 5-year bRFS values: group 1: very low-risk (bRFS > 90%), group 2: low risk (bRFS: 80-90%), group 3: intermediate risk (bRFS: 60-79.9%), group 4: high risk (bRFS < 60%) [Figure 1]

Conclusions: This systematic analysis of a large database allowed to identify unforeseen correlations that can generate new hypotheses. These results justify further analysis of large series of patients with PCa treated with RT, possibly performed with more advanced statistical analysis methods.

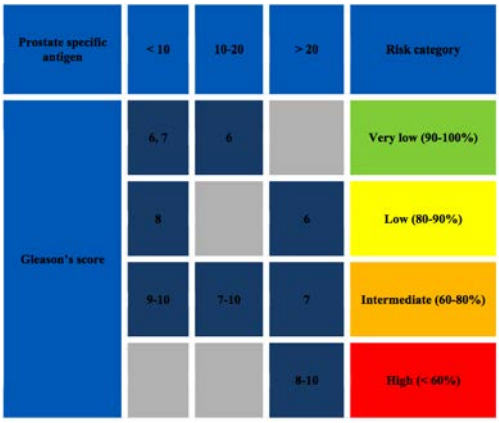

Figure 1.

P176

POSTOPERATIVE RADIOTHERAPY OF PROSTATE CANCER: ANALYSIS OF PROGNOSTIC FACTORS AND DEVELOPMENT OF A RISK STRATIFICATION SYSTEM

M. Buwenge[1], S. Bisello[1], F. Deodato[2], N. Ominsky[1], G. Tarantino[1], M. Ntreta[1], S. Cilla[3], G. Siepe[1], L. Cavallini[1], A.R. Alitto[4,5], L. Strigari[6], A.G. Morganti[1], S. Cammell[1], G. Macchia[2]

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Background: The aim of this study was to analyze the prognostic impact on clinical outcomes of patients with prostate cancer treated with postoperative radiotherapy based on a comprehensive analysis of parameters related to tumor, patients, and treatment characteristics. Furthermore, we aimed to develop a simple risk stratification system based on real life data from a large patient population

Material and methods: A retrospective analysis of 381 patients enrolled in an observational study was performed. Endpoints of the study in terms of clinical outcomes were biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS). Variables with P value less than 0.05 or with a trend ($p < 0.1$) at univariate analysis (log-rank) were entered into a multivariate Cox's regression model.

Results: Multivariate analysis showed a lower risk of biochemical recurrence in patients older than 61 years, with pN0 pathological stage, and with lower levels of postoperative PSA. In terms of Gleason score, only patients with a value of 7 (4 + 3) showed a lower risk. In terms of LC, multivariate analysis confirmed a higher risk in patients with lymph node metastases, similar to what was observed for RC. In addition, a higher risk of regional relapses was observed in patients with preoperative PSA levels higher than 10 ng/ml. We designed a predictive model of biochemical outcome using two age categories, two nodal stage categories, and four PSA categories to define 16 different groups of patients. These 16 groups were arranged in only 3 categories based on 5-year bRFS values: group 1: low-risk (bRFS > 95%), group 2: intermediate risk (bRFS: 76-95%), group 3: high risk (bRFS: < 76%). [Figure 1]

Conclusions: This systematic analysis of a large patient's series allowed to identify unforeseen correlations that can generate new hypotheses. These results justify further analysis of large series of patients with prostate cancer treated with postoperative radiotherapy, possibly performed with more advanced methods of statistical analysis.

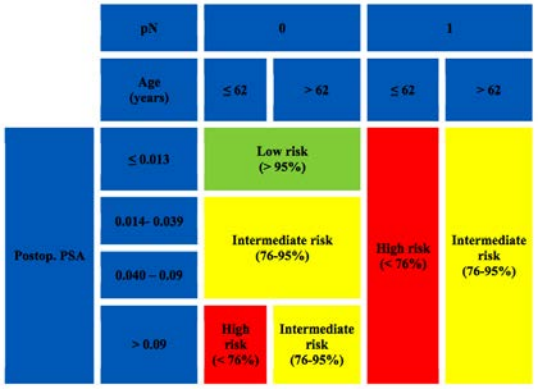

Figure 1.

P177

PROSTATE CANCER TREATED WITH SALVAGE RADIOTHERAPY: ANALYSIS OF PROGNOSTIC FACTORS AND DEVELOPMENT OF A RISK STRATIFICATION SYSTEM

M. Buwenge[1], S. Bisello[1], G. Macchia[2], A.R. Alitto[4,5], G. Tarantino[1], M. Ntreta[1], S. Cilla[3], G. Siepe[1], S. Strolin[6], F. Tabarrini[1], L. Cavallini[1], E. Scirocco[1], A.G. Morganti[1], S. Cammelli[1], F. Deodato[2]

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Background: The aim of this study was to analyze the prognostic impact on outcome of patients with prostate cancer (PCa) treated with salvage radiotherapy (RT) based on a comprehensive analysis of parameters related to tumor, patients, and treatment characteristics. Furthermore, we aimed to develop a simple risk stratification system based on real life data from a large patient population

Material and methods: A retrospective analysis of 454 patients enrolled in an observational study was performed. Endpoints of the study were biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS). Variables with P value less than 0.05 or with a trend ($p < 0.1$) at univariate analysis (log rank) were entered into a multivariate Cox's regression model.

Results: Multivariate analysis showed a higher bRFS rates in patients with pN0 stage, lower Gleason score (GS) and treated with prophylactic nodal irradiation (PNI). Moreover, it showed improved LC in patients treated with hypofractionated regimens. In terms of RC, multivariate analysis showed better results in patients with lower GS and worse results in patients with negative surgical margins, treated with IMRT/VMAT technique, and not receiving PNI. The analysis on MFS showed a better outcome in pN0 and low GS patients and a higher failure risk in patients receiving adjuvant ADT. Higher DFS rates were confirmed in patients with pN0 or low GS or low PSA levels at salvage treatment as well as in patients treated with cone-beam CT. Furthermore, multivariate analysis showed better DFS rates in patients receiving PNI. OS rates were higher with IMRT/VMAT techniques. We designed a prognostic model using 4 Gleason score categories, 2 nodal stage categories, and 2 nodal irradiation categories to define 16 different groups of patients. These 16 groups were arranged in only 4 categories based on 5-year bRFS values: group 1: low-risk (bRFS > 80%), group 2: intermediate risk (bRFS: 60-80%), group 3: high risk (bRFS: 40-59.9%), and group 4: very high risk (bRFS: < 40%). [Figure 1]

Conclusions: This systematic analysis of a large patient's series allowed the identification of unpredictable correlations potentially useful to generate new hypotheses.

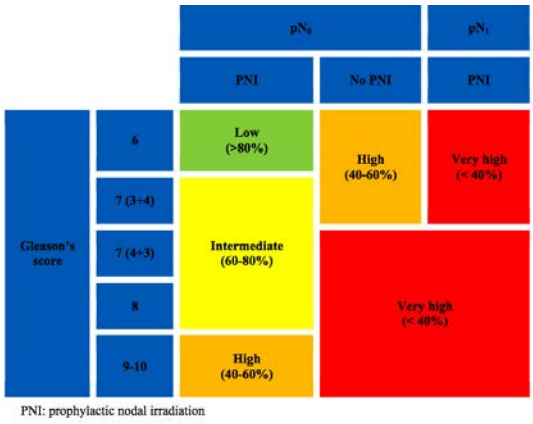

Figure 1.

P178

RADIOTHERAPY OF PROSTATE CARCINOMA: A COMPARISON OF THE PREDICTIVE ROLE OF EAU VERSUS NCCN RISK STRATIFICATION SYSTEMS

M. Buwenge[1], S. Bisello[1], F. Deodato[2], N. Dominsky[1], G. Tarantino[1], M. Ntreta[1], S. Cilla[3], G. Siepe[1], L. Cavallini[1], A. Arcelli[1], E. Scirocco[1], A.G. Morganti[1], S. Cammelli[1], G. Macchia[2], A.R. Alitto[4,5]

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Introduction: The aim of this analysis was to evaluate the predictive efficacy on different clinical outcomes, according to the NCCN and EAU risk stratification systems, in three different treatment settings: definitive, adjuvant, and salvage radiotherapy (RT) of prostate cancer.

Material and methods: Data from a multicentre observational study (311/2019/Oss/AOUBo, ICAROS-1 study) were collected and analysed. The predictive efficacy of the NCCN and EAU stratification systems was evaluated on the following end points: biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS).

Survival estimates were calculated by the Kaplan-Meier product-limit method and compared with the log-rank test.

Results: In this analysis, we included 1909 prostate cancer patients treated with definitive (1074), adjuvant (381), and salvage RT (454). Both NCCN and EAU systems accurately predicted bRFS (p<0.001), MFS (p<0.001 and p: 0.003, respectively) and DFS (p<0.001 and p: 0.006, respectively) in patients treated with definitive RT. In the same patients' group, only the NCCN system significantly correlated with LC (p: 0.023). In the adjuvant setting, both systems failed to significantly predict bRFS and all clinical outcomes. In the salvage setting, only the NCCN system was able to significantly predict bRFS (p: 0.002), MFS (p: 0.002), and DFS (p: 0.006).

Conclusions: This analysis confirms the efficacy of both risk stratification systems in definitive RT setting. Moreover, our analysis suggests the utility of the NCCN system also in the salvage setting but not in the adjuvant one. Therefore, further studies aimed at defining new risk categorization systems in the post-operative setting are needed.

P179

DUCTAL PROSTATE ADENOCARCINOMA: MULTICENTRIC, RETROSPECTIVE ANALISYS OF 81 PATIENTS

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Aims: Prostate cancer (PCa) is the most frequent malignancy among men. Several rare histotypes are described, among them ductal prostate (pure and mixed form) adenocarcinoma (DPA) represents less than 5% of all new diagnoses of PCa. Previous studies have shown that DPA has a more aggressive behavior, with greater tendency to metastatic diffusion and consequently worse prognosis in comparison to the common acinar variant. Aim of present study is to investigate outcomes and prognostic factor related to this rare cancer.

Methods: Eighty-one patients with a proven diagnosis of DPA were evaluated in a multicentric retrospective study. Patients who had undergone surgery or radiotherapy or chemotherapy or combined treatments were considered eligible for the study. We assessed the outcomes in terms of overall survival (OS) and disease-free survival (DFS).

Results: Median follow up was 62,8 months (range 3-206). Twenty-six patients died during the follow up time, 23 of which due to prostate cancer. Pure DPA and mixed ductal-acinar adenocarcinoma were seen in 35,8% and 64,2% of patients, respectively. At our analysis 3y and 5 y- OS were 73% and 52%, while 3y and 5 y- DPFS were 66,7% and 48%, respectively. Pure form is associated with an increased risk of stage IV at diagnosis and worst prognosis.

Conclusions: Present work is one of largest retrospective study of patients with DPA. Our study confirm more aggressive behavior, with a worse prognosis of DPA, especially in the presence of the pure form. Both surgery and radiation therapy have been shown to be equivalent treatments, while no benefit has been demonstrated in the use of hormone-therapy. Large retrospective database are needed to understand the best therapeutic approach.

P180

ACUTE AND LATE GASTROINTESTINAL AND GENITOURINARY TOXICITY OF MODERALTELY HYPOFRACTIONATED DEFINITIVE RADIOTHERAPY FOR ORGAN-CONFINED LOW-RISK PROSTATE CANCER:PRELIMINARY ANALYSIS OF A RETROSPECTIVE SERIES OF 73 CONSECUTIVE PATIENTS

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Aims: To assess acute/late gastrointestinal (GI) and genitourinary (GU) toxicity of a MHFRT regime for the definitive treatment of localized low-risk prostate cancer in a retrospective series of 73 consecutive pts.

Methods: Between January 2013 and November 2019, 73 consecutive pts, median age 74 yrs ± 4.6 SD, received definitive MHFRT with 70 Gy in 28 fractions at 2.5 Gy/fraction for organ-confined (T1a-T2a) low-risk prostate adenocarcinoma. Gleason score was 3+3=6 in 66 pts and < 6 in 7 pts; median initial PSA: 5.10 ng/mL ± 2.07 SD; 22/73 (30%) pts received adjuvant hormone therapy concomitant with MHFRT; 21/73 (29%) pts had been submitted to previous transurethral resection of the prostate before MHFRT; several comorbidities were recorded in 65/73 (89%) pts. All pts were treated with volumetric modulated arc therapy (VMAT) up to 70 Gy in 28 fractions to prostate ± seminal vesicles (27/73 pts); CTV to PTV margins were 9 mm but for posteriorly (8 mm); median PTV volume was 204.3 cc ± 45.7 SD. Prescription dose was 95% of PTV to be covered by at least 95% of the prescribed dose. All pts were irradiated with empty rectum and full bladder according to a protocol applied before CT-simulation and prior to the delivery of each treatment fraction. CBCT daily images were taken for the first 5 MHFRT

sessions and once a week thereafter, applying set-up corrections whenever needed.

Results: Median follow-up was 32.2 months ± 15.6 SD (range: 7.6-76.2 months). Toxicity (CTCAE V 4.0) was as follows: acute G1 and G2 in 21.9% and 1.4%, respectively for GI and in 45.2% and 5.5%, respectively for GU; late G1 and G2 in 8.2% (both) for GI and in 17.8% and 4.1%, respectively for GU; there were no ≥ G3 acute/late reactions. All pts are alive and biochemically controlled at the time of this analysis.

Conclusions: The MHFRT regime used in our series showed both a mild acute/late toxicity profile and promising biochemical control that need confirmation in a larger series with a longer follow-up, also with the aim of investigation of possible clinical/dosimetric predictors for toxicity.

P181

ADJUVANT AND SALVAGE RADIOTHERAPY IN PATIENTS WITH PROSTATE CANCER: THE SURVIVAL AND TOXICITY DATA IN OUR CASISTIC.

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[1]Radioterapia ed Oncologia clinica "G Cozzaglio" Istituto Clinico Sant' Anna, Italy

Aim: To analyze survival and toxicity data in patients (pts) treated with a personalized radiotherapy (RT), affected by prostate cancer previously treated with surgery.

Methods: Our casistic involved 72 pts, who underwent salvage or adjuvant RT between 2012 and 2018, after surgery and/or biochemical relapse (BRL). We evaluated toxicity data according to CTCAE v5.0. Statistical assessment was performed with SPSS®.

Results: The median age was 67 years (range 43-78). Forty-two pts (58%) were treated after biochemical relapse with salvage RT and 30 pts (42%) underwent adjuvant RT after surgery. Twenty-three pts (32%) were included in a very high risk category; 21 pts (29%), 12 (17%), 9 (12%) and 7 (10%) were in high risk, unfavorable intermediate, favorable intermediate and low category, respectively. Seventy-four pts (89%) underwent also ormonotherapy (OT). The other 8 pts suffered by comorbidities that not allowed the association. Tailored VMAT-RT to the prostate bed was performed in 61 pts (85%) with a PTV prescribed dose of 70 Gy/2 Gy per fraction in 45 pts (63%) and 72-74 Gy/2 Gy per fraction in the other pts. In 11 cases (15%) was prescribed a normo-fractionated RT to the pelvis and a boost to the prostate bed. Regarding to acute toxicity, 34 pts (47%) did not show any degree of dysuria, while 34 (47%) and 3 (4%) pts reported grade 1 and 2, respectively. In only 1 case we registered G3 event. Forty-three pts (60%) developed an increase of G1 urinary frequency, while 28 (39%) and 1 (1%) pts showed G0 and G2 event, respectively. Nine pts (13%) developed acute diarrhea, with G2 cases in only 2 pts. Regarding chronic toxicity, no pts developed fecal incontinence or rectal stenosis. Sixteen (22%) and 3 pts (4%) showed G1-G2 urinary incontinence, respectively. Only 1 pts suffered of G3 event, but it appeared firstly from surgery. In 2 pts we had G1 sexual impairment. After a median follow up of 38 months, only 6 (8%) and 2 pts developed BRL and metastasis events, respectively. At Chi-square analysis, there was no correlation with initial risk factors. We did not register any disease-related death. Two and 5 years overall survival (OS) was 95% and 92% respectively. There was no statistical difference between OS in salvage or adjuvant RT. We also related OS and OT, with better survival in pts who underwent the association (p= 0.021).

Conclusions: The casistic evaluation showed a good survival profile in front of an adequate personalization of treatment delivery.

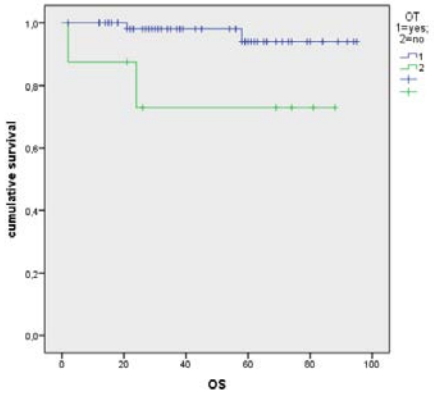

Figure 1.

P182

SBRT FOR ELDERLY PATIENTS WITH OLIGOMESTATIC PROSTATE CANCER: IMPACT ON QUALITY OF LIFE

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Unità Operativa Radioterapia, Azienda Ospedaliero Universitaria Pisana, Italy

Aims: Prostate cancer patients are usually elderly, with multiple comorbidities, which can affect quality of life and compliance at the treatments. In this study, we analyzed patients with oligometastatic prostate cancer treated with SBRT; all patients had an onco-geriatric evaluation before and after treatment to assess the impact of treatment on quality of life.

Methods: Patients with oligometastatic prostate cancer (<4 active lesions at [(18)F]Choline PET/CT) were clinically evaluated and assessed with KPS and G8 (screening tool that was developed to identify elderly cancer patients who would benefit from comprehensive geriatric assessment (CGA).That allowed us to understand if the patient could tolerate treatments. At each control the patients were newly evaluated with the same methods to notes if there was a change in the gen-

eral conditions due to the treatments, to refer them to the oncogeriatrician specialist if necessary.

Results: From January 2018 to today 55 patients have been treated with SBRT, for a total of 71 treatments (40 treatments in 2018 and 31 treatments in 2019); 39 treatments for bones lesions, 32 for lymph node metastasis. The patient who was treated on more lesions at the same was treated on 4 rib bone lesions. After an initial disease response at this level, the 6-month follow-up showed a frank progression of disease therefore the patient started systemic therapy. It should be noted that of these 55 patients, 4 were treatment again 6-18 months after the previous SBRT but on other lesions; of them currently 2 are NED and 2 are in PD. Actually the patients are all alive although 37 NED and 18 in progression, and have started systemic therapy. At the moment all patients treated with SBRT have excellent general conditions, with G8 test above 14 and KPS above 80, without modification of these scores after the SBRT.

Conclusions: The geriatric analysis has shown that SBRT does not entail a worsening of the patient's clinical condition, and is therefore strongly recommended also to potentially fragile patients. From the analysis of the data we have at our disposal, it appears that the treatments had a 95% of local control. We can confirm that SBRT treatments can be offered safely in oligometastatic patients, with a curative intent that allows the systemic treatment to be postponed for at least 6 months

P183

EVALUATION OF PATIENTS SETUP ACCURACY AND DETERMINATION OF PTV MARGIN IN HYPOFRACTIONATED VOLUMETRIC ARC THERAPY (VMAT) OF LOCALIZED PROSTATE CANCER USING CBCT

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Aim: To determine the inter-fraction setup error and the prostate motion relative to the bony anatomy assessed with daily kilovoltage cone beam computed tomography (CBCT) to evaluate the accuracy of PTV margin in prostate cancer patients treated with radical hypofractionated VMAT radiotherapy.

Methods: 1024 total treatment fractions (CBCT sessions) from 40 patients were evaluated. PTVs were obtained by using anisotropic expansions of CTVs, applying 7-mm in left-right (LR), superoinferior (SI) and anterior (A) and 5-mm in posterior (P) directions. Systematic and random components of the shifts were retrospectively evaluated by comparing two matching modalities: pelvic bones (clipbox) based on chamfer algorithm and grey-value soft tissue (mask). Motion of the prostate relative to the pelvic bony anatomy was defined as the difference between mask and clipbox values. For the entire patient population, the mean value of the average deviation, the group systematic error and the group random error were computed for clipbox and mask match and for organ motion.

Results: The systematic rotations of the bones, as well as the rotations of the prostate relative to the bones with respect to the three axes were negligible. Group deviations M, representing inaccuracies in treatment preparation repeated over multiple patients, were all on the order of 1 mm or less. The systematic and random components of the shifts in mask and clipbox misalignment were very similar, with the AP axis as the largest contributor. Average deviations caused by internal prostate displacement were smaller along each axis. The systematic and random errors for the prostate motion were 2 mm in AP and SI direction and 1 mm in the LR direction. Overall, the percentage of treatment fractions that would be delivered outside the PTV margins is about 5%, especially in the posterior direction.

Conclusion: The online soft-tissue image-guidance correction based on daily CBCT during VMAT radiotherapy of prostate cancer patients is a fast and efficient procedure. Due to the large random displacement of the prostate with respect to the bony anatomy, daily CBCT appears mandatory for high dose and high gradients treatments. Considering the residual organ motion of the prostate, our findings are in good agreement with the PTV margins, confirming the accuracy of the set up procedure.

P184

MODERATE HYPOFRACTIONATED RADIOTHERAPY WITH HELICAL TOMOTHERAPY FOR PROSTATE CANCER: 5-YEARS-RESULTS OF A SERIES OF 430 PATIENTS

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Aims: External beam radiotherapy (EBRT) represents a milestone treatment for prostate cancer (PC). Moderate hypofractionated (MH-RT) schedules are increasingly used due to the low alpha/beta value, which differs prostate PC from other solid tumors. TomoTherapy HI-ART system is a Linear Accelerator equipped with a megavoltage imaging system mounted in the gantry head of a spiral CT, allowing accurate verification of the position before and during each treatment session (IG-IMRT). In Italy, the AUSL-IRCCS Reggio Emilia was one of first centers to use TomoTherapy to perform MH-RT for PC. The purpose of this work is to investigate the outcomes and toxicities of hypofractionated treatments delivered with

tomotherapy in patients with PC.

Methods: Retrospective analysis of a series of patients with PC treated in our institution with exclusive Thomoterapy IG-IMRT between 2008 and 2019 were collected. All Patients received MH-RT with total dose of 70 Gy in 28 fractions (2,5 Gy for fraction). Adjuvant and salvage radiotherapy treatments were excluded. We assessed outcomes in terms of overall survival (OS), and progression-free survival (PFS) and toxicity. Co-relationship uni-multivariate analysis with clinical outcome and toxicity are being investigated.

Results: 430 patients with PC underwent to MH-RT with TomoTherapy as exclusive treatment, of which 84 (19.5%) also received pelvic lymph nodes irradiation. The median follow up was 63,1 months (range 2,9 – 132,1). 5y OS and PFS were 89% and 90% respectively. 52 patients (12%) had biochemical recurrence. The observed recurrence was: 1 local, 23 (5.3%) locoregional lymph-node and 36 (8.4%) distant metastasis. Genitourinary (GU) and gastrointestinal (GI) acute and late toxicity greater of G3 were in 2 (0,5%), 2 (0,5%), 12 (2.7%) and 3 (0.7%), respectively. Three patients experienced urinary stenosis which required surgical interventation.

Conclusions: According to our knowledge this is one of the largest retrospective studies of patients with prostate cancers treated with MH-RT Tomotherapy. This preliminary analysis, focused on the long-term effect, disease control and survival, confirms that a moderate hypofractionated program managed with the HI-ART technique achieves good local control with a low toxicity profile.

P185

REPORT OF TOXICITY AND CLINICAL OUTCOME OF MODERATE HYPOFRACTIONETED POSTOPERATIVE HELICAL TOMOTHERAPY IN A ELDERLY COHORT OF PROSTATE CANCER: A MONO-ISTITUTIONAL ANALYSIS

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Aims: To evaluate toxicity and clinical outcome of a retrospective series of 77 prostate cancer patients treated with moderate postoperative hypofractionation delivered by Helical Tomotherapy (HT).

Materials and Methods: From April 2013 to May 2020, 77 patients with median age of 70 years (range, 65–84 years) were treated with hypofractionated radiation therapy after prostatectomy. Adjuvant treatment was performed in 42 (54.5%) patients and salvage therapy in 35 (45.5%) patients, delivering to prostate bed a total dose of 63.8 Gy (equivalent dose in 2-Gy fractions=67.4 Gy) using 2.2 Gy fractions. Whole-pelvis irradiation was performed in 53 (68.8%) of cases (median dose, 49.3 Gy; range, 48-55.1 Gy). ADT was administered in 39 (50.6%) patients. All 77 patients completed the planned treatment without any interruption, with good tolerance. Common Terminology Criteria for Adverse Events (version 4.0) was adopted for acute and late genitourinary (GU) and gastrointestinal (GI) toxicity evaluations. Biochemical progression was defined as PSA level increase of ≥0.2 or more above the postoperative radiotherapy (RT) nadir.

Results: With a median follow-up of 28 months (range, 12-68 months), we found acute G2 GU toxicities in 2.6%, detecting no G≥3 events. For acute GI toxicity, we recorded G2 grade in 2.6%. Late toxicity GI G≥2 was detected in 5.2% and G≥2 GU in 5.3%, including two patients who underwent surgical incontinence correction. Actuarial 2- and 3-year biochemical recurrence-free survivals were 93.5% and 94.8%, respectively, for the entire population.

Conclusion: In our experience, many men with prostate cancer are elderly. In the physically fit, treatment should be the same as in younger patients. We report that moderate hypofractionated postoperative RT with HT is feasible and safe, with reports of low incidence of toxicity and promising biochemical control rates.

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THE IMPACT OF THE 18F-FLUCICOVINE PET-CT IN THE THERAPEUTIC DECISION FOR PATIENTS WITH PROSTATE CANCER AFTER BIOCHEMICAL RELAPSE

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Aims: Recent data demonstrated the utility of the 18F-Flucicovine PET-CT for the planning of salvage radiotherapy in patients with prostate cancer. The aim of this retrospective study is to evaluate the impact in the therapeutic decision of the 18F-Flucicovine PET-CT after biochemical relapse in patients radically treated for prostate cancer.

Methods: From March 2019 to March 2020 20 patients, with biochemical relapse of prostate cancer treated with Prostatectomy or Radiotherapy, underwent 18F-Flucicovine PET-CT after multidisciplinar discussion. 65% were classified in the unfavorable intermediate/high/very high risk groups. 15 patients underwent

radical prostatectomy (RP), 5 definitive radiation therapy (RT) with or without androgen deprivation (ADT); after Prostatectomy 5 patients underwent adjuvant or salvage radiotherapy. At the time of the CT-PET the average age was 73 years (range 62-85); the average value of the PSA was 0,86 and median was 0,77 (range 0,06-1,62 ng/ml).

Results: 10 exams were positive: 2 with positivity in the prostate bed, 7 with nodal relaspe (5 pelvic and 2 lomboaortic nodes), 1 in the dorsal vertebra column. In 2 patients with CT-PET negative for clinical relapse we had confirm with a multiparametric RMN of the pelvis. Globally in the 50% of the patients we had modified the terapuetic strategy after the 18F-Flucicovine PET-CT. Table 1 shows the change or the confirm of the initial therapeutic strategy after the 18F-Flucicovine PET-CT. For 5 patients the 18F-Flucicovine PET-CT allowed us to find nodal and bone oligometastasis, in order to use stereotactic technique with radical intent.

Conclusions: It is not possible to draw definitive conclusions from our case studies due to small numbers of data. However, in our experience we believe that 18F-Flucicovine PET-CT can be a valid aid in patients in whom it is believed that the therapeutic decision may be influenced by the result of the examination, in the aim to personalize medicine after multidisciplinary discussion.

Table 1. Schematic distribution of thetherapeuticdecision after the 18F-Flucicovine PET-CT.

	Therapeutic strategy proposed before 18F-Flucicovine PET-CT				
	ADT		RT		
PET-CT result	confirmed	changed	confirmed	changed	N° pts
+	2	6	1	1	10
-	1	4	3	2	10
N° pts	3	10	4	3	20

ADT: androgen deprivation therapy, RT: Radiation therapy

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ANALYSIS OF DOSIMETRIC PARAMETERS IN PATIENTS TREATED WITH VMAT (VOLUMETRIC ARC THERAPY) RADIOTHERAPY METHOD. OUR EXPERIENCE

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Purpose: Future challenges in oncology increasingly involve the development of predictive models able to support clinical decision. The aim of our preliminary results was to analyze some dosimetric parameters to predict late bladder toxicity and of the rectal toxicity in prostate cancer patients treated with VMAT (Volumetric Arc therapy) radiotherapy method.

Methods: Between the 2019 and March 2020, 94 prostate cancer patients were treated with radiotherapy using Volumetric Arc therapy (VMAT) by Simultaneous Integrated Boost methods in our Radiotherapy Department. Clinical Target Volumes (CTV) included: prostate gland (CTV1, 76 Gy) and seminal vesicles (CTV2, 74 Gy). Late bladder and rectal toxicity data were collected and analyzed through cumulative Dose Volumes Histograms (DVH) that has been exported for each patient. Data were analyzed by using in house developed software. A p value < 0.05 was used as level of significance. The data taken into consideration for our analysis were Vd (a value of dose to a specific volume of OAR) and Dv (a value of Volume relativo a specific value of dose).

Results: Data from a total of 94 patients were collected for analisys. in the subset of patients with late bladder toxicity grade ≥ 2 (in terms of haematuria, cystitis and dysuria), we observed a correlation with a Vd equal to 55 Gy (p.value 0.021). Relating to patients with late rectal toxicity grade ≥ 1 (in terms of proctitis, tenesmus) we observed a correlation with a Vd equal to 48 Gy (p.value 0.03). Local control was 99.1% (mean 4 months of follow-up) but we are aware that a long follow-up is needed to assess completely both local control and late toxicity.

Conclusions: Nowadays the search for models to predict toxicity, which increasingly favor the use of more personalized treatments, is the aim of modern radiation therapy. Our results could help to optimize treatment planning in view of a more efficient personalize treatments such as to further reduce both acute and late toxicity.

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MACHINE LEARNING-BASED MODELS OF RADIO-INDUCED TOXICITY IN PROSTATE CANCER ULTRA-HYPOFRACTIONATED RADIOTHERAPY

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This retrospective study was part of the research notified to our Ethics Committee (UID 2; 410). This study was partially supported by two research grants from the Associazione Italiana per la Ricerca sul Cancro (AIRC), namely "Radioablation ± hormonotherapy for prostate cancer oligorecurrences (RADIOSA trial): potential of imaging and biology" registered at ClinicalTrials.gov NCT0; 39; 402; 3; 5, and IG-1; 3218 "Short-term High Precision Radiotherapy for Early Prostate Cancer With Concomitant Boost on the Dominant Lesion", registered at ClinicalTrials.gov (NCT0191; 3717)The study was

also supported by the Italian Ministry of Health with Ricerca Corrente and; 5x1000 fundsSV and JLI are students of the SEMM (Scuola Europea di Medicina Molecolare) MZ received a research grant from Accuray Inc(Data collection and analysis of Tomotherapy® and CyberKnife® breast clinical studies, breast physics studies and prostate study) outside the current studyThe sponsors did not play any role in study design, execution and data analysis.

Aims: In the last decades, radiotherapy (RT) treatments have become safer and more effective, allowing for dose escalation to the target volume without jeopardizing the sparing of surrounding organs at risk (OARs). However, effective toxicity prediction tools are essential in the era of tailored treatments. The purpose of the study is to test machine learning (ML)-based predictive models of toxicity in prostate cancer (PCa) patients (pts) treated with ultra-hypofractionated RT regimens.

Methods: Two cohorts of 61 and 186 non-metastatic low-intermediate risk PCa pts (from AIRC IG-13218 prospective trial and "Give me Five" retrospective trial, respectively), who underwent ultra- hypofractionated RT (35 Gy/5 fractions), were considered (Ethics Committee Notification UID 2410). Dosimetric and clinical features were used to train different ML models to predict genitourinary (GU) and gastrointestinal (GI) acute toxicities. The area under the receiver operating characteristic curve (AUC) was used to compare the model performances.

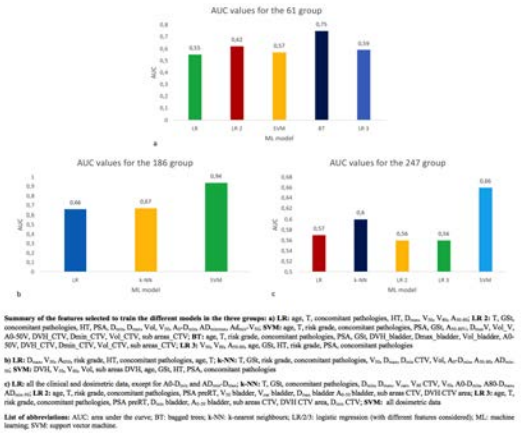

Figure 1. Machine learning-based models performances within the three different patients groups (a: 61; b: 186; c: 247).

Results: Separate analyses of the three groups (61, 186 and 247) were carried out. Bagged trees outperformed all the others on the 61 cohort (Figure 1a), with an AUC of 0.75, while SVM resulted the best algorithm on the 186 (Figure 1b) and 247 cohort (Figure 1c), with an AUC of 0.94 and 0.66, respectively. Overall, the best performing algorithm was LR, since, among the 8 best results, 4 were achieved with this one. The most predictive features were found to be T-stage, age, OARs volume and DVH punctual values. No significant correlation with the outcome was found for sub-areas under the DVH. Overall, the models achieved better AUC values when the two subgroups of pts were considered separately. The study presents some limitations, such as the relatively low occurrence of toxicity events, often resulting in a scarce capability of identifying true positives, and low AUC values in certain configurations.

Conclusions: In the era of personalised medicine and tailored treatments, a model that accurately predicts toxicity could represent a useful clinical tool for better patients' selection. The study shows that the performance of the predictive models is highly dependent on the choice of classifier, features and training/testing sets. Differences between groups can be due to the different characteristics of trials. Further analyses should focus on features and classifiers selection, to improve the performances and generalizability of the models.

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COULD PLANNING ORGAN AT RISK VOLUME FOR THE RECTUM USING CONE BEAM COMPUTED TOMOGRAPHY BE USEFUL IN DAILY CLINICAL PRACTICE FOR THE TREATMENT OF PROSTATE CANCER?

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Aims: Highly conformal dose distribution techniques, such as Volumetric Modulated Arc Therapy (VMAT), are the standard of care in prostate cancer patients submitted to radical radiation therapy (RT). The use of Image-Guided RT (IGRT) technologies, such as cone beam computed tomography (CBCT), improves daily target localization leading to a more precise dose delivery. As the position of the prostate and seminal vescicles mainly depends on surrounding organs, patients self-administer an enema and fill the bladder with adequate fluid amount before the planning CT and RT sessions. If imaging shows gas/fecal mass in rectum, patients repeat preparation and imaging until standards are matched. These procedures increase patient time at the LINAC, patient discomfort and the radiation dose due to ionizing IG. To reduce above downsides we assessed if Planning organ at Risk Volume for the rectum (PRV-r) could be useful for optimizing daily RT sessions.

Methods: We analyzed 7 prostate cancer patients submitted to radical hypofractionated RT with VMAT in March - June 2020. Total radiation dose to the prostate and seminal vescicles was 72 - 63,6 Gy/30 fractions in 4 patients and 67,5 - 60 Gy/25 fractions in 3 patients. IGRT was realized with daily CBCTs. The PRV was generated adding automatic expansion of the planned rectum of 5 mm in anterior, right and left later-

al directions. If QUANTEC dose-volume constraints for rectum toxicity applied to PRV were satisfied, PRV was accepted. Otherwise margins were reduced until PRV fulfilled the constraints. During CBCT evaluation, if bladder filling was adequate and rectum was included in its PRV, the RT treatment was delivered. Differently the patient repeated bladder and/or rectal preparation. We analyzed every CBCT in all the patients assessing how often the presence of PRV-r helped us to allow the treatment delivery.

Results: IGRT treatment data of each patient are shown in table. In 4 patients PRV-r was accepted with 5 mm margins, while in 3 patients with 4 or 3 mm. 261 CBCTs were acquired. Inadequate rectal preparation caused more repeated CBCTs than bladder preparation. PRV-r was useful in 40-100% of RT fractions. Radiation dose was safely delivered following the first daily CBCT in average 62% and 35% of fractions with PRV-r expansion of 5 mm and 3-4 mm, respectively.

Conclusions: Our preliminary results show that PRV-r has benefits in prostate cancer treatment with VMAT and daily CBCT, especially if PRV-r margins are 5 mm.

Table 1.

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EARLY SALVAGE RADIOTHERAPY. STANDARDS AND FUTURE PERSPECTIVES IN THE TREATMENT OF PROSTATE CANCER. A MONOCENTRIC RETROSPECTIVE STUDY OF 67 PATIENTS.

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Aims: About half of men who have undergone radical prostatectomy may have a biochemical recurrence. Last year 2 randomized trials (RADICALS, RAVES) and a Meta-analysis (ARTISTIC) were presented regarding the role of adjuvant radiotherapy or early salvage radioyherapy after radical prostatectomy. all have demonstrated a clinical benefit of early salvage radiotherapy (eSRT). This is a monocentric retrospective study to evaluate the role of pre-RT PSA as a prognostic factor predicting the 5-year "biochemical failure free survival" (BFFS) in patients undergoing salvage radiotherapy "SRT".

Methods: 67 patients diagnosed with biochemical relapse of prostate cancer after radical prostatectomy underwent Salvage Radiotherapy in association or not with androgen deprivation therapy (ADT). All patients included in the study had a PSA> 0.2 ng/mL at the time of radiotherapy. The radiation therapy dose varied from 66 to 74 Gy in 2 Gy per Fraction. Follow-up included serial PSA assessments (every 3 months in the first 2 years, every 6 months thereafter).

Results: 5-year BFFS was 53% (35) for all patients included. 5-year BFFS increased with the decrease of the pre-SRT PSA level: 69% for patients with a pre-SRT PSA <0.5 ng/mL (n = 21), and 44% for those with a PSA > 0.50 ng/mL (n = 14).

Conclusions: Numerous studies have already shown, in this regard, that the efficacy of the salavage radiotherapy is greater as the PSA is lower at the time of treatment.[1] Recently, the American Society for Radiation Oncology (ASTRO) and American Urological Association (AUA) jointly published a consensus paper stating that salvage radiotherapy "should be administered at the earliest sign of PSA relapse". Salvage radiotherapy allows a better disease control when administered at a PSA<0,5 ng/ml.

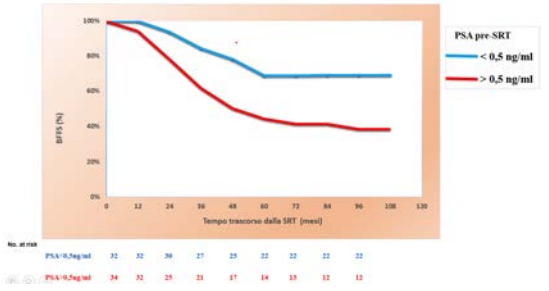

Figure 1.

Reference

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ADJUVANT RADIOTHERAPY IN NODE POSITIVE PROSTATE CANCER PATIENTS: A DEBATE STILL ON. WHEN, FOR WHOM?

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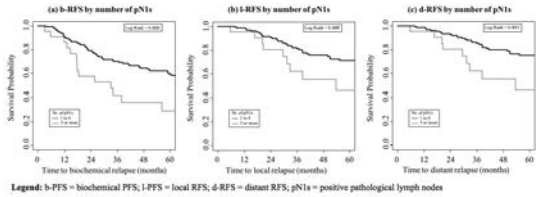
Aims: To evaluate the impact of adjuvant radiotherapy (RT) (aRT) in prostate cancer (PCa) patients with pathological positive lymph nodes (LNs) (pN1s) after radical prostatectomy (RP) and extended pelvic lymph nodes dissection (ePLND) in terms of distant recurrence-free survival (d-RFS) according to the main tumour pathological characteristics and the number of pN1s. Biochemical-RFS (b-RFS), local-RFS (l-RFS), overall survival (OS) and acute and late toxicity were assessed as secondary endpoints.

Methods: A retrospective cohort of 187 consecutive patients with pN1 were treated with aRT. aRT on tumour bed and pelvis was administered within 6 months from RP in patients with locally advanced PCa. Androgen deprivation therapy (ADT) was prescribed following the guidelines. Univariate and multivariate analyses for b-RFS, l-RFS, d-RFS and OS were performed to assess whether the number of pN1s represented an independent prognostic factor. Youden index was computed to find the optimal cut-off number of pN1s able to discriminate between patients with and without relapse. This study was part of the research notified to our Ethic Committee (nr N79).

Results: At 5 years, l-RFS, d-RFS, b-RFS and OS were 68%, 71%, 56% and 94% respectively (Figure 1). The median follow-up was 49 months. The number of PN1s was significant associated with b-RFS, l-RFS and d-RFS. The best threshold for discriminating between patients with and without relapse was found to be 5 pN1s. In multivariate analysis, the number of pN1s was confirmed to be an independent predictor of b-RFS, l-RFS and d-RFS, but not of OS. Multivariate analysis showed also an increased risk of b-RFS for increasing values of initial prostate-specific antigen (iPSA) and in patients with tumour vascular invasion. l-RFS and d-RFS also correlated with significantly reduced risk for International Society of Urological Pathology (ISUP) grade < 3 (group 1 or 2 compared to group 3). OS correlated only with the increase in iPSA value.

Conclusions: Our data confirmed the excellent outcomes of pN1 PCa patients treated with adjuvant treatments and the key role represented by the number of pN1s in predicting b-PFS, c-PFS and d-PFS. Large prospective cohort studies and randomized clinical trials are needed to confirm these results and identify the subgroup of pN1 patients who might most benefit from aRT.

Figure 1. b-RFS (a), l-RFS (b) and d-RFS (c) by number of pN1s



Legend: b-PFS = biochemical PFS; l-PFS = local RFS; d-RFS = distant RFS; pN1s = positive pathological lymph nodes

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SHORT AND LONG-TERM GENITOURINARY AND GASTROINTESTINAL TOXICITY SALVAGE POST-PROSTATECTOMY IMAGE-GUIDED VMAT RADIOTHERAPY

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Aims: To report the short and long term late tolerance of men receiving image-guided VMAT in a salvage post-prostatectomy (SRT) setting.

Methods: The records of 101 men treated with prostatectomy and subsequent SRT to the prostate bed were selected. Only men with a pre-RT PSA between 0.2 and 2 ng/mL was selected. Men were treated with image-guided VMAT. Tolerance to treatment was determined from the chart and graded according to RTOG scale. Multivariate logistic regression was used to explore the variables influencing the GU and GI toxicity. Significance was defined as two tailed p-value <0.05.

Results: The acute toxicity was assessed 15 days after SRT. Fifteen days after RT, 20 men (19,8%) suffered from G1-2 acute GI toxicity. Of these, 8 men (7,9%) suffered from G2 acute GI toxicity. Higher acute GU toxicity than GI toxicity was observed. Thirty-one men (30,6%) suffered from G1-2 GU toxicity. Ten men (9.9%) suffered from G2 acute GU toxicity. No acute grade 3 or higher GU and GI toxicity was detected. Incidence of late GU and GI toxicity two years after the end of postoperative RT was assessed in 70 men. Only 10 out 70 patients (14,3%) treated with SRT suffered from G1-2 late GU toxicity. Seven men suffered from G2 late GU toxicity. No grade 3 or higher GU toxicity was detected. Late G2 GI toxicity was observed in 3 men (4,3%) with no grade 3 or higher GI toxicity was detected. Multivariate logistic regression indicated that the cumulative dose (66Gy vs 70 Gy) (OR=1,78; CI95% 1,23 to 2,4) and higher bladder volume (OR: 1.45; CI 95% 1.12 to 1.89) were two independent prognosticator for higher acute any grade of GU toxicity. These two variables did not significantly impact on the late GU and GI toxicity.

Conclusions: With a low rate of relevant acute and late GI and GU toxicity SRT confirms as well tolerated treatment. However longer follow-up will be necessary to confirm our results.

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ACUTE AND CHRONIC TOXICITIES IN PROSTATIC CANCER PATIENTS TREATED WITH MODERATE HYPOFRACTIONATION AND SIMOULTANEUS INTEGRATED BOOST (SIB) BY INTENSITY MODULATED RADIOTHERAPY (IMRT), OUR EXPERIENCE

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Aims: The aim of this study is to evaluate pain, chronic genitourinary (GU) and gastrointestinal (GI) late toxicities in patients treated with pelvic intensity-modulated radiation therapy (IMRT) and Simoultaneus Integrated Boost (SIB) for prostatic cancer.

Methods: We retrospectively analyzed 52 patients treated from January 2017 from May 2020. All of them have been treated with Intensity Modulated Radiotherapy and applying moderate hypofractionation and SIB on the prostate. The median age at the time of treatment was 77 years (range 66-85 years). Toxicities were assessed through a phone questionnaire at a median time of 31 months from the date of treatment. Toxicities were assessed using the Radiation Therapy Oncology Group (RTOG) scale.

Results: Patients were treated with a fractionation of 170 cGy / 29 fr. on the pelvic lymph nodes, 190 cGy / 29 fr. on prostate and seminal vesicles and 240 cGy / 29 fr. with a SIB on the prostate area. One patient was treated with a dose of 240 cGy/12 fr. on the pelvic lymph nodes, prostate and seminal vesicles. In two patients a SIB was delivered at a dose of 240 cGy/ 29 fr. and in one patient with a dose of 270 cGy/12 fr. on PET positive lymph nodes. The median V50 of the bladder was 12,83%, while the median V40 was 45,43%. 16 patients developed acute GU toxicities: G2 8 patients (50%), G3 7 patients (44%) and G4 1 patient (6,26%). 6 patients developed chronic GU toxicities: G2 5 patients (83%) and G4 1 patient (7%). A volume of 230 cc of the intestine absorbed a median dose of 33,86 Gy. Acute GI toxicities were reported by 28 patients: G1 18 patients (64,28%),G2 6 patients (33,3%) and G3 4 patients (22,22%). Chronic GI toxicities were reported by 11 patients: G1 5 patients (45,5%), G2 4 patients (36,36%) and G3 2 patients (18,18%).

Conclusions: Our data confirm the excellent tolerability and low profile of late toxicity of IMRT treatments delivered with a moderate hypofractionation on prostate and are consistent with the literature data on the subject.

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CHOLINE PET/CT GUIDED STEREOTACTIC RADIOTHERAPY IN ELDERLY PATIENTS WITH RECURRENT PROSTATE CANCER

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Aims: Prostate cancer is the most diffuse malignancy in elderly patients; therefore, the management of such a tumor must be tailored on the basis of the presence of comorbities. Once primary curative treatment failure, at the time of tumour recurrence, the best timing concerning the administration of Androgen Deprivation Therapy (ADT) is still debated. In the last years, the use of Choline PET/CT in clinical decision making of patients with recurrence Prostate Cancer has been increased, in selected cases, the so called oligometastatic patients, active metastatic lesions are treated with stereotactic body radiotherapy in order to achieve a PSA control and, therefore, postpone the beginning of ADT by almost 3 years. The aim of the present study was to demonstrate how stereotactic body radiotherapy (SBRT) guided by choline PET/CT can impact on patient's ADT free survival in elderly patients with recurrent prostate cancer.

Methods: We included in the present retrospective analysis oligometastatic prostate cancer patients (1 to 3 simultaneous lesions), aged over 70 years and treated with SBRT on all active lesions revealed by choline PET/CT (functional imaging was repeated after a new PSA increase). All lesions were treated with Radiosurgery (24 Gy delivered in a single fraction) or 27 Gy delivered in 3 fractions. Kaplan Meier were used for OS.

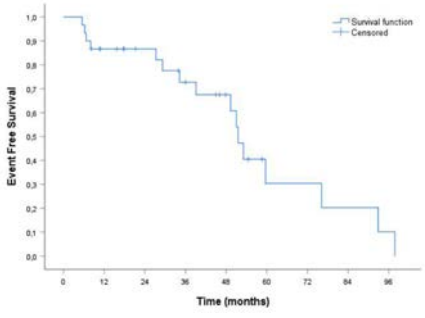

Figure 1.

Results: Data analysis was performed in June 2020. We analized data from 30 oligometastatic prostate cancer patients treated between 2010 and 2020. A total of 49 lesions were treated; 18 patients had lymph node relapse,10 had bone metastases and 2 both sites. Moreover, 4 patients had 2 simultaneous secondary sites

while the remaining 26 had only 1 metastatic location. 27 patients performed a single cycle of Radiotherapy, 1 performed two,1 performed five and the last one performed four. After a median follow up of 35 months, the average ADT-free survival was 51 months. 16 patients became plurimetastatic and started ADT while the remaining 14 never needed to undertake it.

Conclusions: Our experience underlines the diagnostic importance of choline PET/CT in selecting oligometastatic patients candidate for local treatment rather than systemic therapy. A biochemical control allows to postpone the need for systemic therapy which, especially in the case of the elderly subject, would risk compromising his balance and consequently also allows to postpone the phase of resistance to castration of the illness.

P195

SAFETY AND EFFICACY OF BLADDER-PRESERVING THERAPY FOR MUSCLE INVASIVE BLADDER CANCER: A MONOINSTITUTIONAL EXPERIENCE

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Aims: Tri-modality therapy (TMT) represents a radical treatment option for selected patients with muscle-invasive bladder cancer (MIBC) suitable or not for a surgical approach. Aim of our study is to retrospectively evaluate side-effects and efficacy of a multimodal approach in patients with non-metastatic MIBC

Methods: Ten patients (pts) were referred to our Institute with a histological diagnosis of high grade MIBC. Median age was 75 years. Nine pts were male and one female. Nine pts were former or still active smokers. All pts were staged by cystoscopy and chest abdominal CT scan; four pts were also submitted to 18FDG PETCT scan and 1 to bone scintigraphy. Two pts were found with nodal loco-regional disease at the final staging. All pts were submitted to TURB, while only 1 was submitted to re-TURB before chemo-radiotherapy treatment. Six pts had macroscopic residual tumour after endoscopic procedures. All pts were submitted to radiotherapy with radical intent: 1 received a total RT dose lower than 60 Gy, while nine pts received 60 Gy or more (range 60-66 Gy) with conventional fractionation. Seven pts were submitted to concomitant chemoradiation therapy (3 pts with 5-fluorouracil plus mitomycin C, 1 pt with gemcitabine and 3 pts with cisplatin), while 1pt received chemotherapy before radical radiotherapy (sequential).

Results: At a median follow-up of 16 months, 7 pts are still alive, while 2 died due to other causes than cancer and one due to MIBC disease progression. After the end of radical treatment, 3 pts showed a complete response, 6 pts a partial response, 1 had an apparent local disease progression after CT scan imaging with negative urinary cytology. During the follow up 1 pt experienced local recurrence and another one showed both locoregional lymph node relapse and distant progression (bone e lymph node). No G3 or more acute toxicity were registered (according to CTCAE scale v4.0) (9 pts G1 or G2). Five pts had urinary complications, 3 pts had diarrhea, one had proctitis while 3 pts had haematological toxicity. Only one pt experienced relevant late genitourinary toxicity (Grade 2)

Conclusions: In our retrospective analysis, the multimodal approach appeared to be safe and effective in the short-term management of MIBC in selected pts. Longer follow-up is needed to definitely validate these findings. Prospective or randomized clinical trials are still needed to compare this conservative approach to radical surgery approach.

P196

MODERN RADIOTHERAPY IN TREATING NODAL OLIGORECURRENT PROSTATE CANCER IN ELDERLY PATIENTS: ANALYSIS OF THE OUTCOME AND TOXICITY

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Aim: Oligorecurrent prostate cancer (PCa) with exclusive nodal involvement represents a common state of disease, susceptible to local therapy. Stereotactic body radiotherapy (SBRT) and elective nodal radiotherapy (ENRT) with a simultaneous boost (SIB) are being investigated as nodal-directed treatments in oligorecurrent PCa. Many men with PCa are elderly(>70 years). In caring for these patients who have advanced disease, it is important to assess the health status and his goals of care. The aim of this study is to report oncologic outcome and toxicity of modern radiotherapy (RT) in elderly PCa patients with pelvic nodal (LN) oligorecurrence.

Materials and Methods: In total, 38 LN recurrences in 25 elderly patients (SBRT:17,SIB: 8) were treated between 2011 and 2020. Primary treatment was radical prostatectomy and/or radiotherapy. Prescribed doses for SBRT and schedules of fractionation ranged from 21-50 Gy in 3-5 fractions. SIB schedules were designed to deliver 46Gy (2 Gy/fr) to the pelvic nodes, 59,8 Gy (2,3Gy/fr) to the positive nodes and 70 or 80 Gy (2Gy/fr) to the prostate surgical bed or prostate and seminal vescicles. The choice of radiotherapy was the presence of 2 or more pelvic nodes and the presence of disease in the prostate or prostate surgical bed. Response to treat-

ment was assessed with periodical PSA evaluation. Local response to treatment was scored according to RECIST Criteria 1.1. Acute and late toxicity were evaluated according to RTOG scale.

Results: Median age was 78 years (70-89). Median follow-up was 24 months (3 -90). At the diagnosis the median PSA value was 3.8 (0,04 – 28,51). At the last follow up the median PSA value was 0.08(0,01 –17,52); complete radiologic response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) were observed in 22(58%), 3(8%), 12(38%) and 1 cases (3%), respectively. An objective clinical response (CR+PR) was observed in 25 (66%). The overall clinical benefit (CR+PR+SD) was 97%. 5 patients (20%) showed progressive distant disease. 2 patients had acute grade 2 gastrointestinal toxicity. None of the patients had acute grade 3/4 adverse events or late toxicity. 20 patients (80%) were still alive at time of analysis: 16 are without evidence of disease, 4 with a disease progression.

Conclusions: In our experience, modern radiotherapy can be used to manage oligorecurrent disease in elderly patients to obtain good local control with a low profile of acute and late toxicity.

P197

SALVAGE RADIOTHERAPY IN PROSTATE CANCER: MULTICENTRE RETROSPECTIVE STUDY

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Purpose: The aim of the study is to investigate retrospectively outcome, survival, acute and late toxicity in prostate cancer treated with postoperative salvage intent

Material and method: 152 consecutive patients (pts) were treated in 8 radiotherapy centres. The mean age was 64 years (y), median 65y (range 51-77y). According to 2014 NCCN prognostic classification 10% pts was favourable risk, 41% intermediate risk, and 49% unfavourable risk. The pts were treated with LINAC. The total dose was > 66 Gy with standard fractionation on prostatic bed only (89%) and on prostatic bed + pelvic irradiation (11%). The mean prostate specific antigen (PSA) at the diagnosis was 15 ng/ml; median 8.9 (range 0.59-188). Surgical pathological specimens showed pT2 31% (R1 81%), pT3a 41% (R1 57%, Close 7%), pT3b 26% (R1 72%). Androgen deprivation therapy (ADT) was administrated in 70% of pts. Mean follow-up was 67 months (m), median 55 m, (range 12-160 m). All the pts were clinically evaluated for urinary and rectal late complications according to CTC.AE 4.0 and RTOG/EORTC scale.

Results: Five-year biochemical disease-free survival (bDFS) was 65% and overall survival (OS) was 85%, 20% alive with disease, 7% dead for disease and 8% dead for other cause. Mean PSA at last follow-up was 24, median 1 (range 0-1200). Acute toxicity: genitourinary (GU) ≥ G2 in 12% of pts and gastrointestinal (GI) ≥ G2 in 2% of pts. Late toxicity: GU ≥ G2 in 11% and GI ≥ G2 3%. No pts developed grade 4 GI complication. Urinary incontinence ≥ G2 was 16%

Conclusion: The study confirmed that survival, bDFS, acute and late toxicity was similar to that of the literature. Future prospective studies should be conducted to evaluate and clarify the salvage role and timing of radiation therapy in patients who underwent radical prostatectomy with R+ or detectable PSA after surgery.

P198

RECTUM AND BLADDER INTERFRACTION DOSE VARIATIONS DURING A PROSTATE CANCER TREATMENT WITH TOMOTHERAPY

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Aims: The aim of this study is to evaluate variations of delivered rectum and bladder dose distribution respect to the planned one in prostate cancer patients treated using ThomoTherapy. Dose variations of these organs are linked to their daily changes in volume or a not accurate patient positioning. Dosimetric distribution variations have been studied both fraction by fraction and at the end of all the delivery radiation sessions.

Materials: 20 patients have been involved in the study: the prescription dose was 72 Gy in 28 fractions to the prostate gland. For each patient a comparison between the planned TPS and each daily delivered dose distributions has been performed using MIM Maestro deformable registration algorithms and taking into account the positioning shifts applied during MVCT pretreatment verification. For each of the 28 fractions the acquired MVCT was merged with the planning kVCT in order to transfer the planned dose to MVCT where the bladder and rectum structures were recountured by the radiation physician. The differences in terms of volume and DVHs between the planning CT and each of the 28 radiation session CBCT were evaluated. In addition, a dose accumulation for all the sessions was calculated and compared with the planned one in terms of dose mapping and DVH.

Results: Among the 28 fractions the volume varied between +137% and -23% for rectum and between +177% and -29% for bladder, respect to their corresponding planning volume. Consequently, OAR dose constraints varied over all treatment for each patient. We found:for rectum V50=33%, V60=20% and V65=11% for delivered distribution, rather than V50=27%, V60=13% and V65=5% planned; for bladder V65=0.7% for delivered distribution rather than

V65=15% planned. Over all treatment we verified a decrease in target coverage, homogeneity and conformity index (D95%=93%, HI=0.08 and CI=0.91 and D95%=84%, HI=0.17 and CI=0.69 for planned and delivered distribution, respectively).

Conclusion: Significant interfractions changes in terms of bladder and rectum volumes have been observed. These volume variations imply also dose distribution variations not only for rectum and bladder but also for target. The clinical outcome of all those patients for whom we have experimented a large variation of PTV coverage would be evaluated not in terms of planned dose but in terms of delivered one. Moreover, more attention has to be paid in reproducing the same bladder and rectum size before each radiation session.

P199

REIRRADIATION IN PROSTATE CANCER: EARLY TOXICITY EVALUATION IN MAGNETIC RESONANCE-GUIDED STEREOTACTIC BODY RADIATION THERAPY (MRGRT)

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Aims: A standardized approach in the framework of Prostate Cancer (PC) local failures management is still not defined. New technologies could help to improve re-treatment outcome, reducing side effects, especially in relation to previous treatments. Aim of this study was to evaluate genitourinary (GU) and gastrointestinal (GI) acute toxicity rate in Magnetic Resonance-guided Stereotactic Body Radiation Therapy (MRgSBRT) in Prostate Cancer recurrences (PCr).

Methods: A retrospective analysis was performed on patients affected by PCr. All patients received a re-treatment by Stereotactic Body Radiation Therapy (SBRT) Technique on a low tesla hybrid unit (MRIdian, ViewRay Inc., Mountain View, CA).In order to ensure a reproducible rectal and bladder volume, all patients were instructed to execute a daily enema and to drink 500cc of water half an hour before planning and each delivery fraction. MRgRT reirradiation was performed in 5 fractions by an every other day schedule. The planning target volume (PTV), was defined as isotropic expansion of 3 mm from whole prostate gland/prostate bed (CTV).Daily treatment set-up controls were performed using a 25 seconds true fast imaging with steady-state free precession (TRUFI) Magnetic Resonance (MR). Also PTV online tracking, adding a 3 mm boundary to GTV, was performed to ensure target coverage and Organs at risk (OARs) avoidance.Toxicity was evaluated through the Common Terminology Criteria for Adverse Events CTCAE v5.0, both on daily schedule during treatment and at early follow-up, planned monthly for the first three months.

Results: From June 2019 to February 2020, a total of 6 patients were evaluable for analysis.Median age was 78.5 years (range: 71-85), while median interval from previous treatment was 154 months (range 122 – 206). Total dose delivered to PTV was 30 Gy in 5 fractions in 5 patients (83.3%); in 1 patient total dose delivered to PTV was 25 Gy in 5 fractions (16.7%). Median biologically effective dose (BED) was 210 Gy, considering a α/β of 1.5. No acute GU nor GI toxicity occurred. At the time of the analysis, none of the patients experimented neither biochemical, nor local or distant failure disease.

Conclusions: These preliminary data show that MRgSBRT reirradiation is a safe approach for PCr, as compared to toxicity rates shown by other investigators using Volumetric Modulated Arc Therapy (VMAT) and SBRT (D'Agostino et al. 2019; Jereczek-Fossa et al. 2019). Further analysis, long term toxicity evaluations and larger patients' series are needed to confirm these promising early findings.

P200

COMPARATIVE TOXICITY OUTCOMES OF SALVAGE VERSUS ADJUVANT RADIOTHERAPY FOR PROSTATE CANCER PATIENTS TREATED WITH VMAT AND IMRT TECHNIQUES

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Aims: There is no evidence of different survival and the impact on acute and late toxicity in adjuvant radiotherapy (aRT) or salvage radiotherapy (sRT) after radical prostatectomy. The aim of this study was to assess rectal and bladder toxicity outcomes in a retrospective series of prostate cancer patients treated with VMAT or IMRT in postoperative setting.

Methods: Patients who received aRT or sRT after prostatectomy from 2015 to 2019 were reviewed. They were stratified in two groups: patients treated with aRT and with sRT. Acute and late toxicities were assessed. Differences in proportions between groups were analyzed using the Pearson's Chi-squared test. Univariate logistic regression models predicting rectal and bladder toxicity were used.

Results: 129 prostate cancer patients were examined. 65 patients were submitted to aRT and 64 patients to sRT. All patients were treated with the same radiotherapy protocol (prostate bed delineated according to Radiation Therapy Oncology Group guidelines, IMRT/VMAT technique, total dose 66 Gy). Patients and tumors characteristics were reported in Table 1. Median follow-up was 22 months. Grade 1 acute bladder toxicities were detected in 40 (61.5%) and 30 (46.9%)

patients and grade 2 toxicities were reported in 1 (1.5%) and 6 (9.4%) patients in aRT and sRT respectively. Grade 1 late bladder toxicities were described in 30 (46.2%) and 20 (31.2%) patients and grade 2 toxicities were reported in 6 (9.2%) and 2 (3.1%) patients in aRT and sRT respectively. Acute grade 1 rectal toxicities were reported in 18 (27.7%) aRT patients and 27 (42.2%) sRT patients and 5 (7.7%) and 4 (6.2%) patients developed grade 2 rectal adverse event in aRT and sRT respectively. Regarding late rectal toxicity, G1 was reported in 10 patients (15.4%), G2 in 6 (9.2%) and G3 in 1 patient (1.5%) in the aRT group. In sRT arm, 8 patients (12.5%) and 1 (1.6%) developed G1 and G2 toxicity, respectively. A higher incidence of late bladder toxicity was observed in aRT (55.4% versus 34.4%, p=0.041); a similar trend, although not reaching a statistically significant difference was observed for acute bladder toxicity (63.1% versus 56.2%, p=0.071). In the univariate logistic regression model sRT was associated with lower rate of bladder late toxicity with OR 0.42 (0.20-0.85, p=0.017).

Conclusion: Adjuvant and salvage RT were well tolerated with acceptable toxicity profile in both arms. Lower rates of bladder toxicity occurred in patients treated with sRT.

Table 1. Patients and treatment characteristics in adjuvant and salvage radiotherapy.

	Adjuvant n= 65 n (%)	Salvage n= 64 n (%)
Median age (range)	68 (47-78)	69 (51-81)
Surgery		
• Prostatectomy	26 (40.0%)	40 (62.5%)
• Prostatectomy +lymphadenectomy	39 (60.0%)	24 (37.5%)
Gleason Score		
• ≤6	1 (1.5%)	17 (26.6%)
• =7	34 (52.3%)	30 (46.8%)
• >7	30 (46.2%)	17 (26.6%)
Resection Status		
• R0	14 (21.5%)	37 (57.8%)
• R1	51 (78.5%)	27 (42.2%)
pT		
• 2a	4 (6.2%)	7 (10.9%)
• 2b	0 (0.0%)	8 (12.6%)
• 2c	2 (3.1%)	30 (46.8%)
• 3a	32 (49.2%)	17 (26.6%)
• 3b	27 (41.5%)	2 (3.1%)
pN		
• 0	29 (44.6%)	37 (57.8%)
• 1	10 (15.4%)	2 (3.1%)
• x	26 (40.0%)	25 (39.1%)
Neural Infiltration		
• Negative	11 (16.9%)	24 (37.5%)
• Positive	54 (83.1%)	40 (62.5%)
Vascular Infiltration		
• Negative	48 (73.8%)	51 (79.7%)
• Positive	17 (26.2%)	13 (20.3%)
Lymphatic Infiltration		
• Negative	52 (80.0%)	52 (81.3%)
• Positive	13 (20.0%)	12 (18.7%)
Postoperative PSA (ng/ml)		
Mean ± SD	-	0.3±0.59
Range	-	0.01-4.06
• <0.2	-	36 (56.3%)
• 0.2-1	-	22 (34.4%)
• >1	-	6 (9.3%)
Time Surgery-Radiotherapy Median (IQR)	5.6 months (4.9-6.7)	50.4 months (27.3-93.5)

P201

DOSIMETRIC AND CLINICAL IMPACT OF HYDROGEL SPACER IN PROSTATE CANCER RADIOTHERAPY

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Aims: When hydrogel spacer is placed between the Denonvilliers' fascia and the anterior rectal wall, it pushes away the rectum from the prostate. In particular, in prostate cancer radiotherapy (RT) treatment, it permits to reduce dose to the rectum. The aim of this study was to verify rectal dosimetric improvement in patients (pts) with hydrogel spacer treated with RT for prostate cancer and to correlate it with toxicity.

Methods: Twentyseven pts with unfavorable intermediate risk prostate cancer received prostate hypofractionated RT during 2018 and 2019 at our Department. Of them, 11 pts (group 1) underwent RT after the implant of a hydrogel spacer and 16 pts (group 2) had RT without it. Median age was 74, 75 for group 1 and 74 for group 2. Nine pts (7 in group 1 e 2 in group 2) received a total dose of 70.02 Gy in 2.7 Gy/fraction an 18 pts (9 for each groups) had a total dose of 60 Gy in 3 Gy/fraction. All RT treatments were planned with volumetric modulatet arc radiotherapy (V-MAT) and average D98 and D2 of PTV were 95% and 103% respectively. Primary endpoint was the evaluation in each group of rectal dosimetry; we used V50, V60, V65, V70, V75 as rectal dose constraints and we converted them from the conventional to the hypofractionated dose by EQD2, assuming 5 Gy as alpha/beta ratio. Secondary endpoint was the evaluation of acute and late rectal toxicity, according with CTCAE toxicity scale. Data were analyzed with Wilkoxon Mann-Whitney test.

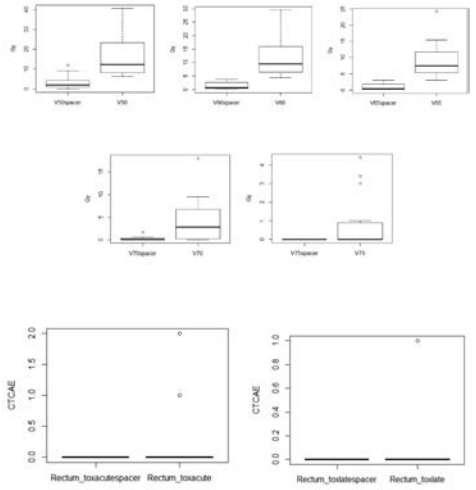

Figure 1.

Results: Rectal dosimetry was evaluated in each group and we obtained better dosimetric results in group 1 than in group 2. We observed in the group 1 respect to the group 2 a statistically significant advantage in V50 (3% vs 17%, p<0.001), V60 (2% vs 12%, p<0.001), V65 (1% vs 9%, p<0.001), and a not statistically significant advantage for V70 (0.4% vs 4%, p=0.030) and V75 (0.1% vs 0.5%, p=0.036). At median follow-up of 12 months, any grade of acute and late rectal toxicity was reported in the group 1 while 2 pts (12.5%) had acute rectal toxicity (G1 in 1 case and G2 in 1 case) and 1 pt (6%) had Grade 1 late rectal toxicity in the group 2; differences between two groups were not statistically significant (p=0.25, p=0.45).

Conclusions: Our experience confirmed that spacer hydrogel significantly improves rectal dosimetry. The clinical impact of this dosimetric gain in terms of acute and late toxicity, despite hopeful results, needs to be still demonstrated, so larger sample and a longer follow up are necessary.

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IMAGE-GUIDED HYPOFRACTIONATED POST-OPERATIVE RADIOTHERAPY AFTER RADICAL PROSTATECTOMY: A MONO-INSTITUTIONAL REPORT ON LONG-TERM OUTCOMES

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Introduction: Prostate cancer (PCa) patients submitted to radical prostatectomy (RP) may be treated with postoperative radiotherapy with adjuvant (aRT) or salvage modality (sRT), according to risk factors and post-operative PSA levels. Hypofractionation schemes in the post-operative setting are less reported in literature compared to the curative scenario. The aim of this study is to report the long-term outcomes of our series of patients treated with Image-guided hypofractionated post-operative RT using volumetric-modulated arc therapy (VMAT).

Material and Methods: From December 2012 to May 2018, 306 patients with PCa treated with RP with or without pelvic lymphadenectomy received aRT, sRT, or esRT. Mean age was 67 years (range 47-83). 160 patients with detectable PSA level were staged with choline (58%) or PSMA (42%) PET/CT. All patients were irradiated using VMAT technique on the prostatic bed as follows: 66 Gy/30 fractions or 67.5-71.4 Gy/30 fractions, in the case of aRT and sRT/esRT respectively. Pelvic lymph nodes were treated if pathologic (pN+) for a median total dose of 52.5 Gy (range, 50.4-54 Gy), in 28/30 fractions. Concomitant androgen deprivation therapy (ADT) was administered in 125 patients for a total duration of 6-24 months, according to risk factors. Acute genitourinary (GU) and gastrointestinal (GI) toxicities were scored according to the CTCAE v4.0. Progression-free survival (PFS) and overall survival (OS) were analysed. Prognostic factors were assessed.

Results: The median follow-up was 36 months. The 4-year OS was 94.8%. The 4-year PFS was 93.7%, 57.5%, and 77.5% for aRT esRT, and sRT, respectively (p= 0.013). The median ADT duration was 23 months for aRT, 23 months for esRT, and 22 months sRT, respectively. At the univariate analysis Gleason score ≥8 was predictive of the worst PFS (4-year PFS 85.4% versus 68.7%; p=0.003), like postoperative PSA level ≥0.5 ng/ml (4-year PFS 80.9% versus 59.4%; p=0.008). Acute GU toxicity was represented by 106 (34.6%) of G1 events, 62 (20.2%) G2, and 5 (1.6%) cases of G3 toxicity, consisting of 3 cases of urinary urgency and 2 cases of bladder incontinence. GI toxicity was mild with 10 cases of G2 proctitis. No late severe toxicity occurred.

Conclusions: Image-guided hypofractionated post-operative radiotherapy using VMAT is feasible and showed acceptable tolerability and limited severe toxicity. PFS was found to be predicted by Gleason Score ≥8 and pre-RT PSA≥0.5 ng/ml. The identification of predictive factors may help to personalize the treatment and increase disease control in the long-term follow-up.

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ACTIVE SURVEILLANCE: MONOINSTITUTIONAL CASISTIC

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Aims: Active surveillance (AS) represents one of the options offered to patients (pts) affected by low-risk prostatic carcinoma. Compared to radiation therapy (RT) or surgery, AS guarantees a similar risk of metastatic spread and mortality and offers the advantage of a better quality of life, ensuring at the same time the possibility to switch timely to an active therapy. Recently, the use of AS in the management of selected cases of intermediate risk prostate cancers has been evaluated. We report here the results of the program of AS that was started in 2008 at our general Hospital.

Methods: Clinical data of 113 men with a histological diagnosis of prostate cancer recruited for AS at our center from 2006 to 2019 were retrospectively analyzed. Most of the study population included low risk prostate cancer (GS ≤ 6, PSA< 10 ng/ml, cT≤2a). In the last 3 years we decided to include also some intermediate risk pts who presented with "limited disease": PSA level between 10 and 20 ng/ml and GPS 3+4 in only 1 biopsy core. Pts aged >80 years were also included. Follow-up schedule was: PSA examination was prescribed every 3 months and clinical evaluation every 6 months in the first two years, afterwards they were

repeated every 6 months. Biopsies were repeated after 18-24 months and then based on PSA doubling time. After the introduction of MRI PIRADS criteria, biopsies were repeated only if MRI PI-RADS score was ≥ 4/5. Drop out reasons included upgrading (GS > 6) or upsizing (> 3 positive cores) at biopsy, or lesions PIRADS ≥ 4 which for any reason could not be confirmed with biopsy.

Results: Median age was 72 years (49-84), median PSA was 5.9 ng/ml (range 0.25-15.95), 48 pts (42%) had at least 2 positive samples at biopsy. Median time on AS is 35 months (2-163). 47 pts (42%) dropped out: 32 (28%) were switched to active treatment, 2 dropped out for other reasons and 13 pts were lost to follow-up. Of 32 pts who were switched to active treatment, 4 received surgery, 24 were treated with RT, 1 received hormone therapy and 3 underwent treatment elsewhere. Among pts treated with RT, 12 were submitted to stereotactic therapy (36.25 Gy in 5 fractions) and 12 received conventional treatment (72-76 Gy in 36-38 fractions).

Conclusions: AS is a safe approach to men diagnosed with low risk prostate cancer and highly motivated to avoid treatment related morbidity. Intermediate risk patients should be carefully selected in order to include only those affected by indolent disease.

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CURATIVE RADIATION THERAPY OUTCOMES OF MUSCLE-INVASIVE BLADDER CANCER PATIENTS: OUR EXPERIENCE

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Aims: To evaluate the clinical outcome and toxicity of muscle-invasive bladder cancer (MIBC) patients treated with curative radiation therapy (RT).

Methods: We retrospectively reviewed MIBC patients submitted to RT with curative intent with or without chemotherapy from April 2013 to June 2020. All patients previously received trans urethral resection of the bladder (TURB) and refused or were defined unfit for radical cystectomy. The genitourinary and gastrointestinal toxicities were evaluated according to the RTOG/EORTC radiation morbidity scoring scheme.

Results: We selected 36 patients (33 males, 3 females) with a median age of 83 years (range 54-90). All patients received TURB before RT. 10/36 patients had a stage cT1N0M0 disease (7 G2 and 3 G3) and 23/36 had a stage cT2N0M0 disease (5 G2, 17 G3, and 1 unknown), whereas for 3 patients the disease stage was unknown. Eight of thirty-six patients (22.2%) received chemotherapy consisting of a local chemotherapy instillation in 4 of them (11.1%), a concomitant radio-chemotherapy (Carboplatin AUC2 weekly) in 3 of them (8.3%) and a sequential chemotherapy in 1 of them (2.7%). The median RT dose delivered was 60Gy (range 29.1-69.6 Gy). 94.4% of the patients completed the planned treatment, while two patients interrupted the course at 36Gy and 54Gy respectively because of unacceptable loco-regional toxicities. With a median follow-up of 17 months (range 1-64 months), 36.1% of the patients showed a complete response whereas two patients were submitted to radical cystectomy due to a local recurrence of disease respectively at 6 and 18 months after RT. The genitourinary acute toxicities occurred in our sample were G1 in 11/36, G2 in 8/36, G3 in 6/36 and G4 in 2/36; 9 patients did not experience any kind of toxicity. The gastrointestinal acute toxicities were low and have been observed in 4/36 patients. No significant late toxicities have been observed.

Conclusions: Curative RT is well tolerated by MIBC patients so that it can be considered an excellent therapeutic option with or without chemotherapy especially in patients who refused cystectomy or considered unfit for surgery due to their comorbidities.

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NEW TECHNOLOGIES FEASIBILITY FOR PROSTATE IRRADIATION: BEST OR NOT?

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Aims: Significant technological advances in radiation therapy (RT) allowed escalating dose to target volumes and reducing Organs at risk (OARs) toxicity. Aim of this work was to compare severe genitourinary (GU) and gastrointestinal (GI) toxicity of prostate cancer (PC) patients treated by Magnetic Resonance-guided Radiation Therapy (MRgRT) with an historic sample of patients treated through Volumetric Modulated Arc Therapy (VMAT).

Methods: Data from intermediate- and high-risk PC patients, according to National Comprehensive Cancer Network (NCCN) risk group, was collected. All patients received a MRgRT treatment on a low tesla hybrid unit (MRIdian, ViewRay Inc., Mountain View, CA). All patients were instructed to execute a daily enema and to drink 500cc of water half an hour before planning and each delivery fraction, to a better repro-

ducibility of bladder and rectal volume. Clinical Target volume (CTV) was defined as Prostate plus/minus seminal vesicles in high risk or proximal part of seminal vesicles in intermediate risk and pelvic lymph nodes for high risk PC patients; CTV to Planning Target Volume (PTV) expansion was 5 mm in all directions. Daily treatment set-up controls were performed using a 25 seconds true fast imaging with steady-state free precession (TRUFI) Magnetic Resonance (MR). Online tracking, adding a 3 mm boundary to GTV, was performed to ensure target coverage and OARs avoidance. This series of patients was compared with a historic comparable sample treated by VMAT on a cone beam computed tomography (CBCT) Linac. Acute and Late severe GU and GI toxicity were collected through the Common Terminology Criteria for Adverse Events CTCAE v4.0.

Table 1. Percentage of patients with acute or late genitourinary (GU) and gastrointestinal (GI) toxicity

	GU TOXICITY				GI TOXICITY			
	ACUTE		LATE		ACUTE		LATE	
Toxicity Grade	MRgRT series	VMAT series	MRgRT series	VMAT series	MRgRT series	VMAT series	MRgRT series	VMAT series
G3	0%	2.63%	0%	5.26%	0%	7.9%	0%	2.63%
G4	0%	0%	0%	0%	0%	0%	0%	0%

Results: From August 2017 to November 2019, 38 patients, treated by MRgRT, with a median age 72 years (range 53-86) were analyzed. Data was compared with a comparable sample of patients, treated between July 2007 and May 2016 (mean age 75 years – range 65-82). The two groups were homogeneous in staging (range T2a-T3b) and dosage (67.5Gy-80Gy). In VMAT series, G3 acute GU toxicity was observed in 2.63% patients and G3 acute GI toxicity in 7.9%. Late GU toxicity was G3 in 5.26% patients, while G3 late GI toxicity was found in 2.63% patients. No G3 or G4 toxicities have been observed in MRgRT series (Table 1).

Conclusions: Our analysis shows that MRgRT is related with low rates of severe GU and GI acute and late toxicity in PC patients, making this a feasible technique even in long course treatment, despite the delivery time. Further analysis and larger series are needed to confirm these encouraging data.

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THE ROLE OF IMMUNOSUPPRESSION THERAPY DURING RADIOTHERAPY IN KIDNEY TRANSPLANT PATIENTS: RESULTS OF A SYSTEMATIC REVIEW AND A CONSENSUS CONFERENCE

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Aim: Immunosuppression (IS) may contribute to cancer development and some authors propose to reduce it in presence of viral or IS-related aetiology and in patients undergoing radiotherapy (RT). The present abstract reports the results from a systematic review and a consensus conference session dedicated to this topic.

Methods: A consensus conference was carried-out based on the guidelines by the Italian Istituto Superiore di Sanità. An Organizing Committee, a Scientific Committee, a Work Group and an Expert Panel (EP) were involved in a five-step process including literature systematic review, collection of expert's opinion, conference discussion, voting procedure and results communication. The systematic review was conducted by defining a PICO model (population, intervention, comparator, outcome), a specific search strategy applied on electronic databases (PUBMED, Web of Science and Scopus), following PRISMA statement guideline. Finally, the EP vote was collected following a 2-round voting procedure, asking the members to express their vote according to a 10-point agreement scale. The statement was: "Withdrawing antimetabolites and/or CNI inhibitors and/or mTOR-inhibitors, as opposed to continuing maintenance immunosuppression, improves patient survival in kidney transplant recipients with cancer during standard RT". The agreement or disagreement were strong if they reached 75% or more, and moderate between 51% and 74% (percentage of experts voting the same number-on-the-scale).

Results: The literature search strategy resulted in 566 single citations. After literature screening, 61 records were identified for full-text evaluation. Out of these, 50 were excluded and 9 full text were considered

eligible and were included in final results analysis. There is still no clear evidence that withdrawing antimetabolites and/or CNI inhibitors and/or mTOR-inhibitors as opposed to continuing maintenance IS improves patient survival in kidney transplant recipients with cancer undergoing RT. There are few retrospective studies on small cancer patients cohorts undergoing RT without comparison of different IS treatments and whenever the IS drugs are reported patient survival seems to correlate with stage or type of cancer. The 23.8% of the voting experts assigned ≥7 points, 14.3% assigned 4-6 points and 61.9% assigned ≤3 points. Therefore, a moderate disagreement with the statement was found.

Conclusion: The results of the systematic review do not support the statement and the consensus conference showed a disagreement regarding the withdrawing IS-therapy in kidney transplant recipients with cancer undergoing radiotherapy

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PELVIC RADIOTHERAPY MANAGEMENT IN KIDNEY TRANSPLANT PATIENTS: RESULTS OF A SYSTEMATIC REVIEW AND A CONSENSUS CONFERENCE.

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Aim: The present abstract reports the results of a systematic review and a consensus conference session dedicated to pelvic radiotherapy (RT) management in kidney transplant patients.

Methods: A consensus conference was carried-out based on the guidelines by the Italian Istituto Superiore di Sanità. An Organizing Committee, a Scientific Committee, a Work Group and an Expert Panel (EP) were involved in a five-step process including literature systematic review, collection of expert's opinion, conference discussion, voting procedure and results communication. The systematic review was conducted by defining a PICO model (population, intervention, comparator, outcome), a specific search strategy applied on electronic databases (PUBMED, Web of Science and Scopus), following PRISMA statement guideline. Finally, the EP vote was collected following a 2-round voting procedure, asking the members to express their vote according to a 10-point agreement scale. The statement was: "Kidney transplant patients with cancer should avoid standard RT technique (external beam RT (EBRT), interventional RT (IRT), stereotactic RT, protons), dose on normal tissues and volume in order to preserve the transplanted kidney." The agreement or disagreement were strong if they reached 75% or more, and moderate between 51% and 74% (percentage of experts voting the same number-on-the-scale).

Results: The literature search strategy resulted in 566 single citations. After literature screening and full-text evaluation, 11 papers were considered eligible and were included in final analysis. The median RT total dose for EBRT was 75 Gy (range 60-76Gy). For IRT all studies reported a total dose of 145 Gy. In six studies (54%) no graft rejection was reported. The max dose to preserve transplanted-kidney was reported in one study (10 Gy). Six studies suggested to reduce the target volume in order to avoid side effects such as graft damage, ureteral stenosis or radiation cystopathy. Intensity modulated RT (IMRT) and IRT are reported as good options treatment in patients with localized cancer. The 57.2% of the voting experts assigned ≥7 points, 28.6% assigned 4-6 points and 14.3% assigned ≤3 points. Therefore, a moderate agreement with the statement was found.

Conclusion: The results of the systematic review do not support the statement and the consensus conference showed a moderate agreement regarding the reduction of RT target volume in order to preserve the transplanted kidney.

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THE ROLE OF FOCAL APPROACH AS ALTERNATIVE TO NEPHRON-SPARING SURGERY IN THE TREATMENT OF STAGE I KIDNEY CANCER: RESULTS OF A SYSTEMATIC REVIEW AND A CONSENSUS CONFERENCE.

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Aim: Transplanted patients are followed-up very frequently and, therefore, it is easier to diagnose a renal cancer in T1a stage. Some patients might not be eligible for surgery (comorbidities, tumour site or histology) and are most likely to benefit from an interventional approach, which are of great efficacy in small lesions. The present abstract reports the results and discussion from the conference session dedicated to this topic.

Methods: A consensus conference was carried-out based on the guidelines by the Italian Istituto Superiore di Sanità. An Organizing Committee, a Scientific Committee, a Work Group and an Expert Panel (EP) were involved in a five-step process including literature systematic review, collection of expert's opinion, conference discussion, voting procedure and results communication. The systematic review was conducted by defining a PICO model (population, intervention, comparator, outcome), a specific search strategy applied on electronic databases (PUBMED, Web of Science and Scopus), following PRISMA statement guideline. Finally, the EP vote was collected following a 2-round voting procedure, asking the members to express their vote according to a 10-point agreement scale. The statement was: "In case of cancer below 4 cm of the transplanted kidney, focal treatment (thermoablation, radiofrequency, brachytherapy, electrochemotherapy, cryoablation, stereobody radiotherapy, protons) is a valid alternative to nephron sparing surgery". The agreement or disagreement were strong if they reached 75% or more, and moderate between 51% and 74% (percentage of experts voting the same number-on-the-scale).

Results: The literature search strategy resulted in 331 single citations. After literature screening, and full-text evaluation 21 paper were considered eligible and were included in results analysis. The analysed studies showed that ablative therapy had a good local control and no influence on renal graft function and conservative treatment has been preferred each time it was feasible in order to avoid a return to dialysis. The 85.7% of the voting experts assigned ≥7 points, no experts (0%) assigned 4-6 points and 14.3% assigned ≤3 points. Therefore, a strong agreement with the statement was found.

Conclusion: The results of the systematic review support the statement and the consensus conference showed a strong agreement regarding the use of focal treatment as alternative to nephron sparing surgery.

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ACUTE AND LATE TOXICITY WITH EBRT+SIB INSTEAD OF EBRT+BT IN THE ADJUVANT TREATMENT OF GYNECOLOGICAL TUMOR: A MONOINSTITUTIONAL EXPERIENCE

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Aims: The aim of this study is to evaluate the toxicity of pelvic adjuvant treatment in gynecological cancer using SIB on the vaginal cuff over 25 fraction (5000 cGy to all the pelvis and 5750 cGy localized on the upper two third of the vagina) instead the classical sequential brachytherapy for logistic reason.

Methods: From September 2015 to April 2020, 57 patients underwent Adjuvant Radiotherapy for gynecological cancer (10 after surgery for cervical cancer and 47 for endometrial). The average age was 64 years (range 33-84); all patients underwent radical surgery with a pathological stage from FIGO IA (G3) to IIIC; 31 patients underwent adjuvant Chemotherapy. CT simulation was performed with patients in supine position using knee-ankle immobilization Combifix system, with a vaginal referee. The CTV-pelvis included common iliac nodes, pre-sacral nodes, external and internal iliac nodes, obturator lymph nodes; the CTV-SIB corresponded to the upper two third of the vagina. All OaRs including bladder, anus, rectum, sigmoid, bowel bag, right and left femoral head and neck were contoured. According to NCCN guidelines the dose was 5000 cGy among 25 fractions to the whole CTV-pelvis plus a SIB, with VMAT/IGRT technique, to the vaginal cuff of 5750 cGy in 25 fractions. Boost dose was calculated in order to deliver to vaginal cuff an EQD2 of about 6000 cGy and a BED of about 5900 cGy, using $\alpha/\beta=10$ for tumor and $\alpha/\beta=3$ for the OaRs. This schedule derives from the absence of the Brachytherapy into our Department and the need to ensure a complete treatment to our patients.

Table 1. Acute and Late toxicity.

RTOG/CTCAE	GI ACUTE TOXICY	GU ACUTE TOXICITY	GI LATE TOXICITY	GU LATE TOXICITY
G0	21 pts	28 pts	42 pts	38 pts
G1	25 pts	8 pts	0 pts	1 pts
G2	26 pts	17 pts	1 pts	1 pts
G3	5 pts	4 pts	0 pts	3 pts

Results: Acute and late toxicity were evaluated according to the RTOG and CTCAE scale (table 1). No patients had to interrupt the treatment for severe acute toxicity; all symptoms were treated with local or systemic drugs with resolution or improvement of them. After treatment 6 patients dies, only one for tumor metastasis; 7 patients completed the EBRT during the last six months and 5 were loose at the follow up. The late toxicity was evaluated above 43 patients (Table 1); only 1 patient actually alive has progression disease.

Conclusion: EBRT with SIB to the vaginal cuff in the Adjuvant treatment for endometrial and cervical cancer have acceptable acute toxicity and allows us to treat our patients without send them to other Radiotherapy center for Brachytherapy, with a better compliance.

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RADIOCHEMOTHERAPY IN CERVIX CANCER AND SEVERE PSORIASIS: A CASE REPORT

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Aims: To report a case of patient with a history of psoriasis treated with radiochemotherapy for cervical cancer.

Methods: A 53 years old woman with a history of psoriasis since 1992 developed cT2b cN1 cervical cancer. The patient was taking methotrexate therapy for severe psoriasis, which was suspended to administer neoadjuvant chemotherapy. For worsening psoriasis, retinoid therapy (Acitretin) has been started. The patient underwent VMAT radiotherapy with radical intent for a total dose of 52.5 Gy on the pelvic lymph nodes and 50 Gy on the uterus, vagina and cervix, respectively. Since brachytherapy boost could not be performed due to fibrosis and stenosis of the cervical canal, a dose-escalation on the small pelvis was obtained with external beams up to a dose of 60 Gy, by adding 5 more fractions of 2 Gy each. No radiosensitizing chemotherapy has been administered due to psoriasis. Acute toxicity was assessed with CTCAE v.5.0.scale.

Results: The patient experienced a mild gastrointestinal and urogenital toxicity (G1) and grade 2 cutaneous toxicity. Unexpectedly, we did not observe severe skin toxicity with the use of retinoids. Retinoid therapy has partially controlled skin symptoms and arthritic pain in the hands, but psoriasis has progressively worsened and the patient resumed methotrexate therapy as soon as she completed the radiotherapy course. She was re-evaluated 3 months after the end of the radiation treatment only with CT (she refused 18-FDG PET and MRI for claustrophobia), that showed a complete disease response.

Conclusion: This patient with severe psoriasis with the need for systemic therapy (methotrexate), completed the curative radiochemotherapy for cervix cancer with the support of retinoid therapy with moderate toxicity, especially at skin level.

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RADICAL PELVIC RADIOTHERAPY ALONE IN STAGE III VAGINAL CARCINOMA: A CASE REPORT

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Aims: To report on the effectiveness of radiotherapy alone in vaginal cancer with lymph node metastases in a patient with neutropenia secondary to antiepileptic therapy.

Methods: A 51 years old woman was referred to our Radiotherapy Department for a vaginal carcinoma cT2 cN1 (bilateral iliac and left obturator nodes, maximum diameter 45 mm). A chemotherapy treatment was contraindicated due to neutropenia, caused by antiepileptic therapy with lamotrigine. The patient underwent external beam radiotherapy alone. Dose to the pelvic lymph nodes was 58.8 Gy and 50.4 Gy to the vagina and uterus. To improve the efficacy of the therapy and to reduce the dose to the organs at risk (OARs) the VMAT technique has been adopted with daily control with cone beam CT. Subsequently, the patient was submitted to a vaginal brachytherapy for a boost dose of 15 Gy in 3 fractions. Acute toxicity was assessed with CTCAE v.5.0 scale.

Results: The patient experienced only a mild (G1) gastrointestinal and urogenital acute toxicity. However the treatment was interrupted for two weeks due to further worsening of neutropenia, although febrile neutropenia was not documented. The patient was re-evaluated 3 months after the end of the radiation treatment with 18F-FDG PET CT that showed a complete disease response, both for lymph nodes and vaginal tumor. Nine months after radiation treatment, the patient developed a recurrence in the left supraclavicular lymph node. Due to persistent neutropenia, chemotherapy could not be administered and the patient underwent curative radiotherapy, for a total dose of 54 Gy in 27 fractions. The patient is alive 18 months after the diagnosis of vaginal carcinoma and currently asymptomatic.

Conclusion: This patient with vaginal carcinoma developed progressive neutropenia from the start of antiepileptic therapy which prevented the possibility of administering a chemotherapy before and during the radiation course. Although radiotherapy was delivered alone, the use of advanced techniques such as VMAT and brachytherapy, led to a complete and durable remission of the pelvic disease with an acceptable toxicity profile. The absence of systemic treatment did not control the development of distant disease.

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PALLIATIVE HYPOFRACTIONATED RADIOTHERAPY IN ELDERLY FRAIL PATIENTS WITH VULVAR SQUAMOUS CANCER: A MONOINSTITUTIONAL EXPERIENCE

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Aims: Vulvar cancer is an uncommon gynecologic tumor, typical of elderly women; squamous cell carcinoma represents more than the 90% of cases. The treatment is mainly surgical but chemoradiation or radiation

only is an effective alternative in advanced disease or in unfit patients for surgery due to comorbidities. Aim of this retrospective study was to evaluate efficacy and toxicity profile of a palliative hypofractionated radiotherapy schedule (39 Gy in 13 fractions) in elderly frail patients with vulvar cancer.

Methods: Between June 2014 and October 2019, 22 elderly patients with histological diagnosis of squamous vulvar cancer unfit for surgery were consecutively treated at the Radiotherapy Department of National Cancer Institute in Milan. Thirteen of 22 patients with comorbidities (cardiovascular 46%, oncological 38%, diabetic 20%), performance status ≥2 (ECOG scale) and a G8 score ≤ 9.5, after a multidisciplinary evaluation have been proposed for palliative radiotherapy. Radiation treatment was delivered according to a schedule of 39 Gy in 13 fractions (3 Gy/fx) to the primary tumor and loco-regional nodes. Only two patients had concurrent radiosensitizing platinum based chemotherapy. The most common symptoms before the treatment were itch, pain and bleeding.

Results: Thirteen patients with vulvar cancer were considered for the study. Median age was 83 (range 67-93). All patients completed the treatment without interruptions. Median OS was 12.5 months (range 6-30); median PFS was 4 months (range 2-26). The most common site of relapse was loco-regional (46%). According to CTCAE4.02 score, acute genitourinary toxicity was G1-G2 in 53%, gastrointestinal toxicity was G1- G2 in 13% and skin toxicity was G1- G2 in 76% of the patients. There were neither G3 nor G4 toxicities. Two months after the end of the treatment all patients had a complete resolution of the pre treatment symptoms.

Conclusions: Our analysis confirms that this protocol is well tolerated by elderly frail vulvar cancer patients and provides a good palliation of itch, pain and bleeding improving in this way the quality of life, which is the primary end point in this setting of patients.

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RADIOMICS PREDICTS CLINICAL OUTCOME IN FIGO STAGE IB2-IVA CERVICAL CANCER TREATED WITH EXCLUSIVE CHEMO-RADIOTHERAPY

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Aims: The aim of this study was to analyze radiomic nomogram, using MRI images, that includes radiomics and clinical parameters for predicting the patterns of recurrence and the clinical outcome of patients with locally advanced cervical cancer (LACC) treated with exclusive chemo-radiotherapy.

Methods: We analyzed radiomic features from MRI images performed before and after treatment in 60 women (median age of 54 years), affected by FIGO Stage IB2-IVA cervical cancer, underwent definitive radio-chemotherapy 45-50.4Gy (in 25-28 fractions).Thirty-nine (65.0%) received also (4-20Gy) EBRT sequential or concomitant boost on primary tumor site and 56 (93.3%) received (6-28Gy) HDR-BT boost (daily fractions of 5-7Gy). Moreover, 71.7% of patients received dose-dense NACT consisted of TAX (80 mg/m2) plus CBDCA AUC 2 every week for 6cycles and 85.0% of patients weekly concurrent 40 mg/m2 cisplatin. The GTV(Gross Tumor Volume) was defined on T2-weighted sequences features extracted using a dedicated software and their prognostic value was correlated with clinical information. T-test was used to compare features with progression and survival. Multivariate analysis based on binary logistic regression by step-wise method was used to detect predictors of dependent variables Significance was fixed at 0.05.

Results: In univariate analysis, after a median follow-up of 28 months (range, 6-84months), age ≥ 60 years and FIGO stage IB2-IIB were significantly associated with better PFS (p=0.022 and p=0.009, respectively). There was a trend for significance for worse OS in patients with positive nodes (p=0.062). In multivariate analysis, only age and FIGO stage IB2-IIB reached statistical significance for better PFS (p=0.031 and p=0.011 respectively) and lymph node involvement (p=0.023) for worse OS. Neoadjuvant or concomitant chemotherapy gave no significant vantages. Moreover, twenty-nine features were extracted from each T2-weighed MRI images performed before and after treatment. In multivariate analysis, the feature PRE Gray Level p75 was significantly associated with PFS (p=0.047), PRE D3D Value with OS (p=0.049) and PRE Information Measure Of Correlation1Value with LC (p=0.031).

Conclusions: Our results suggest that radiomics constitutes a great promise to use quantifiable imaging characteristics to predict the behavior and the prognosis of LACC but further research in MRI-based radiomics are required to validate the use of reproducible features in prognostic models.

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LOBULAR CARCINOMA OF THE BREAST WITH METASTASIS TO THE UTERINE CERVIX: A CASE REPORT

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Aims: The uterine cervix is an uncommon site for

metastasis and the frequency is approximately 4% for all tumours. However, the frequency of cervical metastasis of breast cancer is much lower and is estimated to range between 0.8 and 1.7%. The objective of the current study was to report a clinical case considered rare in literature, as well as discuss its implications and peculiarities.

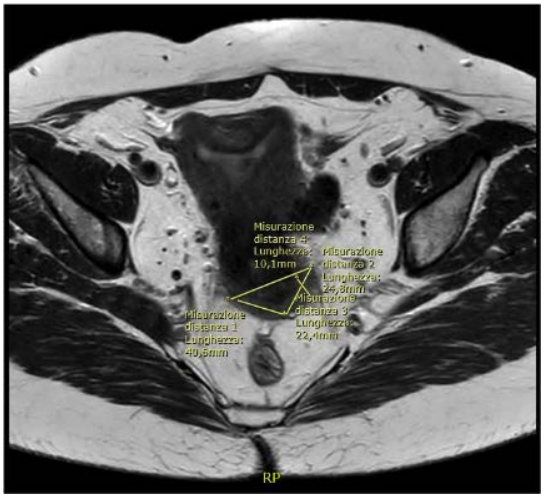

Figure 1. T2W_TSE_HR.

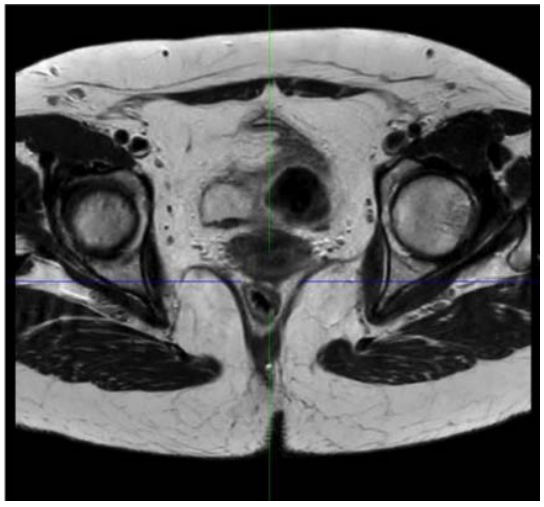

Figure 2. T2W_TSE_HR.

Methods: A 54-year-old female sex, patient was diagnosed with Grade-2 lobular carcinoma of the left and right breast 9 years ago and underwent mastectomy with dissection of axillary lymph nodes. The tumor stage was: pT2(m),pN3a,M0 on the left and pT3(m),pN3a,M0 on the right. Immunohistochemistry (IHC) revealed that the tumor was: estrogen-receptor positive (ER) (40%), progesterone-receptor positive (PR) (70%), human epidermal growth factor receptor-2 (HER-2-receptor) negative (1+), ki-67 (15%), CK5 negative, Topisomerasi II Alpha positive (15%) and p53 focal positive (30%) on the left and ER positive (40%), PR positive (60%), HER-2-receptor negative (1+), ki-67 (15%), CK5 negative, Topisomerasi II Alpha positive (10%) and p53 focal positive (10%) on the right. After the patient was treated with chemotherapy, radiotherapy and hormonal therapy. During follow-up the patient had abnormal uterine bleeding and underwent computed tomography and magnetic resonance imaging that showed a cervical tumor 4 x 1 cm with parametrial involvement and extension into the vaginal fornix (Figures 1-2). Pathology analysis shown that the sample was compatible with metastatic breast carcinoma. On IHC, the tumor was GATA 3 positive, cadherin-negative, ER positive (90%), PR positive (70%), Ki-67 (15%)%), HER-2-receptor negative (1+). Treatment with chemotherapy was started and after the patient underwent radiotherapy at the dose of 45 Gy to gross disease, parametria, and uterosacral ligaments and boost of an additional 5 Gy to gross disease.

Results and conclusions: The distinction between metastatic and primary carcinoma is crucial for the therapeutic definition. IHC is crucial for differentiating primary cervical malignancy from the metastatic cervical malignancy. In conclusion, we would recommended to maintain a high index of suspicion in all women with a history on breast cancers, and metastatic involvement of the female genital tract, including the cervix, should be considered when vaginal bleeding or an enlarged uterus is present.

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IMRT-VMAT VULVAR CANCER RADIOTHERAPY TREATMENT: A RETROSPECTIVE SINGLE-CENTER EXPERIENCE

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Aims: Radiotherapy treatment (RT) in vulvar cancer (VC) is a therapeutic option for advanced disease as

well as in the adjuvant setting. Intensity Modulated RT (IMRT) and Volumetric Modulated Arc Therapy (VMAT) enable more conformal dose distribution, delivering higher doses to the target and lower doses to organs at risk than 3D Conformal radiotherapy. We retrospectively analyzed clinical outcomes and toxicity in VC patients treated with these advanced techniques in our center.

Methods: Patients who underwent adjuvant or definitive RT (IMRT or VMAT) for VC in our institution have been included in the study. Toxicity, local control (LC), overall survival (OS), progression free survival (PFS) and pattern of recurrence were evaluated.

Results: A total of 29 patients were analyzed. Median age was 79 years (range 45-93). Most part of them were treated with IMRT, from 2016 to 2020. Adjuvant RT was delivered in 41.4% patients and definitive RT in 58.6%. RT dose to vulva ranged between 39.6–65 Gy and 45-65 Gy respectively; RT dose to inguinal nodes was 32.4-66 Gy and 32.4-66 Gy respectively. Moreover 51.7% of patients were treated for a recurrent VC. Most patients showed grade 2 (27.6%) or 3 (69%) of skin acute toxicity. Treatment was not completed in 6.9% of patients. Gastro-intestinal and genitourinary toxicities affected few patients, with low grades of intensity. Clinical outcomes were not satisfactory in these patients, above all in those treated for a recurrent disease. Total LC was 63.8% at 1-year and 43.1% at 2-year, with better results in the adjuvant setting (2-year LC 77.8%). As per OS, the difference between adjuvant e definitive RT was less evident, in fact 2-year OS was 42.3 and 32.4% respectively.

Conclusions: VC is a rare disease with the vast majority of evidences based on retrospective studies. Despite IMRT allows to enhance tumor control, our data suggests that in an elderly population it is not always possible to deliver a proper treatment with satisfactory clinical outcomes and recurrent disease still represent a complex challenge. Moreover, skin toxicity represent the major limit to deliver the high doses needed to eradicate the tumor.

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FACT-CX FOR LONG TERM QUALITY OF LIFE COMPARISON BETWEEN TWO DIFFERENT APPROACHES IN LOCALLY ADVANCED CERVICAL CANCER

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Aims: To compare Quality of Life (QoL) long term follow-up in 2 groups of locally advanced cervical cancer patients undergoing different approaches of curative treatments.

Methods: Patients who underwent pelvic chemoradiation followed by brachytherapy (eCRT) or radical surgery (nCRT) in two different radiotherapy departments with a follow-up ranging from 2 to 5 years were enrolled in a questionnaire-based study. QoL and bladder, intestinal, and sexual dysfunctions were evaluated with the Functional Assessment of Cancer Therapy-Cervix (FACT-Cx) consisting of the Functional Assessment of Cancer Therapy (FACT-G) plus a cervix cancer-specific subscale (CxCS), and the Trial Outcome Index (TOI).

Results: 50 patients filled out the 42-items questionnaire. Significant differences between the 2 groups were found in CxCS scores concerning morbidity and adverse events from treatments (p: 0.004), in FACT-Cx TOI scores concerning mainly changing in physical/functional outcomes (p: 0.017), and in FACT-Cx total score, a multidimensional aggregated score of physical, functional, social, emotional and cancer-specific status (p: 0.035) in favor of nCRT. Moreover, the item by item detailed comparison of each FACT-G and CxCS subscales resulted in some differences (nausea, feeling bad, closeness to partner, sleep, vaginal discharge, fear of treatments and appetite), all in favor of nCRT group. Conversely, no significant differences between brachytherapy boost and radical surgery were found concerning sexual function.

Conclusions: QoL scores measured by FACT-Cx questionnaire during a long-term follow-up period results clearly in favor of nCRT compared with eCRT treatment in locally advanced cervical cancer patients.

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SALVAGE EXTENDED NODAL RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST ON PET/CT POSITIVE LYMPH-NODES FOR RELAPSED GYNECOLOGIC TUMORS

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Aims: To report outcomes and toxicity of salvage extended nodal radiotherapy (ENRT) with simultaneous integrated boost (SIB) based on fluoro-deoxy-glucose positron emission tomography/computed tomography (PET/CT) positive lymph nodes in gynecological cancer patients (pts) with lymph-nodal (LN) recurrence.

Methods: From 03/2007 to 04/2020, 25 gynecological cancer patients with LN relapse after previous rad-

ical therapies were treated with salvage ENRT and SIB PET/CT-guided in our Institution. Primary tumor was: ovarian cancer for 11 pts, endometrial carcinoma for 9 pts, cervix carcinoma for 4 pts and vulvar carcinoma for 1 patient. A simulation PET/CT scan in treatment position was performed in 23/25 pts to identify the gross tumor volume PET (GTV-PET); in two pts GTV-PET was identified on diagnostic PET/CT. A 5 mm isometric margin was added to GTV-PET to obtain the planning target volume (PTV)-PET. Clinical target volume (CTV) included the lymph-nodal chain of interest: pelvic, para-aortic or mediastinal. A 7 mm isometric margin was added to CTV to obtain the PTV. The prescription dose to PTV was 50.4Gy/28 fractions. A SIB was prescribed to PTV-PET at mean dose of 61.01 (50.4-65.5)Gy. The treatment was delivered with TomoTherapy® (Accuray, Sunnyvale, CA) or RapidArc® (Varian Medical Systems, Palo Alto, CA). Daily set-up correction with MVCT and kVCT was performed.

Results: Median follow-up was 41.4 (2.7 – 123.4) months, in this period 16% of pts had local recurrences and 60% developed systemic progression. The 6 month follow-up PET/TC scans showed complete response in 76% of pts and partial response in 16% of pts. At the last follow-up 72% of pts were alive, while 28% were dead due to disease progression. Median disease free survival (DFS) was 27.1 (0.5-108.1) months. In one patient the metastatic disease was diagnosed during radiotherapy. Acute toxicities were: nausea- G1 in 40% of pts, G2 in 20% of pts; hematological toxicities- G2 lymphopenia in 4% of pts and G3 lymphopenia in 8% of pts, G1 anemia in 8% of pts; genital skin toxicity- 8% G1 and 4% G3 dermatitis of vulvar and inguinal region. No rectal toxicity was observed. Only few patients experienced a low grade late toxicity: 12% G1 nausea, 8% G1 lymphopenia, 4% G1 proctitis and 4% G1 vaginal dryness.

Conclusions: Salvage ENRT with SIB for PET/CT positive lymph-nodal relapse in gynecological cancers is feasible and ensures a good (84%) long- term local control, with negligible toxicity.

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MULTICHANNEL VERSUS SINGLE CHANNEL: COMPARISON DOSE DISTRIBUTION IN HIGH DOSE RATE BRACHYTHERAPY

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Aim: To retrospectively compare the potential dosimetric advantages of a multichannel vaginal applicator vs. a single channel one in intracavitary vaginal high-dose-rate (HDR) brachytherapy after hysterectomy.

Material and methods: We randomly selected ten patients median age 73 (IC95% 62-78) with endometrial carcinoma, who received adjuvant vaginal cuff HDR brachytherapy after hysterectomy, using multichannel vaginal applicator consisting of one central and 6 peripheral channels. The peripheral channels can produce an asymmetric dose distribution. The clinical target volume (CTV) as the organs at risk (OARs) were delineated on axial CT images for each patient and each brachytherapy fraction. A mean brachytherapy dose of 5.6 Gy/per fraction (5-7 Gy) was prescribed to CTV. Retrospectively for each patient, for two brachytherapy fractions, two treatment plans were created alternatively loading the central single or the multiple peripheral channels : the dose distributions of the rival plans were compared. For dose comparison, using a central channel, the lateral channels were de-activated, leaving only the central channel activated. All plans were optimized by using the same constraints: for CTV (5 mm expansion of the applicator surface) coverage: 95% of the volume receiving the dose prescription; dose to D2cc of bladder and dose to D2cc of rectum were limited to 80% and 75%,respectively, of the prescribed dose during plan optimization. Doses to 2 cc of OARs were statistically compared with paired t-Student test.

Results: Dose-volume-histogram (DVH) were analysed for OARs rectum and bladder at the same coverage of the CTV (D95 of CTV). Multichannel applicator provides a dose reduction, when compared to single channel, statistically significant for rectum with an average dose reduction at 2cc rectum = 0.27 Gy (4.65 vs 4.91 Gy) $p < 0.0001$ and an average percentage dose reduction at 2cc rectum = 4.65% Gy (82.55% vs 87.20%) $p < 0.0001$. On the other hand, bladder DVHs between multichannel and single channel were not statistically significant, with an average dose reduction at 2cc bladder = 0.05 Gy (3.82 vs 3.87 Gy) $p = 0.255$ and an average percentage dose reduction at 2cc bladder = 1.00% Gy (69.5% vs 70.5%) $p = 0.254$

Conclusions: Multichannel applicator provides dosimetric advantages over single channel, by reducing the dose to organs at risk especially in rectum, minimizing potential late rectal complications without compromising target coverage.

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MORPHOLOGICAL CHANGING ON T2-WEIGHTED IMAGES MRI AND RADIATION-INDUCED VAGINAL STENOSIS IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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Aims: Chemo-radiation therapy (CRT) is an important treatment modality for locally advanced cervical cancer (LACC). Vagina represents one of the organs at risk (OARs). In the setting of cervical cancer radiother-

apy (RT), a common side effect is vaginal stenosis, defined as morphological changing on MRI in length and tightening because of fibrosis after RT. Aim of this study was to analyze vagina morphological changes on early pelvic MRI that could be related to radiation-induced vaginal stenosis.

Methods: Patients with LACC treated with exclusive CRT in our Institute were retrospectively evaluated. MRI before radiotherapy (bMRI) and MRI after 4 weeks from the start of radiation treatment (4wMRI) were examined by radiologists for vagina morphological changes (width, length and signal alterations), analyzing T2-weighted (T2-W) images. Vaginal stenosis was clinically evaluated during follow-up by gynecological evaluation using CTCAE v4.03 scale toxicity.

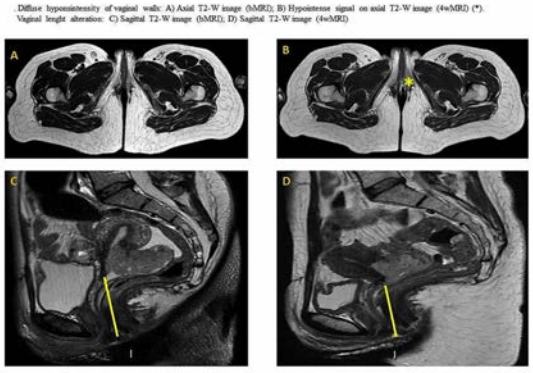

Figure 1.

Results: All the 14 examined patients were treated with IMRT/VMAT with a RT dose of 4500 cGy on the pelvis up to 5500 cGy (SIB on N+, 21.4%); sequential boost was administered in 14.3%, brachytherapy boost in 57.1%. Median age was 58 (range 34-85) and all the sample showed performance status (Karnofsky scale) of 80-100%. With a median follow-up of 10.5 months (range 3-33), clinical vaginal stenosis was reported in 10/14 patients (71.4%): vaginal stenosis ≥ Grade 2 was recorded for 7 patients (70.0%), Grade 1 for 3 patients. In 10/14 patients (71.4%) vagina morphological modifications were observed on T2-W images as below: 1) median width: bMRI = 29.0 mm (range 23.0 - 40.0) vs 4wMRI = 27.0 mm (range 20.0–35.0); 2) median length: bMRI = 50 mm (range 45-70) vs 4wMRI = 45 mm (range 36-60); 3) in all the same patients a diffuse hypointensity of vaginal wall on 4wMRI was detected. Vagina morphological alterations are represented in Figure 1.

Conclusions: Pelvic RT could be responsible of acute vaginal damage; indeed, in our experience, vagina morphological changes (width, length and signal alterations) on early compared to baseline T2-W images MRI were observed in patients with late vaginal stenosis. On the other hand, in literature, early morphological variations on T2-W images have not been confirmed as strong predictive parameters of radiation-induced side effects. Then, further analysis with functional imaging (DW-MRI) could support our data offerring an early prevention of radiation-induced vaginal stenosis.

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EARLY RADIATION-INDUCED MORPHOLOGICAL CHANGES OF ANAL SPHINCTER COMPLEX AND BLADDER NECK ON MAGNETIC RESONANCE IMAGING IN CERVICAL CANCER PATIENTS DURING RADIOTHERAPY

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Aims: Chemoradiotherapy is a standard of care in the treatment of locally advanced cervical cancer (LACC), but can induce pelvic sequelae that have an impact on the quality of life of patients. Radiotherapy can cause an inflammatory process responsible of early morphological changes and subsequent functional alterations of pelvic floor structures, correlated to the dose. The purpose of the study was to evaluate early radiological changes of anal sphincter complex and bladder neck, and to compare them with dosimetric parameters and clinical effects.

Methods: Fourteen patients with LACC treated in our Institute were analyzed. They all performed a Magnetic Resonance Imaging before RT and 4 weeks after the start of RT (4wMRI), to evaluate early treatment response. The anal sphincter complex and bladder neck were delineated on Simul-TC and reviewed by radiologist. Early radiological changes of these structure on 4wMRI were examined by the radiologist. Data were compared with toxicity and dosimetric parameters according to literature.

Results: Mean age was 58 years (34-85). All the patients were treated by VMAT with a total dose of 45Gy on pelvis, concomitant to cisplatin-based chemotherapy. A simultaneous boost (up to 55Gy) on nodes was executed in 6 cases. A sequential EBRT boost was prescribed in 24.4% of cases and a brachytherapy boost in 57%. Diffuse hypointensity on T2-weighted images of anal sphincter complex and bladder neck was found on 4wMRI in 57% and 35.7% of patients, respectively. Only 1 patient had a grade 1 acute genitourinary toxicity. The 35.7% of cases reported an acute low gastrointestinal toxicity, grade 2 (21.4%) or less (14.3%). Overall, none of the patients reported acute toxicity >3 (Table1). Dmax, Dmean and V40 for anal sphincters, and Dmax for bladder neck were considered. No correlation was found between dose received to structures and acute toxicity.

Conclusions: This preliminary data suggest that 4wMRI was useful to detect early radiological changes of sphincters and bladder neck during RT, but no clinical correlation with acute toxicity was found in our experience. Further analysis are necessary to investi-

gate the persistence of alterations in following radiological exams as predictive factor for late toxicity, and integration with qualitative tools like defecography could give more information about functionality. The identification of dosimetric parameters should be prospectically considered to preserve selected structures.

Table 1.

Dosimetric parameters, radiological changes and toxicity (RTOG Scale) in locally advanced cervical cancer patients (n=14)

Characteristics		*N (%)*
DOSIMETRIC PARAMETERS mean, (range)		
Anal sphincters	Dmax	4684 cGy (4564-4765)
	Dmean	2706 cGy (1560-3818)
	V40	30% (9-54)
Bladder neck	Dmax	4654 cGy (4532-4748)
RADIOLOGICAL CHANGES		
Anal sphincters	Yes	8 (57.1%)
	No	6 (42.9%)
Bladder neck	Yes	5 (35.7%)
	No	9 (64.3%)
LOW GASTROINTESTINAL ACUTE TOXICITY		
	Grade 0	3 (21.4%)
	Grade 1	7 (50%)
	Grade 2	4 (28.6%)
	Grade 3	0 (0%)
GENITOURINARY ACUTE TOXICITY		
	Grade 0	8 (57.1%)
	Grade 1	5 (35.8%)
	Grade 2	0 (0%)
	Grade 3	1 (7.1%)

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OUTCOMES OF HELICAL/VOLUMETRIC INTENSITY MODULATED RADIOTHERAPY IN PATIENTS WITH VULVAR CANCER

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Aims: To report outcomes and toxicities in vulvar cancer (VCa) pts treated with helical/volumetric IMRT in our Institute.

Methods: From 08/2006 to 05/2020, 25 VCa pts were treated. Histology was: squamous cell carcinoma in 22 pts, adenocarcinoma in 2 pts, and Paget's disease in 1 patient (pt). Median age was 75 (32-91)years, 76% of pts were older than 70 years. Thirteen pts (52%) underwent postoperative RT for FIGO stages: Tis 1 pt (8%), IB 4 pts (31%), IIIA 4 pts (31%), IIIC 3 pts (23%), and IVB 1 patient (7%). Surgical margins: R1 in 1 pt (8%), <1mm in 6 pts (46%), R0 in 6 pts (46%). Four pts (16%) underwent radical RT (equally distributed in FIGO stages IB, IIIA, IIIB, and IVB). Eight pts (32%) were treated with salvage RT on recurrences after surgery. Clinical tumor volume (CTV) was delineated on CT scan (48%) or PET/CT (52%) including vulva, inguinal and pelvic lymph nodes (LN). Median prescribed dose to PTV was 50.4 (45-62.5)Gy. Simultaneous integrated boost (SIB) was delivered in 13 pts to a median dose of 61.2 (58.8-64.5)Gy on positive PET LN or T. Ten pts received sequential boost: 4 with photons, 6 with electrons to a median dose of 14.4 (9-16)Gy. Three pts received concomitant cisplatin. RT was delivered with helical or volumetric IMRT and daily IGRT was performed.

Results: Median follow-up was 18 (2.4-95.4)months. Acute and late toxicities were graded according RTOG scale (see Table 1). Seven pts had a median of 8 (2-14)days of treatment interruption due to acute toxicity (4 pts with sequential boost, only 1 pt with SIB, 2 pts with concomitant CT). Local control, evaluated with PET/CT, was achieved in 54.5% of pts. Eight pts (36%) presented local relapse (4 vulvar and 4 LN) and 4 pts (18%) distant progression (LN and/or lung metastasis). Average time to local and distant progression were 9.4 and 10 mts respectively. Average overall survival (OS) was 29 mts. Pts treated with adjuvant RT had better outcomes with a median OS of 33.9 mts, followed by salvage RT with 28.3 mts. Radical RT OS was only 6.6 mts, but the median age of pts was 86.3 (79.5-90.2)years.

Conclusions: IMRT for VCa is feasible, SIB reduces the interruptions due to skin toxicity. All pts finished the prescribed treatment. A randomized study is needed to confirm toxicity reduction with SIB and better outcomes with adjuvant RT.

Table 1

	Acute Toxicity (%) 25 pts			Late Toxicity (%) 22 pts		
	G1	G2	G3	G1	G2	G3
Diarrhea	40	16	4	11	0	0
Proctitis	12	0	0	11	0	0
Erythema	8	16	76	23	14	11
Urinary	16	12	0	14	4	0
Haematologic	4	12	4	4	4	0

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A MONOINSTITUTIONAL EXPERIENCE ON VAGINAL CUFF VMAT-SBRT IN ENDOMETRIAL CANCER TREATMENT

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Aims: We investigated the feasibility of Stereotactic Body Radiotherapy (SBRT) delivered using Volumetric Arc Therapy (VMAT) as a boost on the vaginal cuff in patients (pts) with endometrial cancer who refused the Endocavitary Brachitherapy.

Methods: Seven pts affected by stage I and II endometrial cancer where selected for this study. All pts underwent post-operative RT to the whole pelvis (WP) with doses of 50 Gy in 25 fractions. After WP, a sequential boost on the vaginal cuff was delivered with VMAT-SBRT (15Gy/3 fractions on alternate days). The

combined biological effective dose delivered was 68.75 Gy (α/β=10). Pts were scanned with full bladder and empty rectum in supine position. A soft radiopaque transvaginal probe was used to define the vaginal cuff on CT scans. Clinical Target Volume (CTVc) included the vaginal cuff and the upper two-thirds of the vagina. The Planning Target Volume (PTVc) was created by isotropically expanding the CTVc of 3mm. Bladder, rectum, small bowel and femoral heads were contoured as Organs at risks (OARs). All SBRT plans were optimized on the basis of radiobiological cost functions in the Monaco planning system (v.5.11.03). Final Monte Carlo dose calculation was done with 1% statistical uncertainty and 0.1 cm grid. Dose was prescribed to the mean of PTVc. SBRT plans were evaluated according to ICRU 91 indices. Treatments were performed on an Elekta Versa HD linear accelerator and daily CBCT. Acute Genitourinary (GU) and Gastrointestinal (GI) Toxicities were assessed through RTOG/EORTC grading system criteria.

Results: Median CTVc coverage evaluated as D95% was 98,1% (range: 95.9%-99.1%) and Median PTVc coverage was 95.7% (range: 94.3%-97.9%). Median PTVc confomality index was 1.3 (1.1-1.4), while median PTVc D2% and D98% were 103.2% (range:102.5%-104.1%) and 95% (range:90.5%-97.1%). Median maximum voxel dose of the rectum, bladder, femoral heads and small bowel were 15.3Gy, 15.4 Gy, 5.7Gy and 15.3 Gy (range: 0.5-15.6Gy), respectively. For 4/7 pts, treatment was well tolerated with G0 GU and GI toxicities. Two pts had G1-G2 GI and 3/7 pts had G1-G2 GU toxicity.

Conclusions: A VMAT-SBRT sequential boost on the vaginal cuff following WP RT is feasible with a good profile in terms of acute toxicity. Given the short follow up, no data were available on late toxicities and tumor control: further investigation on this topic is ongoing at our Centre.

P223

CLINICAL OUTCOME FOR CT-GUIDED HIGH DOSE-RATE BRACHYTHERAPY IN WOMEN WITH LOCALLY ADVANCED CARCINOMA OF THE CERVIX (LACC)

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Aims: To evaluate the outcome and toxicity on LACC patients treated with radiochemotherapy and intracavitary brachyherapy.

Methods: This study includes 67 patients with LACC (range 29-83 years) treated between 2010 and 2018. The most represented stage was FIGO II B. The patients were consecutively treated with pelvic EBRT and boost to the cervix and parametrials, when indicated. Concomitant CHT with CDDP 40 mg/mq was planned. Subsequently, the patients underwent TC-based endouterine brachiterapy. The response was evaluated at 3 months with PET TC and/or pelvic RM with contrast medium. Since then the patients have been followed with clinical- instrumental controls every 4 months for the first 2 years and every 6 months for the following 3 years. Overall survival was defined from the diagnosis to the last follow-up and disease free survival from the complete response data to the relapse or/last follow-up. Outcome and acute toxicity (gastrointestinal and genitourinary within 6 month) were assessed for all these patients.

Results: The dose range of EBRT was 45-50.4 Gy. 42/67 underwent to boost with SIB to the cervix and parametrials up to 61.6-66 Gy . Concomitant CHT with CDDP 40 mg/mq was administred at 56/67 and all patients received intracavitary brachytherapy (dose range 10-28 Gy). We recorded 56/67 complete response. 11/67 showed a not respondent disease. We observed 9/67 relapses (one local and 8 sistemic) with a median DFS of 14 months (range 2-91 months). After a median follow up of 32 months (range 2-118 months). 39/67 patients were alive without disease. Twenty-two patients were dead (15 for disease and 7 for other causes in absence of cervical cancer). The evaluation of the toxicity according to RTOG scale showed G1 genitourinary complications in 22/67 patients and G2 in 5/67, while only one patient complained of G3 toxicity. Gastrointestinal toxicity occurred in 12/67 patients for G1 grade and in 6/67 patients for G2 grade. 9/67 patients showed both genito- urinary and gastrointestinal toxicity at different stages of severity.

Conclusions: Our study confirms the efficacy on local control of RTCHT and intracavitary brachitherapy with an acceptable toxicity profile.

P224

PROGNOSTIC ROLE OF EARLY FDG-PET/CT IN LOCALLY ADVANCED CERVICAL CARCINOMA PATIENTS (LACC): ONGOING STUDY

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Aims: To evaluate in patients with LACC the prognostic impact of FDG-PET/CT (early-PET) after exclusive chemoradiotherapy (CRT) and before intra-uterine brachitherapy

Methods: We included 23 pts with LACC (range 30-75 years) that referred to our institution between

2013 and 2019. Pts were treated with concomitant CRT and subsequent brachytherapy. FIGO STAGE: 1/23 were IIA, 12/23 IIB, 4/23 IIIB, 4/23 IIIC and 2/23 IVA. 9/23 pts had regional lymph node involvement and 2 pt had also positive lombo-aortic lymph nodes. 20/23 pts underwent radiotherapy and concomitant weekly chemotherapy with Cisplatin (40 mg/mq^2), 4 pts received neoadjuvant chemotherapy and 1 patients only radiotherapy. 19/23 pts were treated with IMRT technique and 17 of them received IMRT-SIB (2.2 Gy x 28 fractions on GTV-cervix and GTV-LNs PET-positive, 1.8 Gy x 28 fraction on pelvis ± LN para-aortics). The total brachytherapy dose was 21 or 28 Gy in 3-4 fractions, 7 Gy per fraction, with the aim to obtain a total dose (EBRT plus BT) in the range of 85-90 Gy (6 pt 28 Gy, 17 pt 21 Gy). All pts performed FDG-PET/CT after CRT and before brachytherapy (early-PET). PET images were rated as positive when there was focal uptake with a SUV max >3.

Results: At the end of CRT and before brachytherapy all pts performed early-PET: 14/23 were negative and 9/23 positive. - 2/14 (14.3%) pts with negative early-PET showed a progressive/relapse disease: 1 systemic (lung-bones) progressive disease and 1 cervical, annexial and nodal relapse after 9 months from the end of brachytherapy. - 5/9 pts (55%) with positive early PET-TC had progressive/relapse disease: 4 pts showed systemic (lung-bones) progressive disease and 1 pt showed nodal, cervical and bone relapse after 18 months from the end of brachytherapy.

Conclusions: Our preliminary results showed that early-PET before brachytherapy could have a predictive value in assessing the risk of recurrence/progression in LACC pts. Pts with positive early-PET may benefit from adjuvant systemic treatment.

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"SANDWICH" APPROACH IN ENDOMETRIAL CANCER PATIENTS: A MONOINSTITUTIONAL EXPERIENCE

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Aims: Endometrial Carcinoma (EC) is the most common gynecologic cancer in developed countries. The primary treatment option for stage III disease is surgery and adjuvant Chemo-Radiotherapy. The optimal sequence of administering Chemotherapy (CHT) and Radiotherapy (RT) remains controversial. The purpose of this retrospective study was to evaluate feasibility, efficacy and toxicity profile of administering Carboplatin and Paclitaxel Chemotherapy followed by pelvic Radiotherapy and subsequent consolidation Chemotherapy in the "Sandwich" approach.

Methods: Women with surgically stage III endometrial cancer, treated between May 2012 and March 2019 at the Radiotherapy Department of National Cancer Institute in Milan, were retrospectively analysed. Inclusion criteria were: ≥ 18 years of age with histologically confirmed International Federation of Gynecology and Obstetrics (FIGO) stage IIIA, IIIB and IIIC. All patients undergone hysterectomy, bilateral salpingo-oophorectomy and +/- bilateral pelvic/para-aortic lymph node dissection. Sandwich method consisted of 3 cycles of Paclitaxel (175 mg/m^2) and Carboplatin (AUC5) on a q21 day schedule followed by VMAT (range 45- 50.4 Gy) +/- BRT and three additional cycles of CHT.

Results: Twenty-nine patients with EC were considered for the study. Eight patients completed the treatment with a reduction in chemotherapy and three were treated only with Carboplatin due to allergic reaction to Paclitaxel or to co-morbidity. Median age was 62 (range 40-83). Overall Survival was 35 months (range 12-96), Progression Free Survival was 28 months (range 0-89) with a median follow-up of 28 months (range 4-89). Four patients (13%) experienced distant disease progression (two of them died), in one case (3.4%) was registered loco-regional recurrence, finally one patient had both local relapse and distant disease and she died due to progression. Treatment toxicities were assessed according to CTCAE 4.02 score: acute grade III gastrointestinal toxicity (GI) and genitourinary toxicity (GU) were 10% and 3.4% respectively; acute grade III-IV hematologic toxicities were 20% and 3.4% respectively. Both late grade III GI and GU toxicities were 3.4%.

Conclusions: Our study demonstrates that postoperative adjuvant CHT and RT according to Sandwich approach offers efficacy, acceptably low toxicity and should allow for maximum therapeutic dosing of both radiation and chemotherapy.

P226

EXCLUSIVE RADIOCHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER: EMERGENCY TREATMENT DURING THE COVID-19 PANDEMIC

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Aims: The COVID-19 pandemic had an impact on medical and personnel resources, and patient care access issues. Gemelli University Hospital is one of the larger COVID-19 referral Centre and one of the larger Oncological Centres. Given the lack of anaesthesiolo-

gists as they were engaged in intensive care units, and reduced availability of hospitalization, aim of this paper was to bring back our experience in resource allocation, clinical care and treatment delivery for cervical cancer patients, in the COVID-19 pandemic peak.

Method: Our institution drafted triage practical recommendations about treatment of cervical cancer patients during the COVID-19 pandemic. Patient's stratification and triage were performed before starting treatment. The aim was to achieve the best possible balance between the risk of cancer progression and the risk of infectious disease. Five patients were retrospectively analyzed. All patients had biopsy proven squamous carcinoma and were staged by pelvic MRI, CT-PET and clinic examination according to FIGO 2018 classification. All patients underwent a standard CT-based planning. The low risk clinical target volume (CTV) was treated with intensity modulated technique (VMAT/Rapidarc). A total dose of 45 Gy, 1.8 Gy/fraction was delivered. For positive lymph-nodes a boost was considered (55 Gy, 2.2 Gy/fraction). Weekly concomitant cisplatin was delivered (40mg/m^2/week). After one week, patients were replanned to treat intermediate-CTV (total dose of 14.4 Gy, 1.8 Gy/fraction) followed by Pulsed dose rate (PDR; total dose 34 Gy, 0.5 cGy/h) or High Dose Rate (HDR; total dose 14-21 Gy/2-3 fractions (2 times/week) interventional radiotherapy (IRT). Acute toxicity was assessment by Common Terminology Criteria for Adverse Events v.4 scoring criteria.ticecommendations

Results: Following internal recommendation, after a written informed consent, this treatment modality was proposed and accepted by 5 patients.. All patients completed their treatment. Only one G2 gastro-intestinal toxicity was reported. One patients developed a G3 hematologic toxicity completely recovered during the treatment of intermediate-CTV. Median interruption days were 1 (range 0-2). Chemotherapy compliance was 100%. No patients at the end of treatment showed COVID-19 symptoms.

Conclusion: In order to guarantee the optimal treatment to cervical cancer patients, we discussed how to manage the routinary activities in the new frame of COVID19, in the full absence of specific guidelines for cervical cancer management. A reflection was made on the literature data and on the clinical experience gained in Italy, the first of the western country massively involved after China.

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RETROSPECTIVE STUDY IN A SINGLE INSTITUTION ABOUT STEREOTACTIC RADIOTHERAPY IN BRAIN OLIGOMETASTASES FROM OVARIAN CANCER. PRELIMINARY DATA AND OUR EXPERIENCE.

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Aims: the aim of this study is to evaluate safety, efficacy and toxicity in brain oligometastases from ovarian cancer patients treated with SRS and FSRT.

Methods: this is a single institution retrospective study. We performed analysis of patients with brain oligometastases not susceptible to surgery and after systemic therapy. The types of treatment were in SRS and FSRT modalities with robotic arm Linac (Cyberknife System) to treat in frameless intracrianal target. The contour was manual on the target volum and OAR and we used MRI like co-registration in CT datasets to outline target volume. Follow-up was performed every three months with brain MRI for the first year and every six months thereafter.

Results: We treated in our Centre between 2008 and 2019 11 women and 21 target lesions. The median age was 52 years (range, 44-74). Median prescription dose for brain metastases was of 20Gy/1Fx (range, 16-21Gy) in SRS modality and 30Gy/5Fx in FSRT modality. Moreover the median GTV was 1cc (range 0.17-85) and the median BED 10 was 60 (range 41.6-70.84). One patient underwent surgical resection and 3 patients was administered re irradiation for recurrence. We have not observed G3 and G4 acute and late neuro-toxicities. The median follow-up was 39 months (range, 0-126), the median time to local progression was 24 months (range, 0-35) and the median OS was 15,6 (0-58). Progressive disease was observed in 4 (15%) brain targets. The pattern of failure was predominantly in the bigger lesions in terms of GTV volume size, biologically effective dose α/β <60 Gy and patients with age >60 years.

Conclusions: SRS and FSRT in oligometastatic ovarian patients with brain metastases is an altenative to surgery. Moreover it is a valid approach to maintain local control and delay second line of systemic therapy. It is more likely to apply to the smaller lesion with a BED 10> 60Gy.

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NEOADJUVANT CHEMORADIATION WITH SIMULTANEOUS INTEGRATED BOOST IN LOCALLY ADVANCED CERVICAL CANCER: A SINGLE-CENTER EXPERIENCE

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Aim: To analyze the efficacy and tolerability of intensity modulated radiation therapy (IMRT) simultaneous integrated boost (SIB) associated to cisplatin-based chemotherapy in preoperative setting for patients

with locally advanced cervical cancer.

Methods: Patients with locally advanced cervical cancer were selected for neoadjuvant intensity-modulated extended-field chemoradiation (CRT) plus simultaneous integrated boost. A radiation dose of 39.6 Gy, 1.8 Gy/fraction, was delivered to the pelvis plus a radiation dose to the primary tumor delivered with SIB-IMRT strategy for a total of 50.6 Gy, 2.3 Gy/fraction in 22 fractions. Cisplatin-based chemotherapy was associated to radiotherapy. Radical hysterectomy plus pelvic with or without aortic lymphadenectomy was performed within 6 to 8 weeks from CRT. Statistical analysis was performed using MedCalc software (www.medcalc.be).

Results: From April 2014 to April 2019, 146 patients (median age: 49 years) were enrolled. The 2018 International Federation of Gynecology and Obstetrics (FIGO) clinical stage were IB2(n=5), IIA(n=3), IIB(n=40), IIIA(n=2), IIIB(n=4), IIIC1(n=84), IIIC2(n=3), IVA(n=4), IVB for pelvic peritoneum involvement(n=1). The treatment was well tolerated with a good compliance: no patients had grade 3/4 gastrointestinal or genitourinary toxicity; grade 3 hematological toxicity was reported in 5 cases. pCR was documented in 69 cases (47.3%) and 32 patients (21.9%) had a microscopic residual disease (persistent tumor foci of 3 mm maximum dimension). Among them, eight patients (5.5%) had a pathological nodal involvement. With a median follow-up of 23 months (range: 4-63 months), the 1-year and 2-years local control were 92.7% and 76.1%, whereas the 1-year and 2-years overall survival rates were 99.2% and 96.3% respectively. In pR0 group, the 1-year and 2-years local control were 96.5% and 90.7% respectively with a 2-years overall survival of 100%. In pR1-2 group, the 1-year and 2-years local control were 89.9% and 63% respectively with a 2-years overall survival of 93.4%.

Conclusion: Neoadjuvant chemoradiation with simultaneous integrated boost results in a very encouraging local control rate with a high rate of pathologically assessed complete response and an acceptable toxicity, in according to literature data. Local control and overall survival will be further evaluated with a longer follow-up.

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EBRT WITH SIB TECNIQUE VERSUS EBRT WITH BRT IN THE ADJUVANT RADIATION TREATMENT FOR ENDOMETRIAL CANCER: ACUTE AND LATE TOXICITY IN A MULTICENTRIC RETROSPECTIVE STUDY

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Aims: To evaluate the different toxicity of pelvic adjuvant treatment in endometrial cancer using SIB on the vaginal cuff over 25 fractions versus the standard sequential brachytherapy.

Methods: From September 2015 to December 2019, 79 patients underwent Adjuvant Radiotherapy for endometrial cancer after radical surgery with a pathological stage from FIGO IA (G3) to IIIC: 40 pts underwent EBRT with SIB on the vaginal cuff at the Alessandria's Hospital (SIB Group) and 39 pts underwent EBRT and sequential Brachitherapy at IRCCS Candiolo (BRT Group). The average age was 65 years (range 40-84); 44 pts underwent adjuvant Chemotherapy, 20 in the SIB Group and 24 in the BRT Group. CT simulation was performed with pts in supine position using knee-ankle immobilization Combifix system, with a vaginal referee. The CTV-pelvis included common iliac nodes, pre-sacral nodes, external and internal iliac nodes, obturator lymph nodes; the CTV-SIB/BRT corresponded to the upper two third of the vagina. All OaRs were contoured: bladder, anus, rectum, sigmoid, bowel bag, right and left femoral head and neck. According to NCCN guidelines in the SIB Group, , the dose was 50Gy among 25 fractions to the whole CTV-pelvis plus a SIB, with VMAT/IGRT technique, to the vaginal cuff of 57,50Gy in 25 fractions, SIB dose was calculated in order to deliver to vaginal cuff an EQD2 of about 60Gy and a BED of about 59Gy (α/β=10 for tumor and α/β=3 for OaRs); in the BRT Group the dose was 45-54Gy among 25-30 fractions and sequential Brachitherapy with a dose of 10Gy delivered in 2 fractions.s.

Results: Acute and late toxicity were evaluated according to the RTOG and CTCAE vs 5 scale (table 1). No pts had to interrupted the treatment for severe acute toxicity. No acute or late toxicity higher than G2 were detected. All symptoms were treated with local or systemic drugs with benefit.

Conclusions: GU and GI acute and late toxicity in the two groups demonstrate similar tolerability, with no significant statistically differences (p>0.05), maybe due to the poor number of pts.

Table 1. Results of GU and GI acute and late toxicity in the two groups,

	SIB GROUP		BRT GROUP	
RTOG/CTCAE	GI ACUTE TOXICY	GU ACUTE TOXICITY	GI ACUTE TOXICITY	GU ACUTE TOXICITY
G0	21 (52%)	20 (50%)	23 (59%)	24 (59%)
G1	11 (28%)	12 (30%)	10 (26%)	10 (26%)
G2	8 (20%)	9 (20%)	6 (15%)	6 (15%)
G3	0	0	0	0
	GI LATE TOXICY	GU LATE TOXICITY	GI LATE TOXICITY	GU LATE TOXICITY
G0	40 (100%)	38 (96%)	38 (98%)	32 (82%)
G1	0	1 (2%)	1 (2%)	5 (13%)
G2	0	1 (2%)	0	2 (5%)
G3	0	0	0	0

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EVALUATION OF EARLY REGRESSION INDEX (ERI) AS PREDICTOR OF PATHOLOGICAL COMPLETE RESPONSE IN CERVICAL CANCER: A PILOT-STUDY

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Aims: Several experiences reported the advantage to use neo-adjuvant external beam radiotherapy followed by radical surgery care for locally advanced cervical cancer (LACC) patients, with the aim of removing the residual tumour foci resistant to the previous treatments. There is growing interest in identifying treatment response predictors to early identify poor responders and increase the prescribed dose accordingly, aiming to reduce the risk of disease persistence. Early Regression Index (ERI) is a radiobiological parameter that showed promising results in predicting pCR on T2-weighted 1.5T MR images of patients affected by rectal cancer, modelling early cancer regression combining tumour volumes obtained during treatment simulation (Vpre) and at mid therapy (Vmid): ERI= -ln[(1-(V_mid/V_pre))^(V_pre)] In this study we aim to validate ERI in predicting pCR in the context of low tesla MR guided Radiotherapy for cervical cancer, considering the GTV contoured on MR images acquired at different dose levels for Vmid estimation. We explored optimal timing of MR imaging for pCR prediction, calculating ERI at different dose levels and quantifying its predictive ability in terms of receive operating characteristic (ROC) curve.

Method: A total of 18 patients affected by LACC (FIGO IB2-IVA) were enrolled in this study. All patients underwent MRgRT treatment with a simultaneous integrated boost (SIB) technique, prescribing 50.6 Gy (2.3 Gy/fraction) to PTV1 and 39.6 Gy (1.8 Gy/fraction) to PTV2. TrueFISP MR images were acquired during simulation and at each treatment fraction. GTV was contoured on the MR images acquired at the following dose levels: 11.5Gy, 23Gy, 34.5Gy and 43.7Gy. Pathological complete response (pCR) was considered as absence of any residual tumour cells on surgical specimen after surgery.

Results: 8 patients showed pCR (44.4%). The highest discriminative power of ERI was observed on the first 2 weeks of treatment where 90% sensitivity, 75% specificity and corresponding AUC value of 0.725 (see Table1).

Conclusion: This study confirmed ERI as a simple and promising response biomarker also in the context of low tesla MRgRT for cervical cancer. The second week of treatment represents the best time to predict pCR in LACC treatment. These results, if confirmed on larger cohorts, could facilitate the clinical implementation of ERI in personalized LACC treatment protocols.

Table 1. Predictive performance at different dose levels.

Dose Level (Gy)	Sensitivity	Specificity	Threshold	J_index	AUC	Low_AUC	High_AUC
11,5	90,0	75,0	135,7	0,7	72,5	43,3	100,0
23	90,0	75,0	77,0	0,7	72,5	43,8	100,0
34,5	80,0	75,0	37,8	0,6	70,0	40,9	99,1
43,7	90,0	50,0	31,5	0,4	65,0	36,5	93,5

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HIGH-DOSE-RATE VAGINAL INTERVENTIONAL RADIOTHERAPY WITH CHEMOTHERAPY FOR SURGICALLY STAGED LOCALIZED UTERINE SEROUS CARCINOMA

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Aim: Uterine serous carcinoma (USC) is an aggressive histologic subtype of endometrial cancer. Its treatment is multimodal including surgery, chemotherapy (CHT), and radiotherapy (RT). In stage IA, endovaginal interventional radiotherapy (IRT, also called brachytherapy), in combination with CHT, represents a valid option treatment. The aim of this study is to update our institutional experience with this homogeneous cohort underwent high dose rate (HDR) vaginal IRT and chemotherapy.

Methods: From January 2015 to January 2020, 14 FIGO 2008 stage IA USC patients who had undergone class A radical hysterectomy with bilateral annexectomy, sentinel lymph nodes resection and biopsy of the peritoneum, received 4-6 carbotaxol cycles of CHT followed by endovaginal IRT-HDR. All patients underwent IRT-HDR with 192Ir source, delivered with a vaginal cylinder. The target, delineated on pelvic CT slices, was defined as the proximal 3 cm of vaginal mucosa, the dose was prescribed at 5 mm from the applicator surface; bladder, rectum and small bowel were contoured as organs at risk. Acute vaginal toxicity was evaluated with the CTCAE V4 scale.

Results: Median patient age was 68 years (range 45-

78). Diagnostic endometrial biopsy was performed in all patients, thereafter 13 of the 14 patients underwent class A hysterectomy, sentinel lymph nodes resection and biopsy of the peritoneum. Lymphovascular invasion was present in 2 (14%) patients. Adjuvant CHT consisting of platinum-taxane doublets was administred to 12 patients (86%). Of these, 7 patients (50%) received 6 cycles and 5 patients (36%) received 4 cycles. Two patients (14%) did not receive adjuvant chemotherapy due to comorbidities. IRT-HDR total dose, administered in weekly fractions, was 24 Gy in 12 patients and 21 Gy in 2 patients. Six patients (43%) developed vaginal acute toxicity G1. No acute toxicity higher than G2 was reported. At a median follow-up of 14 months (range 7-49), 14 (100%) patients were alive, one of them (7%) was alive with pelvic recurrent disease.

Conclusion: The present series showed a positive impact of the IRT-HDR plus CHT on stage IA USC. Prospective trials aimed to confirm these data are needed.

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LOCALLY ADVANCED CERVICAL CANCER TREATED WITH DEFINITIVE RADIO-CHEMOTHERAPY AND VALUE OF LEUCOCYTE DISORDERS AT DIAGNOSIS

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Aims: This study retrospectively analyzes the correlation between the value of leucocyte disorders at diagnosis and the outcome in patients with locally advanced cervical cancer (LACC) treated with definitive radiochemotherapy in our Institution in the last 10 years.

Methods: from 2009 to March 2020, 29 patients with cervical cancer, stage FIGO IIA-IIIC2, were treated in our Institution with definitive external beam radiotherapy with or without concomitant weekly chemotherapy (cisplatin 40 mg/m^2) followed by endocavitary brachitherapy. Median age was 60 years (range: 35-87) and 23 patients were over 50 years old (79%). Squamous cell carcinoma was observed in 25 cases (86%), adenocarcinoma in 3 cases (10.5%) and solid carcinoma in 1 cases (3.5%). Grading is known in 20 patients: G2 in 10 and G3 in 10 cases, tumor size is reported in 25 cases: median size is 40 mm (range 18-65 mm) and in 6 patients is ≥ 50 mm. Before treatment, all patients underwent to chest-abdomen TC, pelvic RM, TC PET and complete blood cell count. The dose of 45-50.4 Gy in 25-28 fractions was delivered to the pelvic with 3-field (1 case), box (16 cases) and WMAT (12 cases) technique. Lumbo-aortic nodes was irradiated to a dose of 50.4-52.58 Gy in two cases. A boost was performed on the tumor up to the dose of 55.8-59.4 Gy, on the pelvic lymph nodes up to the dose of 50.4-63 Gy and on the parametria up to the dose of 54-59.4 Gy in 3, 7 and 9 cases respectively. All patients, except 5 (for age over 80 years or co-morbidity), underwent concomitant chemotherapy for a median of 5 cycles (range 2-7). Before brachitherapy all patients underwent pelvic RM to evaluated the response. Brachitherapy with high-dose-rate (HDR) has been performed in 27 cases (only 15 cases in our centre) for a median dose of 30 Gy (range 12-36 Gy) in 2-6 fractions and brachitherapy with pulsed-dose-rate (PDR) has been performed in 2 cases for a dose of 40 Gy. In the 15 patients treated in our Centre, the median HRCTV90(EQD2) has been 88.51 Gy (range 78.96-97.55 Gy) and the median IRCTV90(EQD2) has been in 72.49 Gy (range 68.18-78.71 Gy). The response was assessed with MRI and/or PET after three months from the completion of the treatment. The prognostic value of pretreatment leucocyte disorder was examined. Based on recent studies, leukocytosis and neutrophilia were defined as a leukocyte count or a neutrophils count exceeding 10,000 and 7,500/µl respectively; lymphopenia was defined as the percentage of lymphocytes ≤ 24%, the neutrophil-lymphocyte ratio (NLR) was defined as the absolute neutrophil count (ANC) divided by absolute lymphocyte count (ALC) and it is considered high when it is > 2.8.

Results: complete remission occurred in 90% of cases (26 patients) after treatment. One case (3.5%)has subsequently undergone salvage surgery and is currently on complete remission after 13 months. Relapse was observed in 8 cases after a median of 9.5 months (range 5-50): local relapse associated with bone metastases in 2 cases (after 26 and 48 months), only lumbo-aortic lymph node metastases in 2 cases at 5 months (the patient was treated with radio-chemotherapy and currently she is in complete remission after 90 months) and 50 months, distant metastases in the remaining cases. At a median follow-up of 23 months (range 3-128), 16 patients (55%) are alive with complete remission, 2 patients are alive with disease and 7 patients died for illness. In the remaining 4 cases with complete remission, 2 died for other causes after 8 and 33 months, 2 have been lost to follow-up after 34 and 72 months. We observed leukocytosis, neutrophilia and both in 5, 4 and 3 patients respectively; lymphopenia (≤24%) and high neutrophil-lymphocyte ratio (NLR > 2.8) in 13 and 12 cases respectively. White blood cell alteration was observed in 5 of the 8 patients with disease relapse (62.5%) and consisted of a high NLR and lymphopenia in 4 which in 1 case is also associated with neutrophilia; in addition, one patient, who died from local progression, had neutrophilia and one case with lumbo-aortic node relapse had only lymphopenia. Among young women (age < 50 years) only 2 had relapse and they had leukocitosis and lymphopenia al diagnosis, respectively.

Conclusion: In this retrospective study, we found that lymphopenia and high NLR are the most frequent leucocyte disorder in patients with recurrence as already highlighted in recent studies. Randomized trials with a large number of cases are needed to evaluate the prognostic value of leucocyte disorders.

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ELECTROCHEMOTHERAPY IN KAPOSI SARCOMA: A SYSTEMATIC REVIEW

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Aims: Kaposi sarcoma (KS) is a rare angioproliferative disorder usually associated with human herpesvirus–8 (HHV-8) infection. Electrochemotherapy (ECT) could be an option, such as radiation therapy (RT), in the treatment of KS skin lesions due to the high response rate in neoplastic lesions of different histological types. The aim of this systematic review was to analyse the available evidence on electrochemotherapy in the treatment of KS skin lesions.

Methods: Electronic databases were searched up to October 2019 for studies reporting on patients with KS skin lesions treated with ECT. Papers not reporting tumor response or toxicity nor these outcomes separately from other primary tumors were excluded. The search terms were electroporation, electrochemotherapy, and Kaposi sarcoma.

Results: Three studies including 68 patients were analyzed. The number of treated lesions was reported only in two papers while tumor size was not described. All ECT treatments were performed using intravenous bleomycin. Previous patients' treatments and HHV-8 virological behaviour changes were reported in two papers. Complete response rate was 65% - 100% and the overall response rate was 100% in all studies. Only one study reported local control (2-year: 76.2%). Toxicity was generally mild and transient.

Conclusions: The few available evidence suggests that ECT could be considered an effective and safe treatment option in KS skin lesions, particularly in local relapses after radiotherapy, due to excellent response rate and manageable toxicity, also in previously irradiated regions. However, further studies are needed to better define the role of ECT in this setting particularly as salvage treatment after radiotherapy.

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HYPOFRACTIONATED RADIOTHERAPY FOR NON-MELANOMA SKIN CANCER IN ELDERLY PATIENTS: A MONO INSTITUTIONAL EXPERIENCE

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Aims: Hypofractioned radiotherapy (HRT) is increasingly offered to elderly patients with non-melanoma skin cancer (NMSC), representing a benefit because of their comorbidities, poor PS or for their impossibility to accept a daily treatment. The aim of our retrospective analysis is to evaluate feasibility and tolerance of HRT in NMSC elderly patients.

Methods: We analyzed 30 patients (median age: 91 years; range: 68-110) with 48 lesions, with tumor size ranging from 0.5 to 11 cm. Twenty two patients (73.3%) had a Karnofsky Performance Status (PS) of 70-80%. The mostly prescribed total dose was 2400 cGy (range: 600-3600 cGy) with a weekly single fraction of 600 cGy. Primary endpoints were tolerability, acute toxicity and tumor response, according to Response Evaluation Criteria in Solid Tumors Group. Symptoms response was evaluated according to VAS scale. Overall survival (OS), disease-free survival (DFS) and late toxicity were secondary endpoints.

Results: Patient, tumor and radiotherapy characteristics are reported in Table 1. Radiotherapy intent was definitive in 22 patients (73.3%) and post-operative in 8 (26.7%). Twenty patients (66.7%) were treated with total dose of 2400 cGy, whereas the remaining ten patients were treated with single dose of 600 cGy (2 patients) or with total dose of 1200 cGy (1 patient), 1800 cGy (4 patients), 3000 cGy (2 patients) and 3600 cGy (1 patient). Twenty seven patients (90%) completed the prescribed treatment. Five patients (16.6%) reported G1 acute toxicity (erythema and itch), only a patient (1.4%) G2 toxicity, represented by erythema and patchy moist desquamation, whereas all the remaining 24 patients (80%) had no acute toxicity. With a median follow-up of 9 months (range: 1-73), tumor response was obtained in 26 patients (86.7%), as complete response in 12 (40.0%), partial response in 14 (46.6%), stable disease in 2 (6.7%) and progression 2 patients (6.7%). According to VAS scale and physical examination, 26 patients (86.7%) reported symptoms' response, especially for pain and bleeding. At last follow-up visit, all evaluable patients (30%) had no late toxicity, except for a case of G1 toxicity. Five-year OS and DFS were 40% and 23.3%, respectively.

Conclusions: HRT seems a favorable option for NMSC elderly patients reaching good rates of tumor response, efficacy and tolerability. According to our results a weekly fraction of 600 cGy could be an interesting choice for frail patients with comorbidities and poor PS.

Table 1. Patient, tumor and treatment characteristics (n=30).

Characteristics	*Number (%)*
Gender	
Female	11 (36.7)
Male	19 (63.3)
Comorbidities	
Cardiovascular	16 (53.3)
Autoimmune	1 (3.3)
Metabolic	2 (6.7)
Not reported	11 (36.7)
Performance Status (%; Karnofsky scoring)	
50	1 (3.3)
60	4 (13.4)
70	10 (33.3)
80	12 (40.0)
90	3 (10.0)
Tumour characteristics	
Localization	
Area of cheeks	14 (46.6)
Central face, area of eyes	8 (26.7)
Scalp	2 (6.7)
Legs, feet and hands	6 (20.0)
Primary tumour	17 (56.7)
Relapse tumour	13 (43.3)
Single/Multiple lesions	
Single	22 (73.3)
Multiple	8 (26.7)
Neurological symptoms/Pain	
Pain	6 (20.0)
Itch	2 (6.7)
Loss of strenght	1 (3.3)
Vision impairment	1 (3.3)
No neurological/pain symptoms	20 (66.7)
Bleeding	
Yes	17 (56.7)
Not	13 (43.3)
Homogeneity tumour border	
Yes	5 (16.7)
Not	25 (83.3)
Tumour histology	
Squamous cell	21 (70.0)
Basal cell	4 (13.3)
Kaposi's sarcoma	3 (10.0)
Mycosis fungoides	2 (6.7)
Treatment technique	
Photons	22 (73.3)
Electrons	8 (26.7)
Bolus	
Yes	17 (56.7)
Not	13 (43.3)
Bolus Thickness (17 patients)	
0,5 cm	8 (47.1)
1 cm	9 (52.9)
Immobilization system/Mould	
Yes	19 (63.3)
Not	11 (36.7)

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TOSCO-UMBRO INTERREGIONAL RADIATION ONCOLOGY GROUP (GITUOR) SURVEY TO IDENTIFY TREATMENT MODALITY IN NON MELANOMA SKIN CANCER IN 14 RADIATION ONCOLOGY INSTUTUTES

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Aims: In 2017 the GITUOR sent a questionnaire to Tuscany and Umbria Radiation Oncology centers, focusing the attention on different hypofractionated radiation therapy (RT) regimens used for skin basal and squamous cell cancers (BCCs/SCCs), to know the current treatment practice and to improve the quality of care.

Methods: Data from 14 Radiation Oncology Institutes were evaluated about patients with SCCs/BCCs who underwent definitive or adjuvant RT in 2017. We tried to assess the use of RT and brachitherapy (BT), total dose, fractionation and follow-up regarding local control and cosmetic outcome. Biologically equivalent doses with $\alpha/\beta = 3$ (BED3s) were calculated.

Results: A total of 360 cutaneous skin BCCs/SCCs, across 14 Institutes, were treated with external beam RT or BT. Most of the patients were aged over 80 years old. Among the total of 360 patients, 252 (70%) and 108 (30%) patients had head and neck or trunk/extremities lesions, respectively. We collected data about the percentage of hystological type: 153/360 were BCCs and 207/360 SCCs. In nine Institutes, treatments were provided with linac, in one center with linac or superficial kilovoltage RT, two centers used BT alone and two other centers disposed of all three of them. Data shows that 194 patients were treated with external beam RT, 41 with BT and 125 with superficial kilovoltage RT. Median BED3 was 108, with dose range between 45 Gy/15 fractions and 60 Gy/10 fractions. Mainly used shedules were 35 Gy/5 (BED3 117), 44Gy/10 and 54 Gy/18 fractions (BED3 108). No difference in local control was observed with different schedules, but decreased "good" cosmesis with higher dose for fraction.

Conclusions: We record all the data with the hope to uniform RT dose and fractionation and to improve the quality of care in non melanoma skin cancer. Despite different schedule of fractionations, similar BED3s were used, with no apparent differences in results and cosmesis.

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MERKEL CARCINOMA (MCC): A CASE REPORT

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MCC is a relatively rare cutaneous malignacy predominantly diagnosed in elderly patients (age > 70 years) and its management requires multidisciplinary care for optimal outcome. This report explores the radiotherapy (RT) role as a part of multidisciplinary approach. We describe a case of a 70 years old female patient (pts) with anamnesis of advanced breast cancer treated with chemotherapy for a long period from 2004 until 2007, which in July 2019 presented a red cutaneous nodule on right eyebrow arch. The histopatology report from incisional biopsy describes MCC. She underwent the first RT on nodule of MCC in another center with a total dose of 60 Gy in 30 fractions in July-August 2019 with complete response. In September 2019 the pts showed rapid progression at the lymph node level and underwent immunotherapy with avelumab and after chemotherapy with carboplatin and etoposide without any clinical response. Therefore, due to refractory disease, the pts came to our department of RT in Barletta in November 2019 with a large adenopathy in parotid region and in I and II level of rigth neck that we treated with total dose of 50 Gy in 25 fractions, 2 Gy per fraction daily for 5 weeks with 6 MV photons using intensity modulated radiation therapy (IMRT). The conventional fractionation and dose < 60- 66 Gy for bulky disease was used because of partial overlapping with previous field of treatment. From 27 December 2019 to 7 February 2020 the pts was treated and the treatment planning in this period was recalculated three times as the gross tumor volume was rapidly reducing. The pts presented mild side effects as G2 erythema and edema of face (defined by Common Terminology Criteria for Adverse Event CTACAE version 4). In March 2020 the pts presented new cutaneous lesions on the left eyebrow arch and on the left internal canthus region, thus showing a tendency to metastasize along the subcutaneous lymphatics of the face. These lesions were treated with hypofractionated palliative RT with partial local control but further evidence of new lesions and expired conditions forced us to start the pts for supportive care. Conclusion This report presents a case of an elderly woman affected from MCC who was treated with RT with rapid clinically and radiologically response. The peculiarity of the case is the refractoriness to chemo and immunotherapy and the rapid nodal and extranodal lymphatic subcutaneous diffusion.

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PAGET'S DISEASE OF SCROTUM AND PENIS CASE REPORT OF A RE-IRRADIATION AND REVIEW OF THE LITERATURE

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Aims: Extramammary Paget's disease (EMPD) is a rare cutaneous adenocarcinoma generally arising in the anogenital region. Surgery is still considered the treatment of choice for patients with EMPD, while Radiotherapy is a common alternative for inoperable cases and it's necessary in case of lack of surgical radicality. In this article we described our experience and a review of the literature, with a particular focus on radiation induced toxicity and on the feasibility of re-irradiation.

Methods: Case Report: a 70-year-old patient with EPMD of right hemi-scrotum underwent adjuvant radiotherapy in 2015. The treatment was performed with VMAT technique for a total dose of 50 Gy in 25 fractions of 2 Gy each. After 28 months the patient showed clinical recurrence and he decided to undergo a re-irradiation approach, which was performed with an electron beam and a 10x10 cm square applicator, for a total dose of 50 Gy in 25 fractions. Both treatments were completed with good compliance and without interruptions. Review of literature: a search strategy of the bibliographic database PubMed was performed. The inclusion criteria were case report, clinical prospective or retrospective studies with histological confirmation of EMPD of scrotum and penis; studies with patients undergoing RT; studies in the past 30 years.

Results: At the end of both radiant treatments no G3 (CTCAE v4) toxicity were recorded. In the last follow-up visit at 18 months of second treatment no signs of relapse were reported. At the moment, the patient maintains a good quality of life from a sexual, aesthetic and mobility point of view. The outcome of our patient was in line with data of literature, in fact in most of the 14 reported studies RT was overall well tolerated. The major observed toxicity was G3 skin toxicity in one study.

Conclusions: To our knowledge, there are no other cases of EPMD re-irradiation in literature. Even if several studies have demonstrated its feasibility in clinical practice, it is still not clear which are the skin dose constraints in re-irradiation setting. Our patient showed an excellent response and tolerated very well the high doses of both the radiation treatments. This suggests that the tolerance of skin to re-irradiation following a long period between the two treatments may be comparable to the normal constraints.

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A SMALL CASE SERIES ABOUT SAFETY AND EFFECTIVENESS OF A HYPOFRACTIONATED ELECTRON BEAM RADIOTHERAPY SCHEDULE IN FIVE FRACTIONS FOR FACIAL NON MELANOMA SKIN CANCER AMONG FRAIL AND ELDERLY PATIENTS

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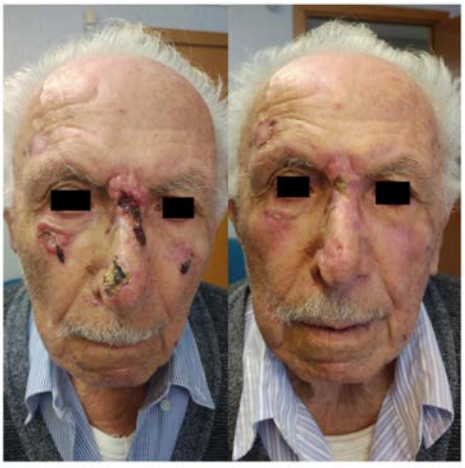
Aims: To evaluate local control and cosmetic results of strongly hypofractionated radiotherapy (RT) with electrons in elderly and fragile patients with non-melanoma skin cancer (NMSC) localized in the face.

Methods: From 1 August 2019 to 1 June 2020, at Malzoni Radiosurgery Center in Agropoli, we enrolled patients aged ≥ 65 years, with histological confirmation of NMSC of the face, that were not amenable to daily RT because of performance status (KPS) and/or compliance and not suitable candidates for surgical treatment due to comorbidities, multifocal lesions with problematic reconstruction or their own choice. Minimum eligibility criteria for RT were a KPS ≥ 40 and a life expectancy ≥ 6 months. The radiotherapy schedule provided for the delivery of the dose of 35 Gy in 5 fractions of 7 Gy / die twice a week for a total duration of treatment of 15 days. The radiotherapy prescription was modulated on the profile of the 6 MeV energy electron isodose based on the tumor depth (100% for cT1-cT2, 90% for cT3-cT4), excluding the use of bolus for inapplicability. The objective response was assessed clinically 4 and 8 weeks after the end of the RT and then monitored every 6 months by means of a photographic report. Side effects were assessed according to the CTCAE scale.



A patient with multiple facial NMSC: on the left pre-RT status, on the right 8 weeks after RT status.

Figure 1.

Results: 12 patients of median age 89.5 years (range 66 - 98) with a total of 23 NMSC cN0 locations (on average 1.9 lesions / patient), of which 8 squamous cell carcinomas and 15 basal cell carcinomas, have achieved a median follow-up time of 6 months (range 1 - 10), with total treatment compliance. 4/23 lesions had been surgically pretreated. 10/12 patients had a 40 ≤ KPS <70 and 2/12 a 70 ≤ KPS <90. 5/12 patients had synchronous lesions. 22/23 lesions were classifiable as T1-T2 and had complete response (CR), 1/23 as T4 with partial response (PR). Within 4 weeks after the end of treatment 12/23 lesions reported toxicity G1, 8/23 G2, 3/23 G3, 0/23 G4, all disappeared 8 weeks later, with or without topical therapy. At the last follow-up (1 June 2020) 1/12 patients died with PR from senile marasmus, 11/12 are alive with CR and with a cosmetic result judged to be good to excellent.

Conclusions: Extreme hypofractionation of the radiotherapy dose for non-melanoma skin cancers of the face is effective, safe and suitable for elderly patients with comorbidities and that cannot be surgically treated.

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RADIOTHERAPY FOR NON MELANOMA SKIN CANCER: OUR EXPERIENCE

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Aims: Radiotherapy (RT) can be considered an efficacious option for unoperable Non Melanoma Skin Cancer (NMSC) with good local control and acceptable cosmetic outcomes. Different fractionation schedules had been used to treat NMSC, according to several clinical and histological parameters. The purpose of this study is to investigate the efficacy and feasibility of RT in the management of NMSC patients, in collaboration with Dermatology Department of the University of Campania.

Methods: We retrospectively analysed NMSC patients treated from January 2017 to March 2020. All cases were biopsy-proven, inoperable, squamous cell carcinoma (SCC) or basal cell carcinoma (BCC), discussed at weekly multidisciplinary tumour board. The treated lesions were located at different sun-exposed anatomical sites (more than half involving scalp). Radiotherapy was delivered with a dose ranging from 55 Gy to 60 Gy with hypofractionated regimen, according to histology, comorbidities and disease site. The RT schedules used were: 55 Gy in 22 fractions (41 patients), 60 Gy in 20 fractions (38 patients) and 60 Gy in 15 fractions (13 patients), resulting in biologically effective doses (BED10) of 57.3 Gy, 60 Gy and 70 Gy, respectively. All the patients were treated with electron beam radiotherapy (ranging from 6 to 12 MeV). Acute and late toxicity was assessed according to CTCAE 4.05 scale. Local control (LC) was considered from the final date of RT to 12 months follow-up.

Results: 92 patients with unoperable NMSC (53 SCC, 39 BCC) were enrolled in the study. Median age was 76 (57-102). 10/92 patients had a previous radiotherapy treatment. 54/92 (59%) patients developed acute skin toxicity. G1 and G2 radiodermatitis were recorded in 34/54 (63%) and 16/54 (30%) patients, respectively, while G3 radiodermatitis occurred in 4/54 (7%) patients . G1 fatigue was experienced by 10/92 (11%) patients and G2 fatigue by 2/92 (2%) patients. Late cutaneous fibrosis was recorded in 9/92 (9,8%) patients. At 12 months FUP, LC was achieved in 73/79

(92%) patients. In particular, 26/73 (36%) patients achieved complete response, 31/73 (42%) partial response and 16/73 (22%) stable disease.

Conclusion: RT represents an excellent and curative option for the treatment of NMSC patient. The evidence utilizing hypofractionated RT in this patient cohort supports RT as a well-tolerated and efficacious option with acceptable toxicity rates.

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HIGH-DOSE-RATE BRACHYTHERAPY FOR THE TREATMENT OF NON-MELANOMA SKIN CANCER, USING VALENCIA APPLICATOR: A SINGLE-CENTRE EXPERIENCE

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Aims: The aim of this study was to evaluate tumour control, toxicity, and aesthetic events of patients affected by non melanoma skin cancer (NMSC) treated with 192Ir High-Dose-Rate (HDR) Brachytherapy (BT), using Valencia applicator at the Division of Radiotherapy, University of Pisa.

Methods: This retrospective study analyzed 84 patients (median age 83 years; range 32-96 years) histological subtypes: basal cell carcinoma (54.8%, n=46), squamous cell carcinoma (34.5%, n=29), Hodgkin lymphoma (5.9%, n=5), Kaposi sarcoma (4.8%, n=4). A total of 155 lesions were treated from January 2012 to February 2020. All the lesions had a diameter ≤ 25 mm (median: 12 mm) and a depth ≤ 4 mm. The appropriate Valencia applicator of 2 cm (58,7% n=91) or 3 cm (41,3% n=64) in diameter was used, depending on the size of the lesions. The prescribed dose was 40 Gy in 8 fractions (5 Gy/fraction) delivered 2/3 times a week. The biological effective dose (BED) was 60 Gy.

Results: After a median follow-up of 14 months (range 3-59 months), 149 lesions (96.2%) had complete response (CR), 3 (1.9%) had partial response (PR) and 3 (1.9%) had stable disease (SD). Five (3.2%) CR lesions had local recurrence. after a median time of 10 months (range, 6-23 months) 11 lesions (7.0%) not CR and recurrent diseases were treated with HDR-BT after failed primary surgery. Radiation Therapy Oncology Group – European Organization for Research and Treatment of Cancer (RTOG/EORTC) G1-2 acute toxicities were observed in 44.5% of the lesions; late G1-G2 toxicities were observed in 32,7%. No G3 or higher acute or late toxicities occurred. An excellent cosmetic result was observed in 82.5% of lesions and about 17.5% had good cosmetic results (moderate asymptomatic fibrosis).

Conclusions: HDR-BT using Valencia surface applicator is a well tolerated and effective modality for NMSC with excellent response rates and acceptable toxicity.

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HIGH-DOSE-RATE BRACHYTHERAPY FOR THE TREATMENT OF NON MELANOMA SKIN CANCER, USING CUSTOM MOULDS: THE EXPERIENCE OF UNIVERSITY OF PISA

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Aims: The aim of this study was to analyze tumour control, toxicity and aesthetic events for non-melanoma skin cancer (NMSC) treated with 192Ir High-Dose-Rate (HDR) brachytherapy (BT), using custom moulds at the Division of Radiotherapy, University of Pisa.

Material and Methods: From January 2012 to July 2019 we treated 33 patients (median age 79 years; range 31-91 years) affected by non-melanoma skin cancer, with histological subtypes: 51,5% basal cell carcinoma (17 pts), 30,3% squamous cell carcinoma (10 pts), 12,2% Kaposi's sarcoma (4 pts), 3,0% cutaneus non-Hodgkin Lymphoma (1 pts) and 3,0% Merkel cell cancer (1pt). We analyzed 36 lesions with a depth ≤5 mm, located in 36,1% Scalp (n=13), 13,9% Nose (n=5), 11,1% Face (n=4), 5.6% Ear (n=2), Trunk1 13,9% (n=5), and Extremity 19,4% (n=7). A customized surface mould was utilized following the contour of the skin surface and size of the lesion, with a median of a 5 catheters (range, 1-9), spaced 1cm apart. The most common fractionation scheme was 40Gy in 10 daily fraction; the biological effective dose (BED) was 65 Gy.

Results: After a median follow up of 23 months (range, 3-74 months) 30 lesions (83.4%) had complete response (CR), 2 (5.5%) had partial response (PR) and 4 (11.1%) had stable disease (SD). Five (13.9%) CR lesions had local recurrence, after a median time of 12 months (range, 6-23 months) 11 lesions (30.5%) not CR and recurrent diseases were treated with HDR-BT after failed primary surgery and /or tailored chemiotherapy. Radiation Therapy Oncology Group – European Organization for Research and Treatment of Cancer (RTOG/EORTC) G1-2 acute toxicities were observed in 65,0% of the lesions, late G1-G2 toxicities were observed in 36,0%. Late G3 cutaneous toxicity was observed in 2 lesions (5,5%) An excellent cosmetic result was observed in 65,0% of lesions and about 29,5% had good cosmetic results (moderate asymptomatic fibrosis). There were only two cases (retreatment) of poor cosmetic results

Conclusions: Surface mould HDR-BT is safe, effective modality for treatment of NMSC. Brachyterapy is well tolerated with very few late G3 toxicity; so this treatment can be considered a good alternative for patients unfit for surgery.

P242

ROLE AND EFFICACY OF EXTERNAL BEAM RADIOTHERAPY (EBRT) IN NON-MELANOMA SKIN CANCER TREATMENT: A SINGLE CENTER EXPERIENCE.

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Aims:In Italy, the incidence of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin is increasing. However, the real incidence is not well studied like as in melanoma. Radiotherapy is one of the treatment options, especially for non-surgical patients. The aim of our study is to report about a single center experience in the use of External Beam Radiotherapy (EBRT) for treating non melanoma skin cancer.

Methods: We reviewed Retrospectively all patients with BCC or SCC diagnosis, treated with radiotherapy in the period 2012–2018. 65 patients were included in the study: 50 male (77%) and 15 female (23%), median age was 89 years (range 76-101). Almost tumors were located in the head and neck region. All tumours were irradiated with external beam therapy, using high energy electrons or photons. We used the photons for deeper location, as parotid and cervical nodes, where the majority of lesions were treated with electrons. Each lesion was treated with personalized shield and customized bolus, often by changing energy of electrons and thickness of bolus during the course of radiotherapy because of lesion modification. The fractionation schemes varied in function of technique, localization and dimension of the lesion and patient performance status: 5000-6600/200cGy, 5000-5500cGy/ 250cGy, 3000cGy/300cGy, 3000cGy/ 600cGy. Special consideration was focused on wound care during the course of treatment with daily medication for limiting biofilm formation.

Results: No grade 3-5 toxicity was observed, only 2 patients stopped the treatment due to performance status impairment. The best results obtained was observed in the treatment of scalp lesions, even in the largest one, with "restitutio ad integrum" of the skin area. In our experience the long course, especially with 5500cGy/ 250cGy fractionation scheme, was associated with the best result. However, the hypofractionated scheme 3000cGy/600 is optimal for limiting commuting and discomfort for most disadvantaged patients. The local control obtained was in the range of 86-96%.

Conclusion: the increase in the incidence of non-melanoma skin cancer should be increase radiotherapy treatment request. Radiotherapy has potential good treatment outcome in terms of local control and toxicity. Therefore, we have started closer collaboration with dermatologist for better individualize the treatment strategy either in earlier stage in these patients, almost of all very old.

P243

HYPOFRACTIONATED RADIATION THERAPY IN ELDERLY PATIENTS WITH NON-MELANOMA SKIN CANCER: EFFICACY AND TOXICITY EVALUATION

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Aims: Radiation therapy can often cure skin cancers and can delay the growth of more advanced cancer. In elderly patients, often of poor performance status, extended daily treatment may be logistically difficult to deliver or are even considered inappropriate. The objective of this study was to assess the rate of tumour response and toxicity of a hyfrofractionated radiation therapy (RT) regimen (8 Gy/fraction on days 0, 7, 14) for elderly patients with non-melanoma skin cancer (NMSC).

Methods: Patients included in this study were deemed unsuitable by the multidisciplinary team for radical surgery for patient factors (age, performance status, cognitive impairment) and/or tumour factors (size, depth of invasion, location). 17 patients with histological confirmation of NMSC and no previous RT to that site were treated with RT from April 2017 to April 2020. Radiotherapy was delivered using electrons with energies of 6-9-18 MeV. A bolus was used to ensure the full dose was delivered to the skin surface. Elective nodal radiation was not carried out. The dose prescribed was 24 Gy in three fractions, delivered on days 0, 7, and 14. The response to treatment was based on the Response Evaluation Criteria in Solid Tumors Group (RECIST). CTC vers. 4.02 scale was used to grade toxicity.

Results: Six patients were affected by basal cell carcinoma and eleven patients of squamous cell carcinoma of the skin. Median age was 85.1 years (range 80-96). All patients completed the treatment and no severe acute and late toxicities were seen. 4 patients had incomplete follow-up data. At the time of last follow-up (median 4.8 months), 84,6% of patients had a complete response (11/13 pts) and 15,4% a partial response (2/13 pts).

Conclusions: This regimen (8 Gy/fraction on days 0, 7, 14) offers impressive response rates and good toxicity profile for elderly patients with NMSC.

P244

SOLITARY BONE PLASMACYTOMA (SBP): A CASE REPORT

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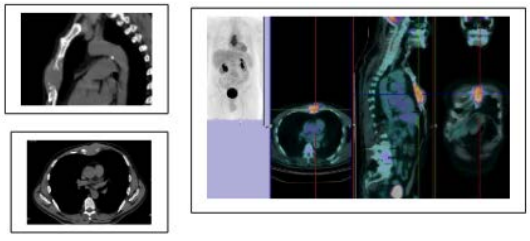
Aims: Solitary plasmacytoma (SP) is a rare plasma cell dyscrasia.The disease more commonly (80%)presents in bone (SBP),less commonly (20%) in an extramedullary site (SEP). These entities are diagnosed by demonstrating infiltration of a monoclonal plasma cell population in a single bone lesion or presence of plasma cells involving a soft tissue,respectively.Patient with bone involvement often present pain, neurologic compromise, and occasionally pathologic fracture. A lytic lesion is typical, with or without adjacent soft tissue mass. The optimal treatment for most patients with SP is a moderate dose of radiotherapy 40 to 50 Gy, and occasionally surgery that should be considered for structural instability. Although adjuvant chemotherapy may be used, there is no evidence that it improves either local control or survival. The most common pattern of relapse is progression to multiple myeloma (MM) and patients with SBP progressed to MM more frequently than those with SEP.



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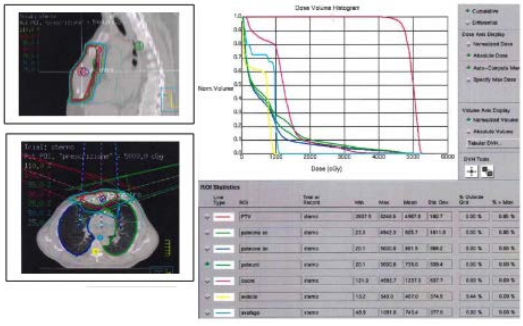

Figure 2.

Methods: We are describing the case of a patient affected by SBP treated with radiotherapy in our institute. A 62-year-old man presented a painful lump on the anterior chest wall. The CT imaging scan showed sternal mass of 7.5 cm x 4 cm x 6 cm with lytic bone lesion. The needle biopsy of pathologic swelling diagnosed the presence of monoclonal plasma cells. Diagnostic evaluation at presentation included physical examination, bone marrow biopsy,serum protein electrophoresis, CT total body and PET-CT (Figure 1) and confirmed no additional pathologic lesions. He had radiation therapy: the treatment was performed with LINAC 6-10 MV x-Rays, with 3D conformal technique at doses of 5000 cGy,200 cGy daily (Figure 2)

Results: After 4 months of completion of therapy he presented a clinical and a CT-PET images partial remission of palpable sternal mass but he progressed to MM.The patient started on biological therapy with Bortezomib and Dexamethasone ongoing and well tolerated.

Conclusions: SBP is a relatively uncommon malignancy. Most patiens are treated with moderate-dose radiotherapy; a subset of these may require surgical intervention. Adjuvant chemotherapy is not indicated. While radiation therapy remains the mainstay of therapy,progress has been made with regard to diagnostic tools available that can risk stratify disease and discern solitary plasmacytoma from quiescient or asimtomatic myeloma at the time of diagnosis. The prognosis is unfortunately affected by progression to multiple myeloma,which justifies rigorous monitoring after treatment and suggests a reflection on the exact role of chemotherapy or novel biological agents.

P245

RT COMBINED RITUXIMAB FOR FOLLICULAR LYMPHOMA: A RETROSPECTIVE ANALYSIS OF TEN YEAR EXPERIENCE

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Aims: In Western countries, Follicular Lymphoma (FL) is one of the most common indolent Non Hodgkin Lymphoma (NHL). For years, Radiation Therapy (RT) alone has been the standard treatment for Ann Arbor Stage I and II, but at present time combined therapy with Rituximab and/or chemotherapy has improved disease control. Our purpose is to analyze our ten- years experience about combined treatment in FL.

Methods: In this retrospective study, we analyzed records about patients treated with Radio-immunotherapy. All patients received 6 courses of Rituximab alone or chemo-immunotherapy (8 R + 6 CHOP) and Involved field radiotherapy (24/40 Gy, 2 gray /die). Total dose was 24-36 Gy if complete response occurred after systemic therapy, and 40Gy in partial response. PET-CT scan was performed in all patients at the time of diagnosis, after the completion of systemic therapy and after the term of RT, and during follow-up. Progressive disease was defined as any progression after RT's end, and overall survival as any death from the same time point. KM curves were adopted for survival analysis, while statistically significant value was set below 5% ($p<0.05$) for univariate analysis.

Results. From 2007 until 2020, 51 patients (median age 59 yr) have been treated at our institution. Patients'

staging revealed : 45% Stage I, 24% stage II; 18% stage III, 13% stage IV. Histological relevant features were Ki 67% (median 30%) and Grading (G1, 6 patients; G2 17 patients; G3, 28 patients). RT site was: 36 inguinal, 5 lomboaortic, 5 iliac, 3 bone and 2 Laterocervical and axilla. PET-CT pre-RT was negative in 42/51 and positive in in 9/51, with residual disease after RT in 2 patients only. Five patients experienced a recurrent disease. Median OS was 113 months, median PFS was 83months. Univariate analysis demonstrated that PET negative before RT was the only factor discriminating PFS results (105 months for PET+ vs NR for PET negative one's). No other factor (Ki-67, stage at diagnosis, grading, dose) influenced PFS and no one OS. Treatment was well tolerated. G0 (no toxicity) was reported in 44 patients, while G1 was reported in 7 patients (4 cutaneous, 2 haematological, 1 gastrointestinal).

Conclusions: Our experience confirmed that RIT is a safe and effective treatment , with long survival. These could open new scenarios in decreasing systemic therapy or RT doses.

P246

EXTRANODAL NATURAL KILLER/T-CELL LYMPHOMA, NASAL TYPE PRESENTING WITH EXTENSIVE LEG ULCERATION: A CASE REPORT

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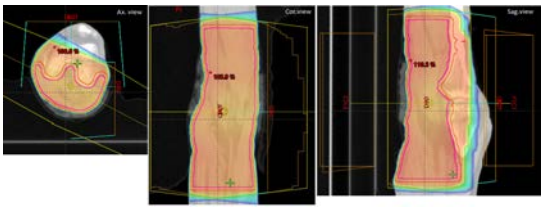
Aims: Extranodal natural killer/T-cell lymphoma, nasal type (NNKTL), accounts for less than 1% of Non-Hodgkin Lymphomas in USA and Europe and belongs to a category of very aggressive lymphomas. It is more frequent in adult male patients, with close association with EBV and expression of both T and NK-cell markers: CD2, CD3, CD45, CD56. It often causes a progressive ulceration and necrosis of the nasal cavity and facial tissues, with poor prognosis due to rapid local progression and metastases. The 5-years survival is reported to be at most 50% in early clinical stages, with a 65% of local control. It can rarely (0.03%) occur out of the nasopharynx. Chemoradiotherapy is the main strategy to treat this condition. Our purpose is to describe a rare case of NNKTL in a 68 years-old man, with onset in his popliteal fossa (PF), managed at our center.

Methods: In December 2017 the patient noticed a swelling in his right leg with a worsening skin ulcer. He underwent ultrasounds and biopsies, but the first diriment diagnosis arrived in July 2018: NNKTL, in hypodermis tissue of right PF. The immunophenotype reported the expression of CD45, CD2, CD30, and FISH was positive for EBV. Subsequent diagnostic investigations confirmed advanced-stage, with right external iliac and inguinal lymph nodes involvement, thus chemotherapy (CHT) based on Cisplatin, Dexamethasone, Gemcitabine, Peg-asparaginase was started, with partial response. However, in October 2018 due to a rapid worsening of the lesion with extensive necrotic ulcer, an urgent radiation treatment (RT) was proposed.



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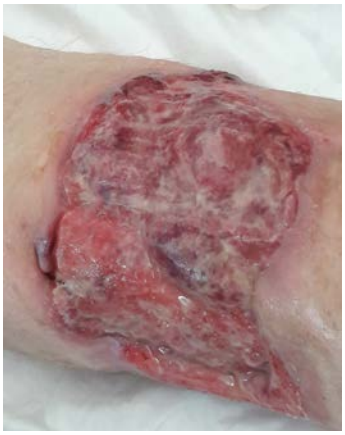

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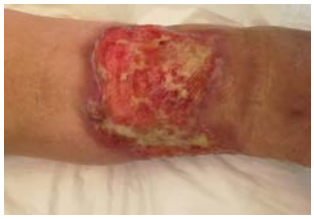

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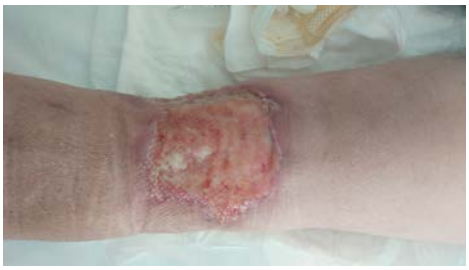

Figure 4.

Results: RT was performed with VMAT technique at the dose of 50 Gy in 2Gy-fractions. The clinical target volume encompassed the entire macroscopic lesion (Figure 1) which progressive response and reduction is shown in pictures (Figures 2-3-4). Following RT, the patient continued CHT and underwent a stem cell autotransplant in September 2019. A month later, a surgical debridement and repair with autologous dermal substitute was performed. The following PET showed a mild hypermetabolism in the subcutaneous layer of right PF, probably related to the surgery itself. Nowadays the patient is alive and continuing his follow-up, without complications associated with the CHT-RT.

Conclusions: We reported a case of a rare lymphoma with an uncommon onset site. It was managed with a multimodal approach as evidence of the importance of integrating and defining times of cares. RT played a crucial role to achieve a local control.

P247

EFFICACY OF RADIATION TREATMENT IN OCULAR ADNEXA LYMPHOMA: A RETROSPECTIVE EVALUATION IN A SINGLE INSTUTUTION

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Aims: Primary lymphoma of the ocular adnexa (OALs) is the most common form of ophthalmic Non-Hodgkin's Lymphoma. Radiotherapy is considered to be the standard treatment with an excellent local control and low toxicity. We reported the results of a large cohort of patients with mucosa-associated lymphoid tissue and follicular OALs treated with radiotherapy over a period of over 30 years. Endpoints of local control, disease free survival, overall survival and toxicity were considered.

Methods: We have retrospectively analysed 81 patients diagnosed and treated at our institution from 1987 and May 2019. Diagnostic material was obtained by pathological (52 patients) or, if not feasible, cytological (29 patients) examination of tissue samples of orbital lesions. We have considered as Stage IAE also patients with bilateral orbital involvement. All patients were treated with radiotherapy: treatment volume included the entire orbit, including the palpebral and bulbar conjunctiva for superficial lesions, without lens shielding. The dose ranged from 23.4 Gy in 13 fractions up to 39.6 Gy in 22 fractions (median 30.6 Gy). After 2001 we use doses < 30.6 Gy.

Results: All patients had stage IAE at the diagnosis and didn't present systemic symptoms, while the majority had local symptoms like swelling (55%), conjunctivitis (17%) and exophthalmos (14%). Gender was equally distributed with 41 females and 40 males. Median age at diagnosis was 63.7 years. All 81 patients obtained a complete remission. Two patients had a local relapse: one had a contralateral eye recurrence 3 years after treatment, the second in the same eye after 16 years. Both patients were treated with radiation therapy obtained again remission. Ten patients relapsed out of the orbits (12%). After a median follow-up of 74.5 months (range 8-309), 63 out of 81 patients (77.8%) are alive, the majority without disease and one in carefully observation. The disease free survival and overall survival are respectively of 85% and 70% with 18 patients died, all for non oncological reasons. The radiotherapy was well tolerated with a toxicity (RTOG scale) ranging from G1 in 36 patients to G2 in 20. The most common late toxicities were cataract (35%) and xerophthalmia (8,6%). A total dose >30,6 Gy resulted associated with cataract (p>0,005). Fifty percent of the patients had no late toxicity.

Conclusions: Our data demonstrates that radiotherapy for patients with indolent OALs is very effective and well-tolerated.

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RADIOTHERAPY FOR THE TREATMENT OF SOLITARY PLASMACYTOMA: 7-YEAR OUTCOMES BY A MONO-INSTITUTIONAL EXPERIENCE

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Aims Solitary plasmacytoma (SP) is characterized by a single mass of clonal plasma cells, without any evidence of systemic involvement or bone marrow (BM) plasmacytosis. It can present either as solitary bone (SBP) or as extramedullary (EMP) plasmacytoma. Definitive RT can result in long-term local control of the SP. Due to the small number of patients (pts) and narrow range of doses, phase III randomized trials are lacking and the optimal dose of radiation for treating SP is not clearly established. The aim of this study is to further support for the potential use of RT for the treatment of SP.

Methods: Clinical data of all pts treated for SP at our Institution between 1992 and 2018 were reviewed. Pts with a diagnosis of SBP or EMP based on a biopsy showing features characteristic of SP along with a normal BM biopsy, and without evidence of systemic disease attributing to multiple myeloma (MM) were considered eligible.

Results: A total of 42 consecutive pts were analyzed. The median follow-up was 84.8 months (range 6.2-265.7 months). Details and characteristics of pts are shown in Table 1. EBRT was used with all pts. The prescribed radiation dose ranged from 20 Gy to 50 Gy, with a median of 46 Gy and a dose per fraction ranging from 1.4 to 4 Gy. The equivalent dose (EQD2) ranged

from 23.3 to 50 Gy, with a median of 46 Gy, calculated by using a ratio of α/β=10. Radiation dose did not differ significantly as a function of sex, type of SP, tumor size; conversely differs significantly as a function of age (p=0.04). The 5y-OS and 10y-OS were respectively 96% and 91%. Local recurrences developed in 21.4% of pts (9/42). 16 pts progressed to MM (38.1%). The 5y-progression to MM free survival (PMFS) and the 10y-PMFS were respectively 68.6% and 61.9%. Impact of several factors on modulating OS was evaluated. Specifically, age at diagnosis was the only significant prognostic factor of OS (p=0.005), whereas type of treatment, surgery, pain and tumor size were not predictive.

Conclusion: Our data confirm the good results achievable with RT to treat SP. Also from our analysis, there is no statistically significant correlation between higher doses and better disease control. Similarly, no correlation between outcomes and type of SP has emerged. No statistically significant correlations were found that could define which pts have the greatest possibility of evolving into MM. Probably other biological factors can influence the outcome of the SP.

Table 1. Patients and tumor characteristics.

Median Age *(range)*	63 *(35-81)*
Sex (M/F)	26/16
ECOG PS (0/1/2)	17/23/2
Median Tumor size *(range)*	4 cm *(0.8-14)*
Tumor size (≤5 cm/> 5 cm)	29/13
Type of SP (SBP/EMP)	30/12
Sites of SBP	
Vertebra	15
Pelvic bones	6
Rib	5
Long bones	1
Skull	3
Sites of EMP	
Nasal/paranasal sinus	4
Nasopharynx	3
Oropharynx	2
Node	1
Other sites	2
Presence of pain (N/Y)	12/30
Spinal cord compression (N/Y)	32/10

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SPLENIC IRRADIATION WITH ADAPTIVE MR-GUIDED RADIOTHERAPY: AN INNOVATIVE APPROACH?

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Aims: Symptomatic splenomegaly is commonly observed in myeloproliferative disorders (MPD) and often associated with abdominal pain, early satiety and pancytopenia. Low-dose splenic irradiation (SI) is a safe and efficacious treatment option when surgery is not feasible. The response of hematopoietic cells to low RT doses can be very marked and cause a dramatic inter-fraction volume reduction. The possibility to apply adaptive RT approaches allows to reduce treatment fields and related toxicity. MR-guided radiotherapy (MRgRT) combines the best tissue contrast resolution offered by on board MR with online monitoring of treatment delivery and possibility to perform daily plan re-optimization. Aim of this study is to describe our experience in SI using adaptive (MRgART).

Methods: We retrospectively analyzed data from patients (pts) affected by MPD, who were treated with MRgART from September 2018 to July 2020. MRgART was delivered with video-assisted breath hold inspiration with a dose of 10 Gy in 10 consecutive fractions. The CTV was the spleen and PTV was obtained by adding an isotropic margin of 5 mm. A specific MRgART protocol has been followed: in case of offline adaptive procedures, the decision to adapt was made offline by reviewing the patient's positioning imaging and a new treatment plan was calculated. In case of online ART procedure, a new treatment plan was optimized on the patient's daily anatomy just before fraction delivery. Average spleen size reduction and patient compliance were evaluated.

Results: Four pts (3 women, 1 man) with MPD were enrolled in the study. Median age was 55,5 (45-60). One patient was affected by primary myelofibrosis, while three pts presented myelofibrosis evolved from previous essential thrombocythemia (1 case) and polycythemia vera (2 cases). ART was performed online for three pts, while an offline ART protocol was applied for one patient, in particular performing two different replanning. At the first fraction the average spleen volume was 2570,52 cc (1049,2 cc-3597 cc); at the end was 1205,41 cc (460 cc-1708,7 cc). The overall average spleen volume reduction was 53,74%. MRgRT was well tolerated by all pts and no acute toxicity has been reported.

Conclusions: MRgRT is feasible in pts undergoing SI through the management of inter-fractional and intra-fractional variability of therapy volumes. ART protocols prevent the occurrence of unnecessary organs at risk irradiation, increasing the safety of treatment and preventing toxicity.

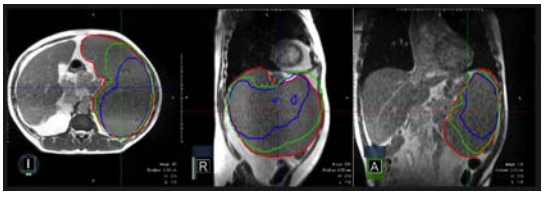

Figure 1.

P250

TAILORED TOTAL LYMPHOID IRRADIATION AS PART OF AUTOLOGOUS STEM CELL TRANSPLANTATION FOR ADVANCED NON-HODGKIN LYMPHOMAS

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Aims: Salvage chemotherapy followed by autologous stem cell transplantation (ASCT) is the standard of care for patients with relapsed/refractory (R/R) non-Hodgkin lymphomas (NHL). Patients with advanced stage at diagnosis, usually have multiple site of relapse during their disease history. The aim of this pilot analysis was to assess feasibility of Helical Tomotherapy TLI (HT-TLI) followed by high dose chemotherapy as a conditioning strategy for ASCT in R/R non-Hodgkin lymphoma (NHL).

Methods: From February 2011 to January 2019, 14 NHL patients with diffuse Large B Cell NHL (n=11) and T-cell NHL (n=3) were treated. Median age was 56 years (range 48-68) and median previous lines of therapy was 3 (range 2-4). Three patients had already received prior ASCT. HT-TLI total dose was 12 Gy delivered in 3 daily, with an optional simultaneous integrated boost (SIB) up to 14 Gy over the region of active residual disease before transplant, if any. High dose chemotherapy was administered 4 days later. Conditioning chemotherapy consisted of high-dose Bendamustine (400 mg/sqm) and Melphalan 140 (mg/sqm) for patients older than 40 years (n=10) and conventional FEAM (Fotemustine, Ethoposide, Cytarabine and Melphalan) for younger patients.

Results: Salvage chemotherapy and HT-TLI induced CR in 4 patients (29%), PR in 4 (29%), less than PR in 6(43%). Six patients (43%) experienced fever of unknown origin and 6 patients (43%) developed grade 3 mucositis. None experienced other grade 3 extra-hematological toxicity. The median number of CD34+ cells infused was 5,5 x 106/kg (range 2,1 -11,6). All patients showed complete engraftment, median time to neutrophil and platelet recovery was 11 (range 9-21) and 12.5 days (range 9-21) respectively. Median follow-up was 64.9 months (CI 95% 22.5-107.3 months). All patients in PR or less before transplant achieved CR. No cases of treatment-related death were recorded. The 3-year overall PFS and OS were 40.5% and 61.0% respectively. Post-ASCT relapse occurred in 7 patients at a median time of 8 months.

Conclusions: Our preliminary results show that HT-TLI is safe in advanced lymphomas, with limited toxicity. With the limit deriving from the small size of this series, we observe that all patients achieved CR after the procedure, even if heavily pretreated, and that relapse rate was relatively low. Overall these results encourage the implementation of HT-TLI in a prospective design to be a part of the conditioning for R/R NHL.

P251

OMNYBUS_ LYMPHOMA PROJECT: EFFICACY OF THE MULTIDISCIPLINARY TUMOR BOARDS IN LYMPHOMA MANAGEMENT ON A PERSONALIZED MEDICINE CHALLENGE. AN OBSERVATIONAL PROSTECTIVE STUDY

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Aim: The aim of the OMNYBuS project was to evaluate the impact of a multidisciplinary tumor board (MTB) on the treatment of patients(pts) with lymphoma.

Methods: During the submission process for presentation at MTB, physicians documented the histological diagnosis, the clinical history, the radiologic data, the timing of evaluation, their current proposal for treatment plan and the main question for the discussion. At least one hematologist, one radiation oncologist, one radiologist and one nuclear medicine physician were involved in the discussion. Alterations in radiologic and medical interpretations were discussed and the initial treatment plan was compared with the MTB final recommendation. Physician's proposed radiological exams or treatment plan MTB recommendation, and documentation of application of recommendations were prospectively recorded in an Institutional Review Board approved schedule (Figure 1).

Results: Between May 2019 and February 2020, 88 pts with lymphoma were weekly presented at the MTB. Eleven pts were presented on more than 1 occasion, resulting in 99 assessments (19 pts with Hodgkin lymphoma,49 with Non-Hodgkin lymphoma, 28 with indolent lymphoma and 3 with other histology). Eighteen cases were presented at diagnosis and the discussion focused on the staging and on the treatment management; 19 were presented at the interim evaluation to discuss about the response and eventually the treatment plan changes; 42 pts at the end of the chemotherapy for the response evaluation and the treatment strategies; 20 cases were presented during the follow-up to evaluate the response or the toxicity. In 17/99 clinical cases MTB recommendations differed from the initial treatment plan.

The MTB was decisive for the treatment or follow-up strategy in ten pts in absence of an initial proposal; an invasive approach as a biopsy was avoided in two cases and approved for other five patients. A new radiological evaluation was recommended in 37 pts, with more requested exams in 13 pts, while in 12 cases instrumental evaluation was avoided; other specialist evaluation were requested in ten cases. The follow-up confirmed that MTB recommendations were followed by 97/99 cases.

Conclusion: This study validates the impact of the MTB for lymphoma pts. MTB recommendations can be successfully initiated in the majority of patients. Hematological cancer patients will benefit from multidisciplinary review and should ideally be presented at tumor board.

OMNYBuS_ LYMPHOMA Project:
*efficacy **O**f the **M**ultidisciplin**N**ar**Y** tumor **B**oard**s** in **Lymphoma** management on a personalized medicine challenge. An observational prostective study*

N° INCONTRO: _____

DATA: / / ***Ora inizio*** : ***Ora fine*** : ***Tempo:*** ***min***

Medico propositore: _____ ☐ **Presente** ☐ **Assente**

Medici presenti: ☐ **Ematologo (N)** ☐ **Medico Nucleare (N)** ☐ **Radiologo (N)** ☐ **Radioterapista (N)**

FINALITà TB ☐ **Assistenza** ☐ **Assistenza e Ricerca**

NOME E COGNOME _____ **In protocollo: 1.SI 2.NO**	**COD. PAZIENTE (C.S.)** _____	**COD. CASO (progressivo)** _____
ISTOLOGIA	1.LH 2. DLBCL 3. Altri LNH B Aggressivi/LNH T 4. LNH B Indolenti 5.Altro	
FASE DI MALATTIA	1.Esordio 2.Valutazione Interim 3.Fine Terapia 4.Follow Up	
ANAMNESI		
Dato TC		
Dato PET		
QUESITO CLINICO	1.Stadiazione 2. Valutazione Risposta 3. Complicanza 4. Trattamento 5. RT 6.Complicanza	
SOLUZIONE PROPOSTA ***(PRE TB)***		
DECISIONE TB		
Discordanza clinico vs Radiologo/Med. Nucleare	☐SI ☐NO Valutazione pre TB:	
ESAMI RICHIESTI	☐ Strumentali ☐ Biopsia ☐ Altro	
ESAMI RISPARMIATI	☐ Strumentali ☐ Biopsia ☐ Altro	
MODIFICA PROGRAMMA RT	☐NO ☐SI Indicazione: Campo: Dose:	
CONCORDANZA CON LINEE GUIDA	☐ SI ☐NO	
APPLICAZIONE ALLA PRATICA CLINICA	☐ S I ☐ NO Motivo: *(Compliance paziente; decisione clinico; altro)*	
QUALITA' VITA PAZIENTE	*da valutare elaborazione questionario dedicato con psico-oncologhe RT*	
OUTCOME	*PFS; OS (?)*	

Figure 1.

P252

RADIATION-INDUCED LUNG SARCOMA OCCURRING AFTER RADIOTHERAPY FOR BREAST CANCER: A CASE REPORT

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Aim: Radiation-induced sarcoma (RIS) is a rare and aggressive complication of breast cancer radiotherapy (RT) whose 10-year incidence rate is about 0.2%. According to literature, RIS typically arise in the context or on the edge of radiation fields. In the latter areas dose is not uniform and may be lower than the one needed to kill cells, thus inducing mutations that can lead to carcinogenesis. Most RIS consists of high-grade tumors with angiosarcoma and non-otherwise specified sarcoma being the most common histological types. Surgery with widely negative margins is the first treatment option. Here we present the case of an undifferentiated lung sarcoma occurring 10 years after RT for breast cancer.

Case description: In March 2009, at S.Orsola Malpighi Hospital, a 46 years-old woman underwent right breast conserving surgery for ductal-lobular infiltrating carcinoma G3, pT1c, pN1 (snt), M0. Adjuvant chemotherapy with FEC 90x3 followed by docetaxel 100x3 and endocrine therapy with tamoxifen were given. The patient received post-operative external beam RT delivered with two opposed tangential 6MV beams on the residual right breast (total dose: 50 Gy in 25 fractions). During follow up, chest X ray and mammography were performed yearly. In 2019 a chest X-ray showed a pseudo-nodular image in the right lung confirmed by a CT showing a nodule of 7x11x10 mm with contrast enhancement in contact with the pleura in the ventral segment of the right upper lobe. FDG-PET/CT showed focal uptake in the same nodule. The patient underwent atypical resection of the lesion and at pathological evaluation an undifferentiated sarcoma of 1cm N0 (0/10) was reported. No adjuvant chemotherapy was given. The patient, now 56 years old, is continuing follow up.

Results and Conclusions: According to Cahan's modified criteria, the new onset of sarcoma as described in this case can be classified as RIS because it occurred after a long latency period (>3years), in the previously irradiated field and had a different histology than the irradiated primary tumor. The described RIS appeared in lung volume which received a total dose ranging between 40 and 45 Gy. The risk of RIS is too low to justify modification of RT prescription. However, the risk of RIS should be considered in patients with irradiated breast cancer during the follow-up.

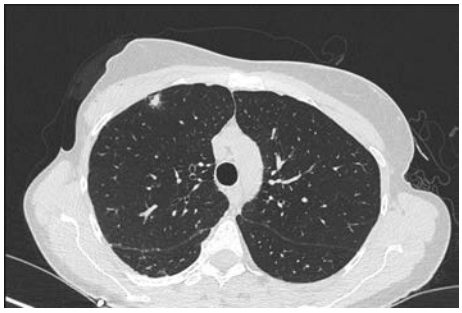

Figure 1.

P253

PRELIMINARY STUDY OF PLANNING COMPUTED TOMOGRAPHY DENSITY OVERRIDE APPROACH FOR CARBON ION RADIOTHERAPY IN SACRAL CHORDOMA PATIENTS IN CASE OF VARIABLE INTESTINAL GAS VOLUME

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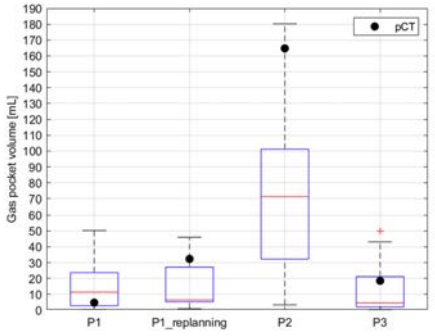
Aim: Particle therapy is sensitive to anatomical density variations of organs with variable filling. This study is a first attempt to estimate the effects of density variations on target dose distribution, mimicking on the planning computed tomography (pCT) different intestinal gas volume conditions as detected on daily cone beam computed tomography (CBCT) acquired after in room setup optimization of patients (pts) affected by sacral chordoma and treated with carbon ion radiotherapy (CIRT).

Methods: Treatment plan robustness against bowel density variation was retrospectively investigated through a CT density override approach. We selected 48 CBCTs from 3 sacral chordoma pts with no spacer implantation treated in prone position with CIRT at ---. Treatment plans consisted of 2 horizontal lateral opposed and 1 vertical beams for two pts and 2 lateral opposed and 2 obliques beams for one pt. Total dose range was 64–73.6 Gy(RBE) in 16 fractions of 4–4.6 Gy(RBE) each, 4 days a week. One pt is enrolled in the ongoing international phase 3 protocol. The proposed strategy is presented as follows: on each pCT gas cavities were virtually filled with mean bowel Hounsfield Unit (44HU) (vfCT), assuming that reproducibility of gas pockets position is not guaranteed during treatment. On each CBCT, gas cavities were semi-automatically segmented and contours were rigidly propagated to the vfCT. A corresponding virtual daily CT (vdCT) was generated superimposing a gas-equivalent Hounsfield Unit (-1000HU) on the vfCT. On each vdCT, dose distribution in the target volume was recalculated in the Treatment Planning System (RayStation®, RaySearch Laboratories). The volume of gas cavities was measured on pCT and on each CBCT. Target coverage differences between pCT and each vdCT were evaluated in terms of D95%, D98% and D99.9%.

Results: The median [range] volume of gas detected in CBCTs was 18.4[0.4; 180.3] mL and it was compared against the volume detected in the pCT (fig.1).These gas cavities variations induced a median [range] dose degradation for clinical target volume of 0 [-0.1; +0.1]% for D95%, 0 [-0.1; +0.4]% for D98% and 0 [-0.3; +0.6]% for D99.9% in vdCT with respect to pCT.

Conclusion: A noticeable interfraction variation of intestinal gas volume was measured. However, for this restricted-cohort analysis, this variation resulted negligible. Further investigations must be carried out to assess the dosimetric consequences of density variations on organs at risk.



Boxplots of gas volume distribution detected on the daily cone beam computed tomography (CBCT) acquired over the whole treatment course for each analysed patient (P=patient). The gas volume detected on the planning computed tomography (pCT) is marked as a black circle. For P1 a re-planning was clinically necessary on an additional planning computed tomography acquired during treatment course

Figure 1.

P254

SPORADIC AND NEUROFIBROMATOSIS 1-ASSOCIATED MALIGNANT PERIPHERAL NERVE SHEATH TUMOR (MPNST): ROLE OF INTENSITY-MODULATED RADIOTHERAPY IN A MULTIDISCIPLINARY APPROACH

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Aims: Malignant peripheral nerve sheath tumors (MPNST) are a rare form of soft tissue sarcoma; they are biologically aggressive, with high mortality and poor prognosis. Main treatment is surgery, but radiation therapy plays an important role in this setting, especially when the excision margins are positive. So the surgical goal is to resect the tumor with negative margins, because it is a strong predictor of survival.

Methods: We are reviewed our clinical archives at PoliclinicoHospital of the University of Catania and found, during a period from 2012 to 2019, a total of six patients with histological confirmed Malignant Peripheral Nerve Sheet Tumors (MPNST). All patients underwent to surgery, but the local extension and the anatomical localization of the disease did not make possible an oncological complete removal for the majority of them. Dose prescription was 46-50 Gy, with conventional 2 Gy/day fractionation, to the PTV and boost volume received additional 10 Gy, to a total of 56-60 Gy. An intensity-modulated irradiation (IMRT) was

obtained through a static step-and-shoot technique, using 5-7 fields, with a variable number of segments (range 32-64, median 48), with an energy of 6 MV X-rays.

Results: IMRT treatment course was completed by five out of six patients; one patient with thoracic localization has interrupted the course of radiotherapy a dose of 4320 cGy due painful symptoms and poor clinical and psychological compliance. Treatment was well tolerated. To date, five out of six patients are still alive. Median Overall survival since the initial treatment was 38 months. Median Survival from the date of diagnosis to the date of last follow-up or death is also analysed and was 41 months.

Conclusions: MPNST has an high tendency to local recurrence, even more than other soft-tissue sarcomas; consequently, its management needs an early and radical approach, to obtain the best chance of survival. A multidisciplinary treatment is the mainstay of the clinical management, with surgery and radiotherapy, to improve local control, patient survival, quality of life, and minimize treatment side effects. Our single-institution experience was developed according to these objectives and a local control was obtained in almost all patients.

P255

PELVIC EWING SARCOMA WITH METASTASES AT TIME OF DIAGNOSIS: ANALYSIS OF A MONOCENTRIC EXPERIENCE

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Aims: Pelvic Ewing sarcoma with metastases at time of diagnosis has a severe prognosis. We retrospectively analyzed our monocentric experience in order to identify outcomes in this subgroup of patients.

Methods: Pelvic Ewing sarcoma patients (pts) with metastases at time of diagnosis treated at our Institution from 2005 to 2015 were collected in this retrospective, monocentric study. Clinical, radiological and therapeutic data were collected.

Results: Twenty-seven patients (pts) (male/female 18/9), with a median age of 20.7 years (range 8-38 years) were enrolled. Median follow up was 23 months (range 1-112). At time of diagnosis 14 pts (52%) had lung metastases, 7 pts (26%) had bone metastases, 6 pts (22%) had both. Twenty-three pts (85%) presented tumor volume larger than 200 ml. All patients received standard chemotherapy (CHT) and 10 pts (37%) had standard and high-dose CHT. Local treatment on primary tumor was exclusive Radiotherapy (RT) in 20 pts (74%) and RT + surgery in one pt (4%). Six pts (22%) died before the beginning of local treatment. Median RT total dose was 54Gy. Median interval time from diagnosis to RT treatment was 5 months. Twenty-three pts (85%) died of disease: 12 (44%) had progressive disease during chemotherapy, while other 11 pts (41%) died after an average time of 12 months from the end of chemotherapy (range 2-22) with controlled local disease until that time. Four (15%) out of 27 pts are still alive with no evidence of disease: one pt had a small primitive tumor (< 200 ml), while the other 3 pts received intensification of local therapy with a stable disease 12 months after the end of CHT: 1 had surgery on primitive tumor in iliac wing at the end of chemotherapy, 1 had surgical excision of lung metastases and 1 had surgery + stereotactic RT on brain metastases.

Conclusions: Long survivor patients had small tumor or intensive metastases treatment. Based on this trend, we suggest an intensification of cures (both RT and surgery on the residual tumor) in patients who had a stable disease 12 months after the end of CT.

P256

ADJUVANT RADIO-CHEMOTHERAPY VERSUS RADIOTHERAPY ALONE IN SOFT TISSUE SARCOMA PATIENTS: A MATCHED COHORT STUDY

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Aims: Standard treatment for high risk soft tissue sarcomas (STSs) is surgery. Neoadjuvant radiochemotherapy (CT-RT) is well studied in terms of safety and efficacy and is used to obtain a better surgical radicality, while in the post-operative setting, even increasing local control, it is still debated because of toxicity. Our study evaluates in a matched cohort of patients with high risk soft tissue sarcoma the differences in clinical outcomes and toxicity between the concomitant radiochemotherapy- (RT-CT) and the radiotherapy alone (RT) group.

Methods: In this retrospective, single center study, 90 patients with STS treated with postoperative intent were included, of whom 45 (50%) received concomitant RT-CT and the other 45 patients received RT alone. Patients were matched on the basis of age, T stage and grading. Overall survival (OS), local recurrence free survival (LRFS) and distant metastases free survival (DMFS) in the two groups were compared. Early and late toxicities were recorded.

Results: OS at 5 years was 88%. Fifteen patients died, of whom 6 (6.7%) in the RT-CT group and 9

(10%) in the RT group. At multivariate analysis age> 65 years was found to be an independent prognostic factor of OS (HR = 3.7, 95% CI 1.2-12.1, p = 0.037). In the whole cohort, 19 patients had local recurrence (21.1%). No difference was observed in the two groups in terms of overall 5-year LRFS, which was 83%. Fourteen patients in the RT-CT group (15.6%) and 15 patients in the RT group (16.7%) developed metastases. Sixty (67%) patients were free from distant metastases after 5 years. Age greater than 65 is the only independent factor influencing distant recurrence (HR = 5.7, 95% CI 2.7-11.9; p = 0.001). There was no difference between the two groups in the development of acute and late toxicity. The main acute toxicity was represented by dermatitis (15 patients developed G3 dermatitis, of which 6 (6.7%) were in the RT-CT group). The main late toxicities were late fibrosis in 12 patients (13.3%), joint stiffness in 3 patients (3.3%) and bone fracture in 1 (1.1%).

Conclusions: Concomitant RT-CT increases LC and DMFS, with acceptable toxicity. In elderly population, which has a worse course of the disease, with a higher risk of developing metastasis, tailored targeted treatments should be considered. Prospective randomized studies are needed, with large size populations and subgroup analysis subdivided by histotype subtypes, to clarify the role of adjuvant CT in STS patients.

P257

NEOADIUVANT RADIOCHEMOTERAPY AND SURGERY OF RETROPERITONEAL SARCOMA. A REPORT ON THE SIZE VOLUME EFFECT ON PATIENT OVERALL SURVIVAL. MONO-INSTITUTIONAL ANALYSIS

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Aim: Retroperitoneal sarcomas are a heterogeneous group of rare tumors which count for 1/2% of all solid tumors. Aim of this study is to evaluate the OS of patient with retroperitoneal sarcoma with lesion size ranging from 33 cc to 5382 cc. in order to evaluate the tumor size's as prognostic index.

Methods: From 2008 to 2017 we treated 35 pts [mean age 68 (min 46 - max 88)] with retroperitoneal sarcoma [lyposarcoma 16; Leiomyosarcoma 18; 1 solitary fibrous tumor),among these 24 primitive and 11 recurrence] . All patients underwent MRI and CT imaging. The pretreatment gross tumor volume was contoured on MRI images aligned to CT. Patients were treated according to ESMO and NCCN International Guide Lines. Radiotherapy was delivered in 2-Gy fractions over 25 sessions for a total radiation dose of 50 Gy. The treatment position offsets were corrected using image guidance. 23 patients were irradiated with Tomotherapy, 12 patients were treated with LINAC.

All constraints for normal tissues were respected according to QUANTEC. After RT, all the patient underwent surgical resection. Kaplan Mayer analysis was carried out with the open source software KMWin based on the statistical software environment R which provides an easy to use graphical interface. Patient were grouped according to the lesion volume (in cc). As lesion volume cut off was used the first percentile, the median and mean value.

Results: The mean follow up was 68 months (range 16-178 m).The log rank test for the data in our study was P = 0,8864 for OS and P= 0,9757 for PD thus the two groups are not statistically significantly different. This is likely because such small numbers in the sample do not have the power to rule out a real difference and avoid a type two error. Despite this, the volume size seems not to be a negative prognostic factor. No cut off was found to make statistically significant the patients into the two groups. One limits of this study is the small number of patients treated in our institute, principally due to the low incidence of retroperitoneal sarcoma. A multicenter study may be necessary to increase the cohort and overcome this limitation.

P258

PRIMARY AND SECONDARY BREAST ANGIOSARCOMAS: A SINGLE-CENTER EXPERIENCE

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Aims: Breast angiosarcomas (BAs) can occur as a primary or secondary tumor associated with radiotherapy (RAAS: Radiation Associated Angiosarcomas). Data of BAs were collected and patients characteristics, tumor related factors and treatment modalities that affected overall survival, local and distant relapse were analyzed.

Methods: Fifteen patients with BAs were treated in a period of twenty years in our istitution. Angiosarcomas were considered RAAS if A) the tumor occurred in a previous radiation field and B) occurred after a delay of at least 3 years from the end of radiation treatment. Seven BAs were classified as primary tumor since there were no known factors associated to the tumor whereas eight tumor met the above criteria and were considered RAAS.

Results: Mean age of primary angiosarcomas and RAAS was 40 years (range: 17-60 years) and 52.2 years (range: 49-86 years) respectively. Mean follow up was 5.6 years (range: 0.1-19.3). All primary angiosarcomas were diagnosed as deep breast mass, whereas RAAS had clinical skin manifestations in six cases. The mean latency period between the radiotherapy treatment and the development of RAAS was 12.5 years (range: 3-26 years). Mastectomy was performed in 6 (40%) RAAS and in 4 (26.7%) primary angiosarcoma; 2 (13.3%) RAAS patients and 3 (20%) primary angiosarcoma patients underwent lumpectomy. At the last follow up 13 patients were alive, one RAAS patient and one with primary tumor have had a cancer related death. Overall survival was 86.7%. One local recurrence occurred in a

RAAS patient, the mean time of local failure was 0.3 years; local recurrence free survival was 92.9%. During the follow up distant metastasis were diagnosed in one (6.7%) primary tumor and one (6.7%) RAAS patient. The mean time of distant progression was 2.5 years (range: 0.4-4.6 years). At the Kaplan Meyer analysis any parameters was statistically significant for overall survival, local and distant recurrence.

Conclusions: In this retrospective study the clinical outcome of primary and RAAS did not differ. Although the incidence of radiation induced angiosarcoma is low, in view of the improved prognosis in women with breast cancer, clinical and radiological evaluations are needed for a long follow up period because early detection is essential given the poor prognosis.

P259

PREOPERATIVE RADIOTHERAPY WITH/WITHOUT CHEMOTHERAPY FOR STS: PRELIMINARY ASSESSMENT AND EFFICIENCY

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Aims: To evaluate local and distant control in a consecutive cohort of patients with extremities and body wall soft tissue sarcomas (STS) treated with preoperative radiotherapy with or without chemotherapy.

Methods: We retrospectively reviewed records of consecutive patients with STS of the extremity or trunk treated at our institution with neoadjuvant intent after induction chemotherapy with Epirubicine and ifosfamide. Patients treated between 2016 and 2017 received radiotherapy alone, subsequent patients treated between 2018 and 2020 radiotherapy and weekly Gemcitabine.

Results: Overall 27 patients were evaluated (M= 59.3%, F= 40.7%), 16 (59%) treated with RT only and 11 (41%) with RT-CT. All patients completed the treatment. Nine patients (34%) received 3 cycle of induction chemotherapy. Grade 3 toxicity was recorded in 0 patients in RT only group and in 1/11 (9.0%) patient in the RT-CT group (thrombocitopenia G3). Of the 22 patients underwent to surgery, Clear resection margins were obtained in 20 (90%) cases. Five patients (19%) achieved complete pathological response. Only four (13%) patients developed wound complications. For the whole group 2 year LC and 2 year PFS were 90.9% (median not reached) and 73.4% (median 29.4 months).

Conclusions: Preoperative radiotherapy with or without chemotherapy resulted well tolerated achieving high rates of clear margins resections without the increasing of wound complications and with a good rate of complete pathological response.

P260

HADRONTHERAPY TREATMENT FOR MOBILE SPINE CHORDOMA

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Aims: Primary spine tumors are one of the most challenging diseases for multidisciplinary oncological approach. Chordoma represents the most common histology. The purpose of this study is to evaluate local control and late toxicity of high-dose protontherapy (PT) and carbon ion (CI) radiotherapy(RT), in patients (pts) with spine classic chordoma.

Methods: We retrospectively analyzed the outcome of 50 pts with histologically proved chordoma treated with PT and CIRT at an Italian hadrontherapy facility between March 2012 and March 2020. Thirty-one pts (62%) were treated with post-operative RT. Residual disease was microscopical (R1) in 6 pts (22.6%) and macroscopical in 24 (77.4%). Four (8%) unresectable pts underwent definitive radiotherapy after biopsy. The most frequent tumor site was the cervical tract (n=25, 50%).Twenty-four pts were irradiated with CIRT to a median total dose of 69.7 Gy(RBE) (range 60-70.4), 10 pts underwent PT to a median total dose of 72.2 Gy(RBE) (range 66-74). The remaining 15 pts (30%) were treated for local recurrence after surgery with (n=7) or without (n=8) post-operative photons RT. Re-irradiation was performed in 11 pts with CIRT to a median dose of 69.7 Gy(RBE) (range 36-76.8), and in 4 pts with PT to a median dose of 74Gy(RBE) (range 60-74). During follow up, pts were evaluated with magnetic resonance every four months.Neuropathy grade was re-assessed according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Primary endpoints were Local Control (LC) and Overall Survival (OS), calculated with Kaplan Meyer method. Statistical significance was assessed by t-test and log-rank.

Results: With a median follow-up of 19,6 months (range 3 - 100.2), 2y-LC were 90% for pts treated for recurrence and 80% for pts treated for primary tumor (p=0.19), respectively. OS was 100% for both two groups (p=0.29). No statistically significant difference was found.All 50 patients developed G1-G2 neuropathy, one of them eventually worsened to G3 peripheral sensory and motor left upper limb deficit, limiting self-care.

Conclusions: In patients with spine classic chordoma, high dose CIRT and PT show favorable results with acceptable late toxicities. In view of slow growth and the biological behavior of chordoma, it is necessary to carry on the follow-up to confirm the long-term local control and the possible onset of delayed neuropathy.

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PALLIATIVE RADIOTHERAPY (PRT) FOR BONE METASTASIS IN END-STAGE CANCER PATIENTS: A INSTITUTIONAL RETROSPECTIVE ANALYSIS TO IMPROVE OUR CLINICAL PRACTICE

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Aims: PRT can improve quality of life in patients with bone metastases and treatment can be delivered with various fractionation regimens. Overestimation of life expectancy may contribute to inappropriate use of aggressive PRT near the end of life. This may be an indicator of poor-quality care. The aim of this study was to investigate the use of PRT for bone metastasis in our Radiotherapy Unit, to find critical points and improve our therapy choices near the end of life.

Methods: We retrospectively reviewed medical charts of patients treated for bones metastases in our Institute. Fractionation regimens, treatment modalities, cancer characteristics were evaluated with respect to death date. Patients who received more than one course of PRT were separately considered for each course. Statistical analysis was performed to identify clinical factors that influence physicians's decision-making.

Results: From January 2010 to December 2017, we performed 1492 treatments for bone metastases. Median age was 69 years (range 30-92). Primitive tumor was breast, lung, kidney, colon-rectum, bladder-urinary tract, prostate and other cancers respectively in 456 (30%), 400 (27%), 85 (6%), 107 (7%), 70 (5%), 184 (12%), 190 (13%) patients. Among all patients, 401 (27%), 657 (44%), 434 (29%) received respectively 1, 2-9, ≥ 10 fractions. Factors influencing choice of schedule were age, primitive tumor and volume of PTV. Median survival after the end of radiotherapy was 6 months (range 0-118). Sixty-eight (5%) patients interrupted radiotherapy for worsening clinical conditions. Among the 219 (15%) patients who died within 4 weeks after the end of treatment, physicians prescrived a single-dose fraction only in 89 (41%) cases and 34 (16%) patients received ≥ 10 fractions. Of 486 (33%) patients who died within 3 months after the end of radiotherapy, 98 (20%) received ≥ 10 fractions.

Conclusions: An accurate survival estimate was essential to adjust treatment choices in PRT, with clinical, ethical and economic impact. Based on our analisys we tend to overestimate life expectancy especially at the end of life, so we changed our clinical practice introducing the use of validated prognostic scores at the first visit to improve physicians's decision-making.

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QUANTIFYING POST-SURGICAL GEOMETRICAL MODIFICATIONS OF TUMOR BED AND BRAIN-STEM DURING PHOTON AND PROTON THERAPY FOR PEDIATRIC TUMORS OF THE POSTERIOR FOSSA: DOSIMETRIC IMPACT AND PREDICTIVE FACTORS

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Aims: Brainstem radionecrosis remains a critical issue during the irradiation of tumors of the posterior fossa. The aim of the present study is to describe post-surgical geometrical variations of tumor bed (TB) and brainstem (BS) and their impact on dosimetry.

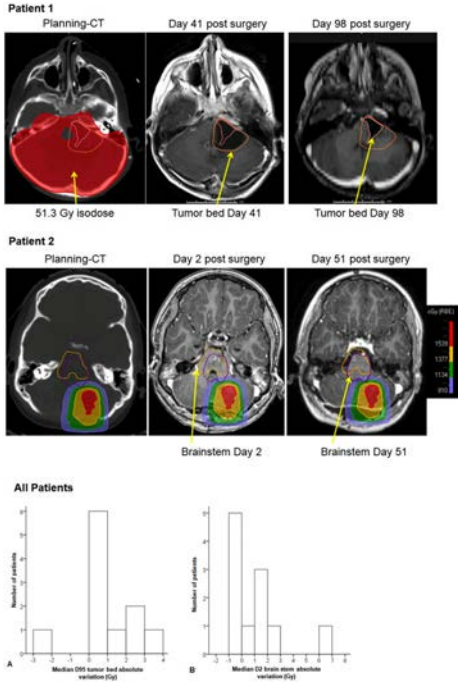

Figure 1.

Methods: Retrospective collection of data from pediatric patients treated at the Centre Antoine Lacassagne (Nice, France) between 2000 and 2019. Accessibility to digitalized medical records for the retrieval of clinical information, as well as the availability of DICOM (Digital Imaging and Communication in Medicine) files from at least two post-surgical, pre-RT gadolinium-enhanced MRIs per child. Only patients with accessible treatment planning data were considered. Qualitative data were represented as percentage, frequency and interquartile range (IQR). Mann-U-Whitney's test was used to compare continuous variables and Chi-Square test for qualitative variables. To provide a comprehensive quantitative assessment of the ROIs modifications over time, the following metrics were selected: 1) Total ROI volume, 2) Dice Similarity Coefficient (DSC): 3) Maximum and Average Haudsdorff Distances (HDs).

Results: Overall, 14 patients were considered for the analysis. They were equally distributed per gender; median age at the time of diagnosis was 8.2 (IQR 5.1-11.3) years. Major post-surgical modifications of TB were quantified by the DSC, HD max and HD average metric, whose values were 0.47 (range: 0.08-0.76), 11.3 (7.7-24.5) mm and 2.6 (0.7-6.7) mm between the first and the second post-operative MRI, respectively. Major post-surgical geometrical variations of the BS were also observed, with DSC, HD max and HD average values of 0.64 (range: 0.08-0.76), 8.5 (4.5-14) mm and 2 (0.4-3.3) mm between the first and the second post-operative MRI, respectively. Coverage to the TB was reduced in one patient (D95: -2.9 Gy), while D2 to the BS was found to be higher for most patients (Figure 1). Predictive factors for greater geometrical changes: Gross Tumor Volume (GTV)> 33mL, hydrocephaly at diagnosis, Luschka foramen involvement and younger age (≤ 8 years).

Conclusion: Major volume changes were observed in this cohort, with some dosimetric impact. The use of a recent co-registration MRI is advised. The 2-3 mm HD average observed should be considered in the Planning Target Volume/ Planning Organ at Risk Volume margin and/or robust optimization planning. Results from wider efforts are needed to verify our findings.

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COMBINED TREATMENT WITH IMRT AND CHEMOTHERAPY / TARGET THERAPY FOR DIFFUSE INTRINSIC PONTINE GLIOMA: CASE SERIES

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Aims: To report our clinical experience in radiation treatment (RT) combined with IMRT and chemo/target therapy for patients (pts) with diffuse intrinsic pontine glioma and to report efficacy, safety and tolerance.

Methods: From May 2013 to April 2020, 7 pts (M:4; F:3), with MRI diagnosis of diffuse intrinsic pontine glioma were treated. Median age was 7 years (range: 3-16). All pts underwent craniospinal MRI. Brain MRI has been used to make a fusion images with simulation CT, in order to optimize the target's and organs at risks contouring. Four pts were treated in combination with chemotherapy and target therapy (vinorelbine and nimotuzumab weekly). Five pts were treated under general anesthesia, depending on age. Static IMRT technique was used in all cases with dose of 54 Gy in conventional fractionation (1,8 Gy/fr).

Results: All pts completed RT. Five patients underwent treatment under general anesthesia, for inability to hold the position with termoplastic mask. One of these, due to clinical improvement halfway through treatment, completed radiation without anesthesia. All pts had skin toxicity (alopecia), one haematological toxicity (low platelet levels). First brain MRI was performed two months after the end of the radiotherapy and demonstrate partial response for three pts and stable disease for four. Time to relapse ranged between four and ten months, according with historical literature data. Reirradiation was performed in one case, with a total of 19,8 Gy/11 fr., after eight months from previous treatment.

Conclusions: Despite advancements in oncologic strategies as well as developments in research, survival outcomes for children with DIPG have not changed significantly over the past 20 years. Radiation therapy remains the mainstay of treatment, with proven but temporary benefit. In our monoistitutional experience, the small sample size and the patients recruitment characteristics cannot allow a real evaluation of progression free survival (PFS). Radiotherapy treatment combined with IMRT and chemo/target therapy for diffuse intrinsic pontine glioma can be considered safe and well tolerated.

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CRANIOSPINAL IRRADIATION DOSE AND PERSISTENT ALOPECIA IN MEDULLOBLASTOMA LONG-TERM SURVIVING CHILDREN: A MONOISTITUTIONAL EXPERIENCE

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Aims: Patients affected by medulloblastoma (MB) can be considered long-term survivals, apart high-risk forms. Craniospinal (CSP) irradiation is part of the treatment, however it brings notable side-effects in spite of technological improvement. In a society where esthetics is one of the primary interests, we tried to define the constraint dose and fractioning for scalp to prevent alopecia in patients (pts), and how we can modulate CSP dose guaranteeing total irradiation objective while reducing this type of side effect.

Methods: We retrospectively analyzed children with diagnosis of MB treated from 1999 to 2018 by intensity modulated radiation therapy (IMRT) or 3D conformational radiation therapy (3DCRT). We gathered data about CSP total dose delivered, daily fraction (fx) and daily dose. A dose between 23.40 Gy and 39 Gy in daily fx of 1.8 Gy or two daily fxs between 1.0 Gy and 1.3 Gy was prescribed to the CSP axis, followed by a boost to the posterior fossa or tumor bed ± metastases boost. Alopecia was graded according to CTCAE v5. Median CSP dose and toxicity grades according to number of fxs were evaluated by Fisher exact test. Finally, we carried out a descriptive analysis about median CSP dose according to number of daily fxs.

Results: A cohort of 38 children, with a median age 7 years and 7 months (range 3 years-16 years and 7 months), was identified. CSP median dose was 25.20 Gy. 18 (pts) did not manifest alopecia (G0), 10 and 10 pts developed grade 1 (hair loss< 50%) and grade 2 (hair loss<50%) alopecia, respectively. 15 of 18 (83%) G0 pts, 4/10 (40%)G1 pts and 1/10 (10%)G2 received a CSP dose inferior or equal to CSP median dose, respectively (P<0,001). As regard analysis of toxicity grade (G0 vs. G1/G2) according to number of daily fxs, 23 pts did a single daily fx and 15 pts with twice daily RT (bid); 16/23 (69.5%) and 7/23 (30%) treated once daily manifested G0 and G1/G2 toxicity, respectively while 2/15 (13%) pts and 13/15 (87%) of the bid group developed G0 and G1/G2 toxicity (P<0.001). In the bid group, all children that developed G1/G2 alopecia received a CSP dose higher than 2520 cGy and all children that did not developed toxicity received a CSP dose lower than 2520 cGy

Conclusions: Alopecia is related to CSP dose, and our data show a relation also to daily fx. Technologic improvement and particularly CSP irradiation with IMRT or proton therapy may improve scalp sparing with dose modulation guaranteeing target coverage.

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MULTIDIMENSIONAL ASSESSMENT FOR PEDIATRIC PATIENTS IN RADIOTHERAPY (M.A.P.-RT) THROUGH THE M.A.P.-RT FORM FOR A CUSTOMIZED TREATMENT PREPARATION: RADAR PROJECT

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Aims: The experience of distress in pediatric patients in radiotherapy can be frequent and combining psycho-social interventions with standard therapies could be one of the strategies for reducing the number of sedations. The RADAR Project aims to monitoring the needs of pediatric patients in order to optimize the treatment preparation. For this reason, a tool for a multidimensional assessment (MAP-RT form) has been implemented to collect information with the aim of recording useful data in a standardized way, providing results that would allow clinicians to provide support and care.

Material and methods: Pediatric patients (0-18 years or 18-21 with cognitive deficits) were considered in the study. Data have been collected retrospectively from patients treated in 2019. Subsequently, data were collected prospectively, through the administration of the MAP-RT form, exploring several thematic areas (Table 1), completed on the first evaluation by the radiation oncologist, the psychologist and the nurse. Feature selection has been performed by Boruta method (random forest classifier), the total significant partial scores achieved in each test subsection have been set in a logistic model to correlate with presence or absence of anesthesia.

Table 1.

		DIMENSION	TOTAL SCORE
A	NURSE OBSERVATION	Pain/distress	0-10
B	AGE SCORING	Developmental	0-10
C	FIRST MEDICAL VISIT INFORMATION	Medical	0-22
D	REPORT ON SKILLS FOR RT	Physical	0-26
E	FIRST ENTRANCE IN LINAC ROOM (CEMS)	Emotional distress	0-25
F	PSYCHOLOGICAL INTERVIEW	Psychological	0-30
	TOTAL SCORE MAP-RT		0-123

Results: Results of logistic regression (LR) have been used to detect the best predictors within the list of score. AUC has been used to detect the best threshold for the scores in the evaluation. Results: A total number of 99 patients were considered for this analysis. The training cohort considered 64 pts enrolled from December 2018 to December 2019, while 35 pts was prospectively analyzed as validation set from January to June 2020. Seventeen over 35 features of MAP-RT form have been selected by the Boruta classifier. In order to predict the need of anesthesia, the best predictive feature was the total score (TS), higher than the single partial scores. The AUC of the ROC using TS was .9875, with an optimal threshold set to 71 (sensitivity = .9574, specificity = .9412) in the training set. In the validation set the AUC using TS was .9467, (sensitivity =

.8, specificity = 1).

Conclusion: This work shows as the use of MAP-RT allows to pre-select patients that can be addressed to anesthesia procedure, considering the multidimensional assessment as a good clinical practice. This tool could be an optimal aid during pediatric patient management procedures. Keywords: Radiotherapy, Distress, Children, Anesthesia, Pediatrics.

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LOW DOSE TOTAL BODY IRRADIATION USING TOMOTHERAPY: IMPLEMENTATION OF METHOD FOR CHILDREN PATIENT

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Aims: Our standard procedure for Total Body Irradiation (TBI) is in a sitting position with lung attenuators, to increase the compliance of the pts (pts) who need to undergo anesthesia treatment we implemented TBI in Tomotherapy. TBI using Helical TomoTherapy (HT) allows to gain better dose distribution and homogeneity, sparing organs at risk (OARs). In pediatrics this can be beneficial to reduce late side effects. We present our treatment technique, dosimetric results and clinical data for our first pediatric pt aged 23 months with Congenital Dyskeratosis receiving dose of 200 cGy TBI as part of the conditioning regimen before second hematopoietic stem cell transplant.

Methods: The pt was immobilized in supine position with 2 thermoplastic masks (Orfit Industries, Wijnegem, Belgium) secured to 2 carbon fiber plates (All in One [AIO] solution, Orfit Industries) in pediatric sedation. The masks covered from head to lower limbs. The hands were within the Orfit. Fiducial markers were placed at shoulder level and lasers marked for treatment positioning. Planning CT scan (SOMATON Confidence-Siemens) was acquired with a slice thickness of 5 mm from 10 cm above the patients' vertex to 10 cm beyond the toes. The whole body was contoured (Eclipse treatment planning system [TPS], Varian Medical Systems, Palo Alto, CA) and transferred to the HT TPS for TBI planning. We have outlined OARs listed in Table 1. To avoid calculating the dose in the skin we created an internal margin of 2 mm below body surface and subtracted it from body, identifying PTV1. To reduce geometrical missing a virtual bolus (VB) of 5 mm thickness was added to patient surface. The area between skin and VB is called PTV2. We assigned to VB a density of 0.4 kg/m3. A VB is a material placed on the skin surface during planning, but absent for the real treatment. VB is declared as low priority target for the optimization algorithm. Dose prescription to the PTV1 and PTV2 was 2 Gy in single dose. The planning parameters were Pitch 0.287, field width 5.02 cm, modulation factor 2. Constraints to be fulfilled was coverage of 95% of the PTV1.

Table 1.

Name	max Dose [Gy]	min Dose [Gy]	Avg Dose [Gy]	StdDev Dose [Gy]	Physical Vol [cc]
PTV_1	2,09	1,94	2,00	0,01	102111,11
Liver	2,05	1,97	2,01	0,01	392,62
Lung R	2,04	1,98	2,01	0,01	156,61
Lung L	2,03	1,98	2,01	0,01	125,12
Brain	2,06	1,95	2,00	0,01	907,33
Body	2,10	1,09	2,00	0,02	11800,78
Lens_L	2,06	2,00	2,02	0,01	0,26
Lens_R	2,04	2,00	2,02	0,01	0,30
Thyroid	2,03	1,98	2,01	0,02	0,55
Testis_L	2,02	1,98	2,00	0,01	0,38
Testis_R	2,03	2,00	2,02	0,01	0,32
Kidney_L	2,04	1,98	2,01	0,01	31,56
Kidney_R	2,03	1,98	2,00	0,01	29,03

Results: Doses regarding PTV and OARs are summarized in Table 1, in particular body maximum dose was 2.1 Gy, minimum dose was 1.09 Gy, median and average doses were 2 Gy and standard deviation was 0.02 Gy. Overall treatment time was 911.9 seconds.

Conclusion: TBI using HT is a satisfactory technique which allows excellent coverage of the target. Moreover, it is possible to differentiate the dose on some OARs of toxicity such as relapse. We are working to use HT also for fractionated TBI and with higher doses.

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BRACHYTHERAPY FOR THE PALLIATION OF DYSPHAGIA IN ESOPHAGEAL CANCER: A RETROSPECTIVE MONOCENTRIC SERIES

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Aims: Carcinoma of esophagus often presents in locally advanced stage with a poor prognosis: among different modalities of palliative treatment, endoluminal brachytherapy could offer a good symptom control. The aim of this study is to evaluate efficacy and adverse effects of brachytherapy in a historical cohort treated in our department.

Methods: We retrospectively collected data from patients with incurable esophageal carcinoma treated with brachytherapy. Age, gender, histological diagnosis, stage of disease, performance status and relevant symptoms were recorded before and after treatment, as well as every objective response data. Overall survival was also reported.

Results: Sixteen patients completed treatment from 01/01/2005 to 31/12/2017. Mean patient age was 66.7 years (range: 46-82) and 13 patients (81%) were male. All patients except two were symptomatic for dysphagia or pain. All patients had undergone other treatments: surgery, chemo-radiotherapy, chemotherapy alone, external beam radiotherapy alone, previous brachyther-

apy or other therapies. Palliative brachytherapy was given in 2 to 4 weekly fractions of 6-7 Gy; 14 Gy in two fractions was the most common schedule. Median overall survival was 24.5 months (1.5 – 105.4 months). After treatment, dysphagia was stable in 5 patients (38%), increased in one patient (8%), decreased or absent in 7 patients (54%).

Conclusions: Esophageal brachytherapy is a suitable palliative option with a better quality of life compared to metallic stents. The toxicity is generally low and it can be performed in combination with other treatments.

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TOXICITY OF POSTOPERATIVE EXCLUSIVE VAGINAL CUFF HIGH-DOSE-RATE [HDR] 192 IR-SOURCE BRACHYTHERAPY IN ENDOMETRIAL CANCER ELDERLY PATIENTS

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Aims: To assess acute/late toxicity, at a median follow-up of 34 months, of adjuvant exclusive high-dose-rate[HDR] 192 Ir-source vaginal-cuff-brachytherapy (VBT) in a retrospective series of 32 consecutive elderly patients(pts)undergoing radical surgery and adjuvant VBT for endometrial cancer.

Methods: During July 2012-April 2020, 32 consecutive pts, mean age 73 yrs(range: 54-86), FIGO Stages IA-II endometrial adenocarcinoma were treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy plus lymphnode sampling or bilateral pelvic lymphadenectomy or without lymphnode pathological staging, with laparotomy (8 pts) or laparoscopy (24 pts) surgery followed by adjuvant VBT HDR alone in 176 consecutive fractions. Pre-existing genitourinary disorders were recorded in 6 pts (age: 70-86 yrs): urinary urgency G1 in 4 pts and urinary tract pain G1 in 2 pts, respectively. A rectal and bladder preparation protocol was used for all patients at each fraction (vaginal applicators diameter 2,5 cm) before 3D CT planning. HDR VBT (MicroSelectron afterloading 192-Ir source) was performed by image-based planning with contouring of organs at risk (bladder, rectum, urethra) and optimization at each fraction; the dose was prescribed at 5 mm from the applicator surface. The dosimetric parameters for all pts are reported in Table 1. Toxicity (RTOG-EORTC and CTCAE v. 4.02) was evaluated at the end of VBT and at f-ups(median:34 months;1-69).

Results: All patients completed the treatment without interruptions or need of medical support measures. Genitourinary toxicity at the end of VBT was reported in 5 pts as urinary urgency G1 (4 pts with pre-existing disorder), and in 7 pts as urinary tract pain G1. At median f-up of 34 months only urinary urgency G1 in the same 4 pts was found. The statistical analysis were performed with Mann-Whitney test for independent samples; for the variable D 0.1cc to urethra a statistically significant difference (p=0.0442) was found.

Conclusions: Confirming a previous preliminary evaluation of toxicity, with a median follow-up of 34 months, our present analysis shows that HDR VBT as exclusive adjuvant treatment for endometrial cancer is well tolerated in elderly patients without detrimental effects on urinary function, particularly in pts of ≥ 70 yrs old with pre-existing urinary disorders.Analysis of a larger patient series should confirm these results and help to find out further potentially predictive dosimetric parameters.

Table 1.

	No toxicity patients (n=27)	Toxicity patients (n=5)
Total dose (Gy)		
Mean Range (min-max)	35.5 25.5 – 41.0	36.0 35.0 – 39.0
Dose per fraction (Gy)		
Mean Range (min-max)	6.5 5.5 – 7.0	6.8 6.0 – 7.0
D0.1cc urethra (Gy)		
Mean Range (min-max)	6,9 1.5 - 11.8	7.6 5.6 - 10.1
D2cc bladder (Gy)		
Mean Range (min-max)	4.5 1.1 - 6.8	4.5 2.1 - 6.3

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STEREOTACTIC RADIOABLATION BY MULTIMODAL IMAGING FOR VENTRICULAR TACHYCARDIA (STRA-MI-VT)- PHASE I/II TRIAL

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Aims: In September 2019, a prospective, spontaneous, open label, phase I\II trial (ClinicalTrials.gov NCT04066517) on single fraction sterereotactic ablation for the cure of refractory ventricular tachycardia has started. Accrual of 15 patients is planned. The primary endpoint of the study is the evaluation of the feasibility, safety and efficacy of this treatment.

Methods: Four patients have already been treated. All patients underwent a diagnostic cardiac computed tomography (CT) scan for substrate characterization, whereas 3 out of 4 patients had an electroanatomical mapping too. A 4D CT simulation is performed and fused with the cardiac CT with medium contrast. The arrhythmogenic substrate, that is the clinical target volume (CTV), is contoured by both a radiation oncologist and a cardiologist. To take into account the respiratory motion, the CTV is then expanded into the internal target volume (ITV). The ITV is further expanded by 3 mm to create the planning target volume (PTV). The prescription dose is 25 Gy and has to be delivered in a single fraction using the intensity-modulated radiotherapy (IMRT) technique.

Results: Four patients have already completed the treatment, and the first one has 9 months follow-up. All patients were treated with Trilogy RapidArc® Varian with 2 or 3 arcs; beam–on time was about 20-25 minutes. The mean CTV was 32,2 cm^3, mean ITV 96.3 cm^3 and PTV 153.2 cm3. In the first patient, the CTV was very close to the stomach, and so the patient experienced nausea and vomit G2 (CTCAE 4.0) in the first week, which were treated with steroids and antiemetic drugs. No acute side effects has been registered in the other 3. Patient 1- and 3 showed a significant reduction of all VT episodes, whereas the second one is showing a progressive improvement in terms of number and characteristics of VT episodes after 5 week follow-up, therefore still in the blanking period. The 4th patient has too short follow up. After 3 months, the first and the second patient underwent a diagnostic CT scan: no radiation-related injuries have been reported; little improvement of echocardiography ejection fraction was registered in 2 patients.

Conclusion: The treatment seems feasible and safe, and accrual is ongoing. Longer follow-up and more robust results are needed to confirm preliminary findings and to consider SBRT as a valid therapeutic option in this setting.

P270

IOERT IN BREAST CANCER AS BOOST: LONG TERM RESULTS OF A PHASE III RANDOMIZED STUDY ON USE OF IOERT FOR EARLY STAGE BREAST CANCER

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Aims: Aim is to present long-term follow up results on local control, esthetic evaluation and toxicity of a prospective study on early stage breast cancer patients treated with intraoperative radiotherapy with electrons (IOERT) boost of 10 Gy versus the same external beam dose and whole breast irradiation (WBI).

Methods: A phase III randomized study to compare IOERT versus external beam boost in early stage breast cancer was conducted in our Institution. Primary endpoints of the study were the evaluation of in-breast true recurrence (IBTR) and out-field local recurrence (LR), toxicity and cosmetic result. Secondary were the valuation of overall survival (OS), disease free survival (DFS) and patient's grade of satisfaction about the cosmetic outcome. Toxicity valuation was assessed using the European Organization for Research and Treatment of Cancer (EORTC) scale. The cosmetic result was rated both in subjective and objective modalities by patients themselves and physicians, respectively, according to the Harvard Scale, without taking photos. Data were examined in June 2019.

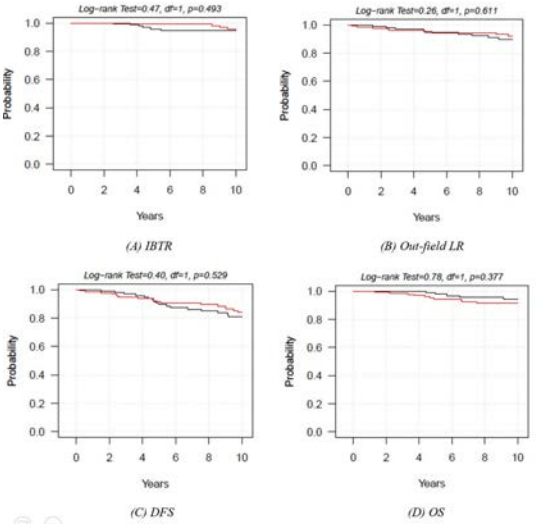

Figure 1

Results: A total of 245 patients was randomized: 133 in the IOERT boost arm and 112 in the EBRT boost arm; the median follow-up was 12 years (range 10-16 years). Four (3.2%) and five (4.5%) IBTR were observed in the IOERT and the EBRT boost arm, respectively. The cumulative risk of IBTR at 5 and 10 years was 0.8% and 4.3% in IOERT group, and 4.2% and 5.3% in EBRT group (p=0.709). The cumulative risk of out-field LR at 5 and 10 years was 4.7% and 7.9% in IOERT group versus 5.2% and 10.3% in EBRT group (p=0.762). All of the IOERT arm recurrences were observed at more than 100 months' follow up, whereas the mean time to recurrence in EBRT group was earlier (55,2 months). As acute toxicity, 7 wound healing problems occurred (7,8%), 3 of them in IOERT

arm. No late complications associated with IOERT were observed, excluding two cases of liponecrosis in the IOERT treatment area. Cosmetic result was very good (objective evaluation 92,8% good or excellent, subjective evaluation 90,2%) and comparable to patients treated with external boost (87,4% good or excellent).

Conclusion: A 10 Gy IOERT boost after breast-conserving surgery provides very high local control rates without significant morbidity. Although not significantly superior in our trial, it is a reliable alternative to conventional postoperative external beam boosts.

P271

ARTIFICIAL INTELLIGENCE AND INTERVENTIONAL RADIOTHERAPY: A REVIEW OF CURRENT LITERATURE IN CLINICAL PRACTICE

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Aims: Artificial intelligence (AI) has gained a pivotal role in fostering Decision Supporting Systems (DSS) and its application in healthcare is rapidly increasing. Aim of our review was to define the role of AI in healthcare with main focus on Interventional Radiotherapy (IRT).

Methods: An in-depth review of existing literature about the topic was carried out through the main electronic databases. The papers identifed were subsequently classified and categorized according to the different phases of the IRT process.

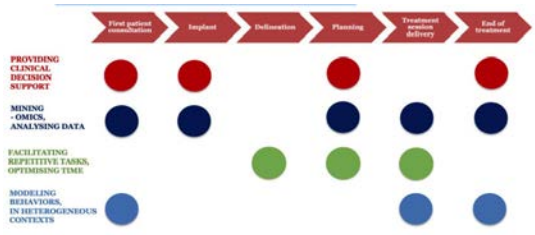

Figure 1. Artificial Intelligence in Interventional Radiation Oncology.

Results: AI may have a large impact in 4 fields: 1) providing clinical decision support, 2) data mining, 3) facilitating repetitive tasks, optimizing time and 4) modelling patients and physicians' behaviors in heterogeneous contexts. AI implementation in IRT should successfully facilitate all the steps of treatment workflow such as patient consultation, implant, treatment volume delineation, treatment planning, treatment delivery, end of treatment/follow-up. A summary of the implementation of AI in IRT is reported in Figure 1.

Conclusions: AI may contribute to improve clinical outcomes through the application of predictive models and DSS optimization. This approach could lead in reducing healthcare costs, time-consuming repetitive tasks, and improving treatment quality assurance and patient's assistance in IRT.

P272

ROLE OF HIGH DOSE-RATE INTERSTITIAL INTERVENTIONAL RADIOTHERAPY AS ADJUVANT TREATMENT FOR ORBITAL RECURRENCES FROM CONJUNCTIVAL MELANOMA: MONOINSTITUTIONAL CASE SERIES

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Aims: Aim of our study was to evaluate local control, functional and cosmetic outcome of postoperative high-dose rate interventional radiotherapy (HDR-IRT) in patients affected by orbital recurrence from conjunctival melanoma.

Table 1.

Step 1: Pre-planning
a. Implant catheters arrangement definition based on pre-procedures CT
b. CT based pre-planning and optimisation
c. Catheter insertion coordinates with reference to bone landmarks
Step 2: Implantation technique
a. Catheter implantation was carried out under general anaesthesia
b. Catheters inserted carefully avoiding injury, especially to prevent extension beyond the orbit
c. The catheters were fixed to the skin for stability
Step 3: Treatment planning and delivery
a. CT based IRT planning and optimization
b. Treatment delivery (3.4 Gy BID in 10 fractions)

Methods: We considered 2 consecutive patients affected by conjunctival melanoma infiltrating the orbit, treated with surgical excision and postoperative HDR-IRT. The therapeutic procedure consisted first of all of surgical excision of the orbital infiltrating nodule which was followed one month after by HDR-IRT. A total dose of 34 Gy was delivered in 10 twice-daily fractions over 5 consecutive days. The entire procedure with its steps is reported in Table 1.

Results: In both patients the treatment was well tolerated and there was no orbital recurrence at a median follow-up of 37-40 months. Postoperative HDR-IRT resulted additionally in an excellent functional outcome, without no significant acute or late side effects.

Conclusions: Postoperative HDR-IRT is a promising feasible, successfull and well tolerated option for selected patients affected by ocular tumors with orbital invasion.

P273

INTRABEAM APPLICATIONS FOR INTRAOPERATIVE RADIOTHERAPY DURING VERTEBROPLASTY FOR VERTEBRAL MESTASTASES

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Purpose: Vertebroplasty is an effective procedure providing structural stability and pain relief in vertebral metastases. In a conducted phase I/II trial the additions of intraoperative radiotherapy to vertebroplasty (V-IORT), provided pain relief in 70% of patients at the first day after the intervention and resulted in local control rates of > 93%. The objective of this study was the preliminary outcomes of the V-IORT treatments with an Intrabeam radiotherapy device for vertebral metastases (VM).

Materials and Method: We retrospectively reviewed 11 patients treated with V-IORT for a 11 painful VM from November 2015 to May 2020. 3 patients had VM from Breast Cancer, 2 patient from Renal Cell Carcinoma, 1 patient from Prostate Carcinoma, 1 patient from Pancreatic adenocarcinoma, 1 patient from a Esophageal adenocarcinoma, 1 patient from follicular Thyroid carcinoma, 1 patient from Colangiocarcinoma and 1 patient from Carcinoma of Unknown primary. All patients were treated with INTRABEAM Photon Radiosurgery System. The median dose and depth of prescription were respectively 8 Gy and 10 mm.

Results: Median patient age was 51 years. V-IORT was successfully performed in 7 of 11 vertebral lesion (63%); In 4 patients (37%) intra-operative radiation could not be applied due to technical difficulties. No severe complications occurred during or early after IORT. The median pain score using a Numeric Rating Scale (NRS) decreased from 5/10 before the procedure to 2/10 at the day 1 after the procedure and median NRS score of 1/10 at the last follow up. After a median follow-up of 8 months, stable disease within the irradiated vertebral body was seen in 6 patients (85%), 1 patient was lost at a follow-up. No re-irradiation due to local progressive disease or pain recurrence was necessary.

Conclusion: V-IORT is well tolerated without severe side effects and provides fast improvement of pain with excellent local control rates in patients with painful VM.

P274

SHORT-TERM OUTCOMES OF INTRAOPERATIVE RADIOTHERAPY USING INTRABEAM SYSTEM FOR PRIMARY LOCALLY ADVANCED AND RECURRENT RECTAL AND GYNECOLOGICAL CANCER: A SINGLE CENTER EXPERIENCE

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Background: The application of intraoperative radiation therapy to the tumor bed after resection of advanced or recurrent rectal and gynecologic cancer often requires multimodality treatment. Intraoperative radiation therapy (IORT) is a focal approach which aims to improve local control. The aim of this study was to present the preliminary outcomes of IORT pelvic treatments with Intrabeam radiotherapy device.

Methods: We retrospectively reviewed 8 patients treated with IORT following definitive resection of a locally advances or recurrent rectal cancer (4 patients), recurrent squamous cell cervical cancer (3 patients) and recurrent vaginal melanoma (1 patients) from May 2019 to March 2020. All patients were treated with the Intrabeam Radiotherapy System (IRS); in 6 patients treatments were performed with surface applicators, in 2 patients with flat applicator. Median collimator diameter was 4 cm (range 3-5 cm). Median dose of 10 Gy was prescribed to a median depth of 1 mm (surface dose range: 9.3-21, median: 11.7 Gy).

Results: Of 8 patients, 7 had a recurrent disease (87.5%) while 1 patient had locally advanced disease (12.5%). Median follow-up after IORT was 3.2 months (range 1-10 months). At the last follow-up 5 patients had no evidence of recurrent disease (62.5%), 1 patientrevealed distant recurrent disease (12.5%), 1 patient had a pelvic recurrence (12.5%) out-field of IORT treatment, and 1 patient had insufficient follow-up at the time of the analysis. No intraoperative complications were attributed to IORT. Median duration of IORT was 5 minutes (range: 4–19 minutes).

Conclusions: The Intrabeam IRS appears to be a

safe technique for delivering IORT in rectal and gynecological cancer patients. IORT with IRS marginally increased operative time, and did not appear to prolong hospitalization.

P275

DEFINITIVE RADIO-CHEMOTHERAPY WITH INTRALUMINAL HDR BRACHYTHERAPY BOOST FOR OESOPHAGEAL CANCER: A CASE REPORT

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Aims: Oesophageal cancer is a relative rare but aggressive tumour with frequent local and distant failure. When surgery is excluded, definitive radiochemotherapy is the standard treatment. Using HDR brachytherapy (BRT) we can give higher doses to oesophageal lesion avoiding healthy tissues.

Methods: We reported a case of a 70 years old male which a March 2019 was diagnosed an invasive squamous cell carcinoma of the thoracic oesophagus. The lesion, at the EGDS evaluation, was extended from 24 to 32 cm from incisors. After endoscopic ultrasound, total body CT and an FDGPET examination the TNM stage was cT2N0MO. Due to comorbidity surgery was excluded and the multidisciplinary board decided for a definitive concomitant radio-chemotherapy with Carboplatin+Paxlitaxel. A prophylactic percutaneous endoscopic gastrostomy (PEG) was placed for nutritional support during the treatment. The patient completed RTE treatment at the dose of 50.4 Gy in 28 fractions to esophagus and locoregional nodes, using IGRT – VMAT. Four weeks after RTE-CT treatment the patient underwent boost to esophageal lesion using intraluminal HDR BRT technique with192Ir source at the dose of 10 Gy in 2 weekly fractions. The proximal and distal borders of the tumour were defined before with a EGDS. The dose was prescribed at 0,5 cm of mucosal surface and a 2D BRT plan was developed. The esophagus applicator was inserted, under analgesia, into the esophagus at the right distance calculated with EGDS, and fixed to the patient's mouth using a bite block. Brachytherapy treatment was performed in remote afterloading.

Results: Two months after RT-CT and boost with BRT technique an endoscopy evaluation showed absence of residual tumour and mild esophagitis. FDG-PET was repeated after 3 months and confirmeda clinical complete response. At the moment of abstract submission, one year after treatment, the patient is in good clinical condition without evidence of disease and late toxicities. Radiotherapy was good tolerated except for grade 2 acute dysphagia requiring partial use of feeding tube to obtain an adequate caloric intake and avoid weight loss. BRT procedure was well tolerated, without necessity of sedation. No severe toxicity occurred.

Conclusions: Definitive radiotherapy with HDR BRT boost seems an effective and well tolerated treatment for medical inoperable squamous cell carcinoma of the oesophagus. More data and longer follow-up are necessary.

P276

PROSTATE CANCER (PC) PATIENTS (PTS) WITH BONE OLIGOMETASTASES (BM): THE ROLE OF STEREOTACTIC ABLATIVE RADIOTHERAPY (SABRT)

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Aims: After choline-PET/CT early diagnosis of BM, we used SABRT with the intent of improving local control.

Methods: Between October 2010 and March 2020, 26 oligometastatic PC pts with a total of 33 BM were submitted to SABRT. Outcome was evaluated using local control and biochemical progression. Median age was 72 years, median Gleason score at the primary diagnosis was 7. Median time from primary treatment to SABRT was 44 months (m) and median PSA value before SABRT 2.3 ng/ml. 15 (58%) pts developed a bone oligorecurrence during follow-up and were submitted only to SABRT, 11 (42%) pts progressed in course of hormonal therapy (HT), 7 (27%) during adjuvant androgen deprivation therapy (ADT) and 4 (15%) during IInd line hormonal therapy (HT). 4 of 7 pts who received ADT withdrawn HT, whereas all 4 pts treated with IInd line HT continued it after SABRT. 4 (15%) pts underwent SABRT for 2 synchronous BM, and other 2 (7.5%) pts for 3 and 4 BM, respectively. The BM sites were: pelvis in 17 (52%), spine in 10 (30%), ribs in 5 (15%) and femur in 1 (3%) cases. Gross tumor volume (GTV) was delineated using choline-uptake and planning target volume was defined as the GTV plus a 5 mm isotropic margin. The fractionation schemes used were: 5 × 8Gy in 16 (49%), 3 × 10Gy in 13 (39%), and 5 × 6Gy in 4 (12%) lesions. Response was assessed with PSA evaluation scheduled every 3 m during the first year and then every 6 m. Pts with a reduction or a stability of PSA level were considered responders, choline-PET-CT was done only when there was a PSA level increase.

Results: After a median follow-up of 27 m (range, 3-115) and the median time of biochemical progression from the end of SABRT was 11 m (range, 3-115). All

pts had a decrease of PSA level after SABRT. 7 pts (27%) maintained biochemical relapse free until last follow up, while others 19 (73%) pts had a PSA increase. In all these last pts choline PET/CT evidenced an out-field progression of disease with a complete disappearance of pathological uptake of the irradiated targets. 5 of 19 relapsing pts with an out-field bone oligoprogression were submitted to SABRT. No SABRT-related acute or late toxicities were observed.

Conclusions: Our experience shows that SABRT of BM is a highly effective therapy with an excellent risk/benefit profile. The high local cancer control rates in bone oligometastatic prostate cancer pts obtained, suggests the use of SABRT to delay adjuvant ADT or IInd line HT.

P277

ELECTIVE NODAL RADIOTHERAPY IN OLIGORECURRENT PROSTATE CANCER: A MONO-INSTITUTION EXPERIENCE

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Aim: The purpose of this retrospective study is to report oncologic outcome and toxicity of elective nodal radiotherapy (ENRT) in prostate cancer (PCa) patients with pelvic nodal oligorecurrence.

Methods: 41 patients were treated with salvage radiotherapy. Six patients received a total dose of 50.4 Gy (28×1.8 Gy) to the pelvic lymph nodes, without a boost to the positive ones. Thirty-fve patients were treated with simultaneous integrated boost (IMRT-SIB) to deliver a total dose of 50.4 Gy (28×1.8 Gy) to the pelvic drainage, 58.8 Gy (28×2.1 Gy) to the positive pelvic nodes, and 63 Gy (28×2.25 Gy) to the prostate bed (in those nine patients who had prostate bed recurrence). At biochemical recurrence after primary treatment, oligorecurrent disease was detected by positron emission tomography (PET) in 94% of the patients. Image-guided intensity modulated radiation therapy (IMRT) was delivered using tomotherapy. 83% of the patients received androgen deprivation therapy (ADT) during ENRT. Survival analysis was performed with Kaplan–Meier method, log-rank test was used to analyze associations between survival end-points and clinical parameters. Multivariate analysis was performed using Cox proportional hazards regression models. Toxicity was registered according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0.

Results: The median follow-up was 33.6 months. At 3 years, overall survival (OS), cancer-specifc survival (CSS), and biochemical progression-free survival (b-PFS) were 89%, 92%, and 53%, respectively. At univariate analysis, all survival end-points were correlated with the number of positive pelvic lymph nodes at oligorecurrence (≤3 vs >3). Biochemical-PFS was correlated with PSA (p=0.034) and PSA doubling time (p=0.004) at oligorecurrence. At multivariate analysis, no independent variable was statistically signifcant. No patient experienced grade ≥2 late toxicity after radiotherapy.

Conclusions: The number of positive lymph nodes and PSA doubling time seems to be important prognostic factors in patients with oligorecurrent pelvic disease. Salvage radiotherapy combined with short-course ADT might be a reliable treatment option.

P278

VMAT-BASED RE-IRRADIATION FOR LOCALLY RELAPSED PROSTATE CANCER AFTER FIRST-COURSE RADIOTHERAPY

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Aim: The management of prostate cancer (PC) recurrence after definitive or post-operative radiotherapy is still controversial. To date, few data about the use of salvage stereotactic re-irradiation are available and mostly based on the use of robotic techniques. Herein we present acute and late toxicity data and preliminary clinical outcomes of a mono-institutional series of 24 patients treated with Volumetric Modulated Arc Therapy (VMAT)-based SBRT for recurrent prostate cancer after previous radiotherapy.

Methods: Inclusion criteria were: previous definitive or adjuvant/salvage radiotherapy, evidence of biochemical recurrence and radiological detection of local relapse (either with MRI or PSMA/Choline-PET), IPSS<10. CTV was delineated as the prostate gland or as the PET+ area within the prostate bed, and PTV was generated by adding a margin of 5 mm in all directions, except for the posterior margin of 3 mm. Re-irradiation was performed with volumetric modulated arc therapy (VMAT) technique. Toxicity was assessed according to CTCAE v4.0. Assuming p values ≤0.05 as significant, Chi-squared tests were applied for statistical analysis. Kaplan-Meier method and log-rank test were adopted for survival estimates.

Results: Between December 2014 and February, 25 patients with median age 75 years (range, 65-89) underwent re-RT for PC. Relapsed disease occurred within the prostate in 13 cases and prostate bed in 12. Median PSA prior to the second RT was 1.23 ng/ml (0.47 – 7.81 ng/ml). Androgen deprivation therapy was administered in 4 patients. Patients were treated with a median total dose of 30 Gy (25-36 Gy) in 5-6 fractions. Twenty-four patients had at least 3 months of follow-up, for a medi-

an length of 21 months (range, 3-69), and are herein assessed. Acute toxicity was: G1 in 8.3%, G2 in 12.5% for GU; no GI occurred. Concerning late events, G≥2 GU occurred in 19.7% including one G3 urethral stenosis. For GI toxicity we observed one G1, no G≥2. Three patients died with 1- and 2-year overall survival (OS) rates of 95%. Median PSA-nadir post-SBRT was 0.23 ng/ml (0.07 – 4.27 ng/ml). Our 1- and 2-year biochemical relapse-free survival (BRFS) and progression-free survival (PFS) rates were 80% and 54.9%, respectively.

Conclusion: Our data support the use of VMAT-based SBRT as a safe re-treatment for locally recurrent PC with one late G3 GU toxicity reported. Preliminary BRFS and PFS rates are encouraging.

P279

TREATING NODAL METASTASIS WITH PALLIATIVE INTENT: STEREOTACTIC BODY RADIOTHERAPY (SBRT) TO POSITIVE CHOLINE PET / CT LYMPH NODES FOR OLIGOMETASTASIZED PROSTATE CANCER (PCA) PATIENTS

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Aims: The purpose of this study is to evaluate the feasibility and toxicity of based stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer (PCa) patients.

Methods: In this study, oligometastasized PCa patients with nodal (≤ 3 lesions) were treated using SBRT in association with androgen-deprivation therapy. All patients were studied with Choline PET/CT before RT. The prescribed SBRT to pathologic lymph nodes was 8 Gray (Gy), delivered in three fraction to have a better control of organ motion (bowel above all) and normalized so that the 80% isodose covers 100% of the PTV.

Results: Between January 2019 and December 2019, nine oligometastasized PCa patients with a total of twenty nodal metastasis were treated stereotactic on positive choline PET / CT lymph nodes. At a median follow-up of 4 (1-10) months, no toxicity was observed.

Conclusions: SBRT to positive choline PET / CT lymph nodes for oligometastic prostate cancer is a feasible treatment modality with minimal toxicity . Further studies with a longer follow-up are needed to better evaluate late toxicity and local control.

P280

RE-IRRADIATION OF LOCAL RELAPSES FROM PROSTATE CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS STUDY

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Aims: Re-irradiation (RiRT) could offer a chance of cure for highly selected patients, although high quality evidences are lacking. The aim of our study is to provide a literature review on the efficacy and safety of this treatment option.

Methods: The systematic review followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). Only studies where RiRT field overlaps with previous radiotherapy(RT) were taken into consideration. A meta-analysis technique over single arm study was performed in order to determine the pooled acute and late G≥3 toxicity rates,2y and 4y overall mortality (OM), 2y and 4y biochemical failure (BF) Heterogeneity was examined by Cochrane Q chi□square test and I2 statistics. Studies with an I2 statistics of 25–50%, 50–75%, and >75% were deemed to have low, moderate, and high heterogeneity, respectively.

Results: 38 studies met the inclusion criteria, 8 of which were prospective, for a total of 1222 pts. Median follow-up (F-U) from RiRT was 30 months (mth)(10-94 mth), only 1 study having 10 mth median F-U. Previous RT was EBRT, BRT and EBRT+BRT in 29, 4 and 5 studies, respectively, with a median RT dose of 72.5 Gy (52-145 Gy). Mean time elapsed since previous RT was 69 mth (30-150). BRT was the most used RiRT method (27 studies), followed by SBRT (9) and EBRT (2). RiRT prescription doses ranged from 19 Gy in single HDR fraction to 145 Gy (interstitial BRT).The pooled analysis result of G≥3 acute toxicity was 1.4% (95%CI: 0.7–3%; I2 = 77.2, P < 0.001). After omitting 11 studies using EBRT- RiRT, the pooled result was 1.3% (95% CI: 0.5-3.4%) (I 2 = 81.4%, P < 0.001). 103 G≥3 late adverse events were reported, with a pooled result of G≥3 late toxicity of 8.7% (95% CI: 5.8–13%; I2 = 78.9, P < 0.001). No differences in heterogeneity were observed when studies using EBRT to re-irradiate were excluded. With regards to OM, the pooled 2y and 4y rates were 2.1% (95% CI: 1.2–3.7%; I2= 49.9%, P<0.001) and 12.2% (95% CI:7.9–18.8%; I 2=86.1%, P<0.001). The pooled 2y BF rate was 23.6% (95% CI:18.8–29.6%) with high heterogeneity (I 2= 82.4%, P<0.001). Excluding studies using EBRT to re-irradiate, the pooled result was 20% (95% CI:15.6–25.7%; I 2=73.9%, P<0.001). Finally, the pooled 4y BF was 35.6% (95% CI: 28.7-44.3%; I 2=87.1%,P<0.001)

Conclusions: RiRT of PC local relapses showed promising OS and biochemical control rates with a safe toxicity profile. Further studies are warranted to confirm our findings.

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STEREOTACTIC RADIOSURGERY WITH A MONOISOCENTRIC TECHNIQUE IN THE SIMULTANEOUS TREATMENT OF MULTIPLE BRAIN METASTASES: DISEASE OUTCOME AND DECISION STRATEGY ACCORDING TO A VOLUME-BASED APPROACH

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Introduction: Radiosurgery (SRS) or stereotactic fractionated radiotherapy (SFRT) is an effective treatment option in the management of multiple brain metastases (BMs). It can delay in some cases the resort to whole-brain radiotherapy (WBRT). The long-term results of the first world-wide experience with the use of a mono-isocenter non-coplanar technique LINAC-based technique in the treatment of multiple BMs is reported.

Materials and methods: Patients with BMs (maximum diameter 30 mm), life expectancy >3 months and good performance status were treated with simultaneous SRS/SFRT with volumetric modulated arc technique and data were retrospectively evaluated. Local progression-free survival (LPFS), intracranial progression (iPFS), overall survival (OS) and intracranial overall survival (iOS) were evaluated. Predictive and prognostic factors were assessed.

Results: 172 patients accounting for 1079 BMs were treated at our Institution from 2017 to 2020. Median treated metastases were 4 (range 1-22). Primary tumor histology was: lung (44.8%), breast (32%), and melanoma (9.4%). The 1- and 2-year local progression-free survival (LPFS) were 86.7% and 71.6%, respectively. BED ≥47.25 Gy12 correlated with higher local control (HR 0.284 (IC 95% 0.106-0.765) p=0.013). Median time to intracranial progression after the first HA cycle was 6 months (range 4.8-7). Having uncontrolled systemic disease and melanoma histology were factors significantly correlated to iPFS. Patients with >10 BMs had a trend towards worst iPFS (HR 2.119 (IC 95% 0.983-4.566) p=0.055). 31 patients received multiple SRS courses (2-7) in case of intracranial progression. The median iOS was 22.4 months, and the 1- and 2-years iOS were 70.3% and 45.7%, respectively. Brainstem metastases and total PTV >7.1 cc were correlated with worst iOS. WBRT was administered in 23 patients and the 1- and 2-year WBRT-free survival were 83.2%, and 61.1%. One (0.13%) patient was operated for radionecrosis 12 months after SRS. Two patients had pseudoprogression to 12 BMs.

Conclusion: The results in a large patient population treated with a mono-isocenter non-coplanar dedicated technique demonstrated its effectiveness and safety also in case of multiple courses. The reduced treatment time and the possibility to spare safely normal brain gives the possibility to safely treat patients with large number of metastases and to deliver multiple courses of SRS/SFRT. In selected cases the administration of WBRT can be delayed.

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TRENDS IN LOCAL MANAGEMENT OF OLIGOMETASTATIC DISEASE AND INTEGRATION WITH SYSTEMIC THERAPIES. A SURVEY ON BEHALF OF TOSCO-UMBRO INTERREGIONAL RADIATION ONCOLOGY GROUP (GITUOR)

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Aims: Oligomestastatic (OM) disease has been recently the object of several prospective trials and new classification of this clinical entity has been provided by European Society for Radiotherapy and Oncology. To evaluate the trends for definition and management of these patients within the GITUOR, we queried expert members of the group with the present survey.

Methods: A 16 questions survey was proposed to GITUOR members representing 14 different institutions across Umbria and Tuscany.

Results: Twelve out of 14 queried experts declared to follow a pre-defined therapeutic and diagnostic workflow for all OM patients and all regularly participate to a weekly multidisciplinary tumor board. Fifty percent of participants evaluate more than 30 OM patients each year, and 29% of them actively enrol these patients in prospective protocols. Regarding patients classification and local management, 79% of experts define OM status based only on number of metastases and 71% perform stereotactic body radiotherapy (SBRT) both in OM and oligoprogressive patients. Thirteen out of 14 participants consider that OM patients should be treated with radiotherapy schedules providing at least 5 Gy per fraction, and choose their treatment balancing between the higher deliverable BED and critical organs at risk. Adapted schedules (e.g., every other day treatment for critical target site) are provided by 64% of participants. All experts carefully consider type of systemic therapy administered, and 79% actively choose a concomitant or sequential schedule based on drug used. Ninety-three percent of participants discuss both about oncological rationale of SBRT and its integration with systemic management, and declared to be available to participate to a prospec-

tive trial enrolling OM patients.

Conclusions: Experts within GITUOR are actively involved in multidisciplinary tumor boards, provide specific therapeutic workflows for OM patients and evaluate a consistent number of these patients each year. Personalised treatment schedules are administered on the basis of target site and critical OARs. Stereotactic ablative approaches are endorsed by GITUOR members. Of note, the majority of participants consider systemic treatments administered in their decisional algorithm. Despite the active participation in treatment workflow, implementation of prospective protocols should be encouraged in order to provide robust data in this particular setting of patients.

Table 1.

Question	n (%)
1. Years of practice	0-5 yr :0 5-10 yr: 2 (14.3) 10-15 yr: 2 (14.3) >15 yr :10 (71.4)
2. Institution of membership	Hospital: 9 (64.3) University Hospital: 4 (28.6) IRCCS-Cancer Care center: 0 Private structure: 1 (7.1) Other (specify): 0
3. Pre-defined therapeutic and diagnostic workflow for all OM	Yes: 12 (85.7) No: 0 In implementation: 2 (14.3)
4. Multidisciplinary Team Implemented?	Weekly: 14 (100) Monthly: 0 No: 0 In implementation: 0
5. Definition of Oligometastatic based on	Number of metastases (≤ 3; ≤ 5;≤10): 11(78.6) Site of metastases: 0 Primary tumor: 0 Patients clinical history: 3 (21.4)
6. Number of oligometastatic patients evalued	≤10: 2(14.3) >10: ≤30: 5(35.7) >30: ≤50: 3(21.4) >50: 4(28.6)
7. Any specific protocol in your institution?	No: 6() Yes, internal protocol for routine management: 4(28.6) Yes, EC approved prospective protocol: 4(28.6)
8. About Oligometastatic setting:	No ablative RT should be recommended: 0 Ablative RT should be recommended only if all lesions are treated: 3 (21.4) Ablative RT could be recommended also for oligoprogressive patients Technique unavailable: 11
9. Fractionation	Conventional (≤3 Gy per fraction): 0 Moderately hypofractionated (>3, <5 Gy per fraction): 1(7.1) Stereotactic (≥5 Gy/fraction): 13(92.9)
10. Do you verify treatment BED based on Alfa/beta ratio	At least BED 100 based on alfa/beta ratio: 1(7.1) Try to use the safest dose/fractionation regimen: 0 Try to find the best compromise between highest BED deliverable and respect of critical OAR constraints: 13(92.9)
11. Preferred dose/fractionation schedule	Every other day: 2 (14.3) Daily: 3 (21.4) Depending on patient (e.g treatment site, OAR criticities, concomitant systemic treatments etc.): 9 (64.3)
12. How to choose correct treatment schedule?	Treatment site: 0 OAR criticities: 0 Concomitant systemic treatments: 0 All previous answers: 14 (100) None of the previous answers:0
13. Systemic treatments (ADT excluded)	Always concomitant Under medical oncologist prescription Discontinuation according to drug half-life: 3 (21.4) According to target site and farmacodinamics: 11 (78.6)
14. Immunotherapy?	Same management of other drugs: 9 (64.3) Specific protocols adopted: 0 You administer treatment between two cycles: 5 (35.7)
15. Within the MDT	You only care for RT management of oligometastatic patient: 0 You manage as well oncological rationale of local ablative management: 1(7.1) You manage as well integration with systemic therapies: 13(92.9)
16. Would you participate to prospective trials on this issue?	Yes: 13(92.9) No, I would not enroll sufficient number of patients: 1 (7.1) No, I think that scientific interest would be negligible: 0

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RADICAL HIGH DOSE RADIOTHERAPY FOR LIMPH NODE OR BONE METASTATIC PROSTATE CANCER: A SINGLE INSTITUTION EXPERIENCE

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Aim: High dose (HD) radiotherapy (RT), with radical intent, is used more and more in prostate cancer (PCa) oligometastatic patients (pts) with good outcomes and low toxicity profile. The aim of this retrospective study is to evaluate the results of HD-RT in only lymph-nodal (LN) versus only bone (B) PCa oligometastatic disease.

Methods: Pts with 1-2 B or 1-5 LN metastases, treated with radical doses, were considered for this analysis. From February 2005 to June 2019, 192 oligometastatic PCa pts (150 LN, 42 B) were treated in our Institute. RT was delivered with helical IMRT (TomoTherapy®, Accuray, Sunnyvale, CA) prescribing high doses, with radical intent. All pts were treated with extended nodal radiotherapy (ENRT) (pelvic in 76 pts, para-aortic in 27 pts, mediastinal in 13 pts, pelvic + para-aortic in 76 pts) to a median dose of 51.8 Gy/28fr. In pts of the LN group a simultaneous integrated boost (SIB) on 11C-Choline PET/CT (PET/CT) positive nodes was prescribed to a median dose of 65.5 Gy/28fr. In B group, bone metastases were treated to a median dose of 51.8 Gy/28 fr. In all patients not previously treated, prostate or prostatic bed was irradiated (median EQD2 88 Gy and 74 Gy respectively). In 83% of pts androgen deprivation therapy (ADT) was prescribed, for a median of 35 months (range 0-84), but 38 of them were already castration resistant. Acute and late toxicities were graded according to CTCAE v 5.

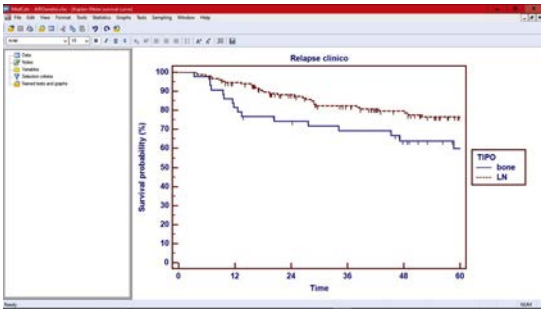

Figure 1.

Results: Median follow up was 59.7 months (range 11.3-148.9). Late toxicity was acceptable and, in all cases, caused by prostate/prostatic bed irradiation: 12 pts presented grade (G) 3 genitourinary (GU) toxicity, 1 patient G 4 GU toxicity and 3 pts G 3 rectal toxicity. At the time of analysis 62 pts were dead, 26 of whom for PCa progression. ADT influences biochemical relapse free survival, thus disease free survival was used for outcome evaluation (see Figure 1). However 41% of pts never experienced a biochemical relapse after RT. The 5 years- DFS was 60% in B group and 77% in LN group (p-value 0.05).

Conclusions: In this large cohort of already metastatic patients with a long follow up, good results in term of systemic tumour control were observed after HD-RT, with radical intent. Apparently LN oligometastatic pts have a better outcome than B oligometastatic pts, but the results are satisfactory also in the later group. Further investigation, already scheduled, is warranted to identify the patients who most benefit from this treatment modality.

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1.5T MR-GUIDED METASTASIS DIRECTED SBRT FOR OLIGORECURRENCES: PRELIMINARY REPORT ON SAFETY AND PATIENT REPORTED OUTCOMES (PROMS)

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Aims: Since October 2019 1.5T MR-Linac has become clinically available at our department for several indications, including treatment of PET-detected oligometastases. Treatment aim for these patients is local control and to delay potentially more toxic systemic therapy. Magnetic resonance-guided stereotactic body radiotherapy (MRgSBRT) could improve tumor target visibility and allows to perform daily adaptive delivery requiring high patient compliance compared to conventional techniques and prolonging treatment times. Our endpoint is to report on feasibility and patient-reported tolerance of SBRT on the 1.5T MR-linac for oligometastases, based on our first clinical experiences.

Methods: Twenty consecutive patients were enrolled in an ethical committee approved prospective observational study (Protocol n. MRI-LINAC 23748) and treated with MRgSBRT on a MR-Linac (Unity, Elekta AB, Stockholm, Sweden) between October 2019 and April 2020. All patients had prostate cancer lymph node or bone metastases detected with Gallium-68 prostate-specific membrane antigen (PSMA) or 18F-choline positron emission tomography (PET) scans. Two different online workflows were used depending on the OARs daily anatomical situation: Adapt To Position (ATP) workflow where the reference plan position is adjusted rigidly to match the position of the critical structures, and Adapt To Shape (ATS) workflow where a new plan is created to improve matching of the daily anatomy. Patient treatment tolerance was prospectively assessed using patient-reported outcome measures (PROMs).

Results: Twenty-five lesions in 20 patients were treated: the most commonly treated anatomic sites were nodal (n=16) and pelvic bone (n=9). Median PSA value pre-MRgSBRT was 1.16 ng/mL (range,0.27–8.9), whereas median PSA value at first follow-up after MRgSBRT was 0.44 ng/mL (range,0.06 – 8.15). At first follow-up, for 16 patients a PET-CT was performed detecting respectively in 6 cases partial response and in 10 cases complete response. The mean dose was 35 Gy in 5 fractions and the mean treatment time was 31 min. Overall, MRgSBRT was safe and well tolerated in the patients population according to the PROMs. No G2 or higher toxicities were recorded.

Conclusions: 1.5T MR-linac MRgSBRT was feasible and safe for oligometastases treatment and well tolerated by all patients. The adaptive workflow allows full online planning based on daily anatomy. Prospective clinical studies with larger patient cohort are necessary to confirm the benefit of MR-guided on-table adaptive radiotherapy.

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SALVAGE ROBOTIC SBRT FOR OLIGOMETASTATIC LYMPH NODAL RELAPSE IN GYNECOLOGICAL CANCER

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Aim: Patients (pts) with oligometastases from gynecological malignancies are considered among the most promising candidates for stereotactic body radiation therapy (SBRT). The aim of this retrospective analysis is to evaluate toxicity and local control (LC) of robotic SBRT (CyberKnife® -Accuray, Sunnyvale, CA-CK), in the management of lymph nodal metastases (LMN) from gynecological cancer.

Material and method: From 02/2018 to 03/2020, 31 LMN from 19 (pts) were treated with CK. Median prescribed dose was 35 (30-45) Gy in 3-5 fractions (fr), at a median isodose of 80% (70-84%). Four (13%) of target volumes were in the same radiation field of previous adjuvant or salvage radiotherapy treatment performed with Image-Guided Intensity Modulated Radiotherapy (IG-IMRT) to a total dose of 50.4 Gy/28 fr. The primary cancer of these pts was: ovarian in 9 (47%) pts, endometrial in 8 (44%) pts, cervical cancer and fallopian tube carcinoma respectively in one (4.5%) patient. Forty five% (14) of LNM locations were periaortic, 26% (8) mediastinal, 16% (5) pelvic, and 13% (4) in other sites (retroclavicular, supraclavicular, axillary and inguinal). Gross tumor volume (GTV) was delineated on the fused CT (slices of 1.25 mm) and PET/CT images in all pts. Planning tumor volume (PTV) was obtained by adding an isotropic expansion of 3 mm to GTV. Radiological/Nuclear Medicine imaging and clinical follow up were performed every 3 months to assess treatment response.

Results: Median follow-up was 9.8 months (range 2.2–26.6). Radiotherapy was safely delivered, all pts completed the prescribed treatment. Tumor response, evaluated with fluorine-18 fluorodeoxyglucose-positron emission tomography (FDG-PET)-computed tomography (CT), was: complete response (CR) in 27 (88%) pts, partial response (PR) in 1 (3%) pts, stable disease (SD) in 1 (3%) pts, and progression of disease (PD) in 2 (6%) pts. The treatment was very well tolerated and no RTOG grade (G) ≥ 2 acute and late toxicities were reported; RTOG G1 dysphagia (associated

with 5 of 9 mediastinic treatments) and fatigue (3 of all 19 pts) were the most common side effects.

Conclusions: Robotic SBRT in oligometastatic lymph nodal relapse of gynecological tumors is a safe approach, with good results in terms of LC. A longer follow up is needed to confirm these findings.

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THE ROLE OF STEREOTACTIC BODY RADIOTHERAPY IN THE MANAGEMENT OF METASTATIC SALIVARY GLAND CARCINOMA- A MULTI-INSTITUTIONAL STUDY OF AIRO - HEAD AND NECK WORKING GROUP

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Aims: The role of radiation therapy (RT), particularly Stereotactic Body RT (SBRT), in the management of oligometastatic disease is currently estabilished in different oncological settings but data on salivary gland cancer (SGC) are lacking. The aim of this study was to investigate the role of RT in oligometastatic SGC patients, focusing the attention on SBRT.

Methods: We performed a retrospective, multicentric analysis of patients with oligometastatic SGC treated with palliative conventional RT or SBRT. Endpoints included response evaluation of the target lesion according to RECIST criteria and local control (LC) for both SBRT and conventional RT.

Results: Between 2006 and 2016, 64 patients were collected from 9 Italian Cancer Centers, on behalf of the Italian Association of Radiotherapy and Clinical Oncology (AIRO) Head and Neck Working Group. Thirty-seven patients (57.8%) were suffering from Adenoid Cystic Carcinoma (ACC) and 27 patients (42.2%) had non-ACC. Thirty-four patients underwent palliative RT (53,1%) and 30 received SBRT (46,9%). The most common metastatic sites were bone for palliative RT and lung for SBRT. We observed an overall clinical benefit (including Complete Response, Response Partial, and Stable Disease) in all patients receiving SBRT, while all PD were observed in patients treated with conventional RT. After a median follow-up of 29.2 months (range 2.3-117.1), LC at 12 months was 57.5% (95%CI 35.1-74.6) for patients treated with SBRT. Considering only ACC patients (n=37), a significant LC benefit was observed for patients receiving SBRT compared to conventional RT technique (p=0.05). The total amount of deaths was higher for conventional RT compared to SBRT.

Conclusion: This is the first multicentric study, focusing exclusively on oligometastatic SGCs patients treated with advanced RT techniques evaluating the outcome after SBRT. We confirmed the potential role of SBRT in the management of oligometastatic SGC patients. SBRT could be a valid approarch to control limited burden of disease considering the lack of truly effective systemic therapies.

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TREATMENT STRATEGY FOR BRAIN METASTASES: RADIOTHERAPY AFTER UPFRONT CNS-ACTIVE SYSTEMIC AGENTS

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Aims: Primary lung and kidney cancers, and melanoma have an high tendency to spread to the brain. Historically, Whole Brain Radiation Therapy (WBRT) has been the most common treatment modality for brain metastases (BM). Stereotactic Radiation Therapy (SRT) offers an effective ablative treatment option for limited BM and its role is expanding in the treatment of multiple metastases too. Since an increasing number of biological therapies has demonstrated to be able to cross the blood-brain barrier, an upfront systemic therapy with CNS-active systemic agents instead of upfront WBRT or SRT could be considered appropriate for these tumor types, especially in asymptomatic patients. In view of the lack of data from prospective clinical studies that compared the timing of biological therapies (TKIs/immunotherapy) and brain radiotherapy (RT), a study was conducted to evaluate the impact of the timing of the two treatment methods on clinical outcomes.

Methods: We retrospectively evaluated patients with BM from non small cell lung cancer (NCSLC), kidney cancer and melanoma treated in our Department with upfront CNS-active systemic agents and WBRT or SRT for intracranial progression disease between 2015-

2019. Neurotoxicity was clinically evaluated with RTOG/EORTC scale. Overall Survival (OS) was defined from the start of biological therapies. Local control (LC) was calculated considering the clinical responses after RT (any response excluding progression disease).

Results: Clinical and treatment patients characteristics of 19 analyzed are detailed in Table 1. Median OS (mOS) was 12 months (range 1-67). For 9 patients who underwent to SRT mOS was 12 months (range 1-67), whereas mOS for 10 WBRT patients was 11 months (range 4-29). Therefore mOS was 9 months (range 1-20) for the 5 symptomatics, mOS of 12 months (range 4-67) for the 14 asymptomatics. Clinical response was evaluated in 15/19 patients: 6 complete responses, 5 partial responses, 1 stable disease and 3 progressions. With a median follow-up of 12 months, LC was 80.0%. Late Grade 1 toxicity (headache and concentration impairment) was recorded in 3 patients. No radionecrosis was observed.

Conclusions: Our data, in line with literature, showed good rates of OS and tolerability in patients treated with upfront CNS-active systemic agents and delayed brain RT for intracranial progression disease. A future prospective study is needed to confirm the effectiveness of this therapeutic strategy for these patients.

Table 1. Clinical and treatment characteristics of analyzed patients (n = 19)

Characteristics	All patients *n* (%)	WBRT *n* (%)	SRS *n* (%)
Gender			
Male	11 (57.9)	5 (45.5)	6 (54.5)
Female	8 (42.1)	5 (62.5)	3 (37.5)
Age (years)			
< 65	12 (63.2)	6 (50.0%)	6 (50.0%)
≥ 65	7 (36.8)	4 (57.1)	3 (42.9)
ECOG PS			
0-1	14 (73.7)	8 (57.1)	6 (42.9)
≥2	5 (26.3)	2 (40.0)	3 (60.0)
Pathological type			
NSCLC	5 (26.3)	4 (80.0)	1 (20.0)
Kidney carcinoma	3 (15.8)	0 (0.0)	3 (100.0)
Melanoma	11 (57.9)	6 (54.5)	5 (45.5)
Number of BM			
1-3	13 (68.4)	4 (30.8)	9 (69.2)
>3	6 (31.6)	0 (0.0)	6 (100.0)
Extracranial metastases			
Yes	15 (78.9)	7 (46.7)	8 (53.3)
No	4 (21.1)	3 (75.0)	1 (25.0)
CNS-active systemic agents			
Immunotherapy	8 (42.1)	6 (75.0)	2 (25.0)
TKIs	11 (57.9)	4 (36.4)	7 (63.6)
Neurological symptoms			
Yes	5 (26.3)	4 (80.0)	1 (20.0)
Not	14 (73.7)	6 (42.9)	8 (57.1)

Legend: BM= brain metastases; PS= performance status; NSCLC= non-small cell lung cancer; RT= radiotherapy; WBRT= Whole Brain Radiation Therapy; SRT= Stereotactic Radiation Therapy; TKIs =tyrosine kinase inhibitors

P288

A RARE SITE OF METASTASIS IN THE SPHENOID BODY IN A OLIGOPROGRESSIVE PROSTATE CANCER: A CASE REPORT

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Aims: Prostate cancer metastasizes most commonly to the pelvic lymph nodes and axial skeleton; on the contrary, metastases in the head neck region are unusual. We evaluated the feasibility and toxicity of IMRT\IGRT with Helical Tomotherapy (HT) for the management of a single sphenoid body metastasis in a oligoprogressive prostate cancer.

Materials and Methods: In August 2016, a 71-year-old man was admitted to our Radiation Therapy Department with biopsy proven diagnosis of prostate adenocarcinoma Gleason Score 9 (4+5) and PSA level: 12.44 ng/ml. From October 2016 to December 2016 he was treated with moderate hypofractionated Helical Tomotherapy (HT) for curative intent (70 Gy in 28 fractions to the prostate, 61.6 Gy to the seminal vesicles and 50.4 Gy to pelvic lymph-nodes irradiation), associated to ADT. In July 2019 due to the PSA increasing (6.9 ng/ml), the patient underwent a PET colin which detected a D3 involvement. Considering the oligoprogressive disease and the castration resistant setting, the patient was eligible to receive abiraterone acetate 500 mg, in association with SBRT on the D3 bone metastasis (30 Gy in 5 fx). In December 2019, another PET colin detected a metastasis in the sphenoid body (SUV max 8.7) and a magnetic resonance imaging (MRI) of the brain confirmed the presence of a 20x16 mm osteolytic area. The PSA at that time was 2.4 ng/ml. Thus, we decided to treat the sphenoid bone with SBRT using Tomotherapy Hi-art system in helical modality with a total dose of 25 Gy in 5 Fractions (5Gy/fx).

Results: Radiotherapy was well tolerated, without acute and late adverse effects according to CTCAE 5.0 tox. At the last follow-up in May 2020, the PSA decreased to 1.8 ng\ml and the last PET colin revealed a metabolic response (SUV 4.9 vs 8.7). The patient continue the treatment with abiraterone acetate 500 mg.

Conclusion: The Sphenoid body is a rare site of metastasis in prostate cancer. We report that SBRT in oligometastatic prostate carcinoma is an effective and well tolerated therapy.

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HYPOFRACTIONATION, ABIRATERONE AND PREDNISONE IN THE TREATMENT OF BONE METASTASES IN PATIENTS WITH HORMONE REFRACTORY PROSTATE CANCER

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Aims: The hypofractionated radiotherapy plays a fundamental role in the treatment of bone metastases. At our center, we evaluated the feasibility and effectiveness of two schemes hypofractionation: 8 Gy single

dose and 8 Gy in two fractions to be made within a week of each other. The two irradiation techniques have been associated with the new molecules used in medical therapy.

Methods: From July 2014 to March 2020 they were treated 52 patients with bone metastases from hormone refractory prostate cancer . The median age of patients studied was 71 years with bone metastasis respectively localized in the dorsal and lumbar spine in 50% of cases, 30% at the level of bilateral lower limbs and the remaining 20% at the level of the pelvis. Radiation therapy was by hand in a single dose in 60% of cases in patients with worse P.S. while in the remaining 40% it was backed bifractionation treatment. All patients were administered simultaneously, the abiraterone acetate 1 g / day, prednisone 10 mg/day in combination with LHRH analogue every three months.

Results: All patients were reassessed after 30-40 days of therapy. In no case were registered signs of toxicity. In 80% of cases there has been a reduction in their analgesic therapy administered dose.

Conclusions: In our experience, the radiotherapy hypofractionated 8 Gy in a single session or, alternatively, 8 Gy in two weekly sessions in conjunction with the abiraterone acetate was well tolerated and had a good impact both as regards the control of the pain is the improvement of quality of life.

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RE-IRRADIANTION FOR LOCOREGIONALLY RECURRENCE IN SMALL CELL LUNG CANCER: A CASE REPORT

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Aims: The aim of the present study was to assess the safety and efficacy of re-RT of the thorax using Volumetric Modulated Arc Therapy-Stereo Body Radiation Therapy (VMAT-SBRT) in a woman affected by recurrence disease Small Cell Lung Cancer (SCLC).

Methods: A 66 year-old woman affected by SCLC (cT2aN2M0, stage IIIA; limited disease) underwent to definitive chemo-radiotherapy (CHT) (45 Gy in 30 fractions-twice daily, concurrently with 4 courses of cisplatin (80 mg/ square) and etoposide (100 mg/square × 3)). She tolerated the chemo-radiotherapy with no serious adverse effects. At the end of CHT, total body CT scan revealed the complete resolution of the mediastinal mass and the brain metastases in the temporal lobe. So, the patient received Whole Brain Irradiation (WBRT) with a dose of 30 Gy in 10 fractions. After 12 months, a loco-regional recurrence on the thorax was detected by FDG-PET/CT total body imaging. Therefore a re-irradiation with an SBRT-VMAT-SIB technique on the uptaking lesion has been planned. Gross Tumor Volume (GTV) was defined as the uptaking lesion on FDG-PET, while a GTVboost was identified as the area of highest FDG uptake.In addition, the CTV on CT during three phases (under normal breathing, and with breath holding during expiratory and inspiratory phases) was superimposed to represent the Internal Target Volume (ITV). The PTV margin for ITV was 5 mm in the lateral and anteroposterior directions and 10 mm in the cranio-caudal direction. SIB consisted of delivering 37,5Gy to the PTVboost while delivering 35Gy to PTV in 5 fractions (on alternate days). In order to minimize the risk of cardiac toxicity, cumulative administered Target doses and Heart Dmean and D(0.1cc) were calculated by summing doses of prior radiotherapy and re-irradiation in term of EQD2.

Results: The Cumulative administered EQD2 (α/β=10) was 97.8Gy and cumulative BED was 117.4Gy. Focusing to cardiac toxicity, Heart Cumulative Dmean (α/β=3) was 45,7Gy (BED=76,2Gy), while Heart cumulative D(0.1cc) was 96Gy (BED=160Gy). The treatment was well tolerated.

Conclusions: Re-irradiation with a VMAT-SBRT technique may represent a safe option for the treatment of locoregionally recurrent SCLC Further research is required to identify the long-term safety and efficacy in a larger number of patients.

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CORRELATION BETWEEN RADIOLOGICAL AND BIOLOGICAL FEATURES AND CLINICAL OUTCOMES IN EARLY PROSTATE CANCER: AN EXPLORATORY SUBGROUP ANALYSIS (AIRC IG-13218 SUBSTUDY)

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Aim: PTEN deletion and Ki-67 expression are two of the most promising biomarkers in prostate cancer (PCa). Multiparametric magnetic resonance imaging (mp-MRI)-guided biopsy is a powerful tool for identifying clinically significant PCa and this method can be used to correctly stage PCa. The aim of the study is to assess whether a correlation can be identified between the pathological stage defined by a mp-MRI-guided biopsy and Ki-67 expression and PTEN deletion. Such

correlation might be useful for the staging and treatment personalization in PCa.

Table 1. Patients tumour characteristics.

Patient index	IPSA (ng/ml)	TRUS Biopsy GS	mpMRI-Biopsy GS	up/down grading	Prostate Volume (cm^3)	PI-RADS max	ECE max	Ki-67 expression (%)	PTEN deletion assessment
1	1.1	4+3	3+4	down	< 50	4	3	18	deletion
2	8.1	4+3	3+3	down	< 50	4	3	18	no deletion
3	5.95	3+4	3+3	down	> 50	3	3	16	deletion
4	6.7	3+3	3+3	confirmed	< 50	5	4	6	no deletion
5	4.08	3+4	3+4	confirmed	< 50	4	1	16	no deletion
6	6.07	3+4	3+4	confirmed	< 50	3	3	40	deletion
7	2.5	3+4	3+4	confirmed	> 50	3	2	10	no deletion
8	12.5	3+4	3+4	confirmed	< 50	4	3	18	no deletion
9	5.35	3+4	3+4	confirmed	< 50	4	3	18	no deletion
10	7.41	3+3	3+3	confirmed	> 50	4	4	20	no deletion
11	6.32	3+3	3+3	confirmed	< 50	3	1	n.a.	no deletion
12	5.3	3+3	3+3	confirmed	< 50	4	2	16	no deletion
13	4.5	3+4	3+4	confirmed	< 50	5	4	20	deletion
14	5.66	3+4	3+4	confirmed	> 50	4	2	20	no deletion
15	11.7	3+3	4+3	up	< 50	5	3	18	no deletion
16	11.2	3+4	4+4	up*	< 50	5	1	35	no deletion
17	7.98	3+3	3+4	up	< 50	4	2	14	no deletion
18	7.7	3+3	3+4	up	< 50	3	3	15	deletion
19	7.5	3+3	3+4	up	< 50	4	2	22	no deletion

*patient who suffered a recurrence. Legend: iPSA = initial prostate-specific antigen, TRUS = transrectal ultrasounds, GS = Gleason score; mpMRI = multiparametric magnetic resonance imaging, PI-RADS= Prostate Imaging reporting and Data System, ECE = extracapsular extension, PTEN = phosphatase and tensin homolog.

Methods: The study has been conducted in the context of the phase II clinical study "Short-term radiotherapy for early prostate cancer with concomitant boost to the dominant lesion" (AIRC IG-13218), Clinical Trials.gov identifier: NCT01913717. Nineteen patients accepted to undergo a further mp-MRI guided biopsy on Dominant Intraprostatic Lesion (DIL), and a new Gleason Score (GS) was assessed. PTEN loss and Ki-67 expression were evaluated on these samples. A correlation between up/downstaging, PTEN loss and Ki-67 expression was analysed and related with PCa outcomes (overall survival, biochemical and clinical relapse). This study was part of research notified to our Ethical Committee (nr N79).

Results: Nineteen patients were included in the analysis (Table 1). For 5 patients an upgrade of GS was found, with 4 patients classified as intermediate-risk instead of low-risk, 1 patient as high-risk instead of intermediate-risk. This patient experienced a local clinical relapse. No correlations between up/down-staging, PTEN deletion and Ki-67 expression were observed.

Conclusions: Further investigations need to be performed towards the identification of a pattern in the tumour aggressiveness-response in PCa treated with ultra-hypofractionated radiotherapy. Moreover, a possible relationship between biomarker analysis and imaging textural features could be also explored.

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LOCAL-CONTROL AFTER EXTERNAL BEAM RADIOTHERAPY (EBRT) ON BONE METASTASES FROM WELL DIFFERENTIATED THYROID CARCINOMA (DTC): REAL-LIFE EXPERIENCE OF A SINGLE CENTER

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Aims: Well differentiated thyroid carcinoma (DTC) is associated with good-long-term prognosis and radioiodine therapy (RAIT) is the definitive treatment of choice. However, bone metastases are associated with worse QoL and overall survival. We evaluated the impact of EBRT combined with RAIT on metastatic bone lesions (BML), in terms of local control and pain relief.

Methods: We retrospectively analysed 30 patients (pts) treated with EBRT on one or more BML from February 2012 to October 2019 at Radiation Oncology Center of S. Orsola University Hospital (Bologna). Contrast enhanced CT (ceCT) or 18F-FDG-PET/CT scans were performed before and at least 2 months after the end of EBRT. Local response to treatment was assessed according RECIST and PERCIST criteria. NRS scale was used to estimate subjective pain response.

Results: Of 31 pts treated, BML were synchronous in 60% (n=18) and metachronous in 40% of pts (n=12). All pts received at least one RAIT (mean cumulative dose: 410mCi, range:900-100mCi). 22/31 pts received intravenous monthly bisphosphonates and 16/31 pts started TKI therapy. A total of 67 BM lesions were treated. EBRT was delivered in 1-25 fractions, with a median dose of 30 Gy (range: 8-50 Gy). 5/67 BML were re-irradiated. 9/67 MBL were also treated with surgery (n=6) or embolization (n=3). Mean FU was 29.8 months (range: 3-82 months). 4/30 pts were lost at FU. Acute EBRT adverse events were mild and rare. FU imaging was performed with 18F-FDG-PET/CT for 39/67 BML and with ceCT for 8/67 BM lesions; restaging for 20/67 BM lesions was not assessed with the same imaging exam, thus local response data are lacking. 18F-FDG PET/CT response assessment was: stable metabolic disease in 16/39 BML (41%), partial metabolic response in 11/39 BML (28%), complete metabolic response in 11/39 BML (28%) and metabolic progression in 1 BML. CeCT showed stable disease in 8/8 BML (100%). Pain was the most frequent clinical presentation and 15/26 pts (58%) were symptomatic. Overall, 3/15 pts had mild pain (NRS score<5) and 12/15 pts had severe pain (NRS>=5). Pain decreased in all pts and completely disappeared in 9/15 pts (60%).

Conclusions: According to literature data EBRT, combined or not with other local therapies, is effective in terms of local control and pain relief in pts with DTC bone metastases.

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HIGH-DOSE SALVAGE ROBOTIC STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR PROSTATE/PROSTATE-BED RELAPSE AFTER PREVIOUS RADIOTHERAPY

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Purpose: To present early outcome and toxicity after salvage robotic SBRT (CyberKnife®, Accuray, Sunnyvale, Ca) re-irradiation of patients with intraprostatic/ prostate-bed failure of pelvic malignancies.

Methods: Between June 2018 and March 2020 10 pts were treated with robotic SBRT for intraprostatic/ prostatic bed failure after previous RT. One patient for a prostate metastasis of rectal mucinous adenocarcinoma after previous neoadjuvant radio-chemotherapy followed by surgery. Three pts for intraprostatic relapse after previous radical RT. Five pts for local recurrence in prostate bed; a sixth patient had two recurrences, one perirectal, the other in front of bladder. Median age at initial diagnosis was 67.5 (47.4-77.7) years. Median initial PSA was 11.00 (3.70-11.46) ng/ml. Median GS score was 7 (6-9). Median prior RT dose was 72 (45-78) Gy and the median interval to relapse was 54 (5-128) months. Median PSA before robotic SBRT was 2.19 (1.14-4.79) ng/ml. Fiducial markers were implanted into the target in 9 of 10 patients. One patient was treated with spinal tracking. Median SBRT total dose was 35 (25-40) Gy in 5 fractions (EQD2=85 Gy, for α/β 1.5). Prescription isodose was 70% (63-81%). Rectal cancer intraprostatic relapse was treated with 40 Gy/ 5 fr at 78.5% isodose. In three patients previously treated with radical radiotherapy a "urethral sparing HDR-like technique" was used, prescribing to the isodose of 63-64%, to escalate the dose inside the target up to EQD2= 199.8 Gy. Four patients received neoadjuvant or concomitant/adjuvant LH-RH analogue and one of them Enzalutamide. Steroid prophylactic therapy was prescribed in 7 pts and alpha-lytic therapy in three pts.

Results: Median follow up was 12 (2.4-24) months. Acute toxicity up to grade 2 genito-urinary and pain (CTCAE v 5.0) was observed in 3 of 10 pts. Only one patient presented late toxicity: G1 nocturia and urinary frequency, six months after the end of treatment. No acute and late rectal toxicity was observed. Median PSA at the last control was 0.17 (0.006-19.59) ng/ml. One patient presented biochemical PD with negative repeated PSMA and choline PET/CT at 12.00 and 19.59 ng/ml. One patient died in an accident 2.4 months after the treatment. All other patients are alive, with disease control.

Conclusions: High-dose SBRT re-irradiation is safe and feasible. Longer follow-up is needed to confirm these good results.

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CUMULATIVE DOSE, TOXICITY AND OUTCOMES OF SPINAL METASTASES RE-IRRADIATION: A SYSTEMATIC REVIEW ON BEHALF OF THE RE-IRRADIATION WORKING GROUP OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims: The main aim of this study was to identify either patient, tumor, or treatment related factors which may affect disease related outcomes of re-irradiation in patients with previously irradiated vertebral metastases.

Methods: A computerized search of the literature was performed by searching terms related to reirradiation (reRT) and spinal tumour or localizations in MEDLINE, EMBASE, OVID, and Cochrane database from 1995 to 2019. Studies including at least 10 patient who had received reRT at the same site of initial radiotherapy for vertebral metastases with localized external beam radiotherapy were included. To determine the pooled ≥G3 acute and late toxicity rate, pain relief, local control and overall survival a meta-analysis technique over single arm study was performed. Heterogeneity across studies was examined by the Cochrane's Q chi□squared test and the I2 statistic. Studies with an I2 statistic of 25–50%, 50–75%, and >75% were deemed to have low, moderate, and high heterogeneity, respectively.

Results: Twenty studies, which included a total of 1241 patients, met the inclusion criteria for this systematic review. One study was a prospective phase I-II trial; all the others were observational studies of either retrospectively or prospectively collected data (16 and 3 studies, respectively). The pooled pain relief, 1-year local control, and 1-year overall survival rates were 74.3%, 78.5% and 55.2% with moderate to high heterogeneity among studies. No difference in heterogeneity was evidenced for both pain relief and local control after omitting studies not using stereotactic body radiotherapy (SBRT) or studies delivering BED < 45Gy10, whereas heterogeneity for 1-year OS was lower after omitting studies not using SBRT and delivering BED < 45Gy10. This finding may be due to the inclusion of patients with longer life expectancy in studies using

SBRT or higher doses. The pooled results of grade ≥ 3 acute and late toxicity were 0.4% (95%CI: 0.1–1.1%) and 1.6% (95%CI: 0.8–34%), respectively with low heterogeneity among studies.

Conclusions: While this systematic review confirmed that reRT is both safe and effective for treating patients with recurrent spinal metastases, it could not identify factors which may affect outcomes of reRT in this patients' population. Analysis of large real-world high-quality datasets may better address this issue.

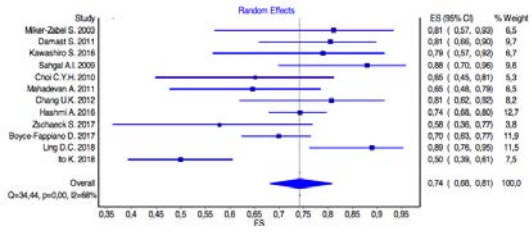

Figure 1. Pooled objective pain relief in re-irradiated patients for included studies.

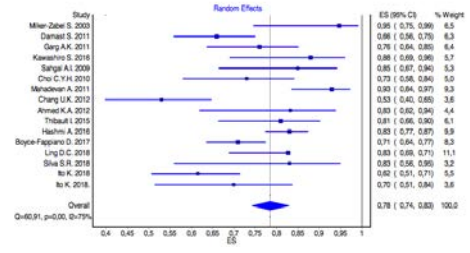

Figure 2. Pooled objective 1-y local control in re-irradiated patients for included studies.

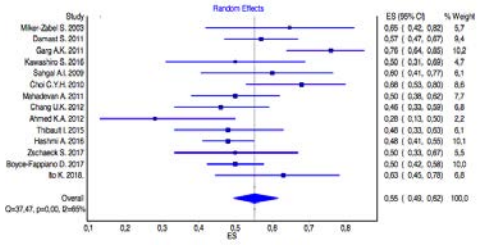

Figure 3. Pooled objective 1-y overall survival in re-irradiated patients for included studies.

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SYSTEMATIC REVIEW OF STEREOTACTIC BODY RADIOTHEREAPY FOR NODAL METASTASES IN OLIGOMETASTATIC PATIENTS.

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Aim: Lymph node metastases (NMs) are a common route of tumor spread. The aim of this analysis was to assess the efficacy of stereotactic body radiotherapy (SBRT) in terms of local control (LC) and progression-free survival (PFS) in this setting.

Methods: A systematic literature search from the earliest date to July 25th, 2019 was performed following PRISMA guidelines and using PubMed, Embase, and Cochrane databases. Papers reporting LC and/or PFS in patients with NMs from solid tumors treated with < 10 fractions of SBRT were selected. The clinical outcomes rates were pooled by means of a random or fixed-effect model.

Results: Twenty-nine studies were eligible (969 patients with NMs: 938 assessable for LC and 698 assessable for PFS). All but three studies were retrospective analyses. LC and PFS results were reported in 28 and 18 papers, respectively. Heterogeneity was observed in terms of patient and treatment characteristics. Pooled 2-year LC reported in 11 studies was 79.3% (95%CI, 72.8%–85.7%) with substantial heterogeneity between studies (Q2 test: p=0.0083; I2 = 57.9%), while pooled 2-year PFS reported in eight studies was 35.9% (95%CI, 22.1%–49.7%) with very high heterogeneity between studies (Q2 test: p<0.0001; I2 = 86.1%). Grade ≥ 3 and Grade 5 toxicity rates were 2.0% and 0.2%, respectively.

Conclusions: SBRT of NMs seems to be safe and effective in terms of LC. However, due to the marked heterogeneity of the included series, prospective studies are required.

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STEREOTACTIC BODY RADIOTHERAPY FOR OLIGOMETASTATIC PROSTATE CANCER

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Aims: Local ablative therapy is proposed as useful treatment for selected patients with limited metastatic burden (1- 3). Stereotactic body radiotherapy (SBRT) is a non-invasive option that may provide good control with minimum toxicity. The aim of the present study is

to evaluate the outcome and toxicitiy of SBRT in patients with oligometastatic disease from prostate cancer.

Table 1. Clinical and pathological characteristics of all patients.

		Pt1	Pt2	Pt3	Pt4	Pt5	Pt6	Pt7	Pt8	Pt9
Age (median, range)	*72(59-79)*	*72*	*79*	*75*	*65*	*71*	*70*	*72*	*59*	*79*
KPS										
80%	4 (44.4)	*80%*	*90%*	*80%*	*80%*	*90%*	*90%*	*90%*	*80%*	*90%*
90%	5 (55.6)									
Gleason Score										
6	2 (22.2)	*6*	*6*	*7*	*7*	*9*	*8*	*8*	*8*	*9*
7 (3+4)	2 (22.2)									
8	3 (33.3)									
9	2 (22.2)									
Clinical T stage at diagnosis										
2	4 (44.4)	*3*	*3*	*3*	*2*	*3*	*3*	*2*	*2*	*2*
3	5 (55.6)									
PSA at diagnosis										
<10	4 (44.4)	*228*	*20.4*	*10*	*8.5*	*7.1*	*45.17*	*7.35*	*17*	*9.93*
10-20	2 (22.2)									
>20	3 (33.3)									
Risk group at diagnosis										
Intermediate	1 (11.1)	*H*	*H*	*H*	*I*	*H*	*H*	*H*	*H*	*H*
High	8 (88.9)									
Lymph node status										
Pos	1 (11.1)	*Neg*	*Neg*	*Neg*	*Neg*	*Neg*	*Pos*	*Neg*	*Neg*	*Neg*
Neg	8 (88.9)									
N° of metastatic sites treated										
1	7 (77.8)	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*3*	*2*
2	1 (11.1)									
3	1 (11.1)									
Pre-SBRT therapy										
Surgery	3 (33.3)	*SRTOT*	*SRTOT*	*SOT*	*S*	*SOT*	*SOT*	*SOT*	*SOT*	*S*
Surgery+OT	4 (44.4)									
Surgery+RT+DT	2 (22.2)									
Time distance between primary treatment and recurrence (median, range)	41mo (3-120)	*120*	*20*	*11*	*73*	*3*	*31*	*41*	*3*	*112*
Type of OT added to RT										
NSAA	1 (14.3)	*ADT*	*ADT*	*ADT*	*No*	*Both*	*Both*	*NSAA*	*ADT*	*No*
ADT (LH-RH analogue)	6 (85.7)									
GTV volume (cc) (median, range)	3.76 (1.06-96.3)	*6.4*	*1.4*	*1.06*	*96.3*	*3.77*	*1.6*	*2.3*	*4.78*	*5.12*
PTV volume (cc) (median, range)	28.62	*19.8*	*31.6*	*7.45*	*140.5*	*26.2*	*9.6*	*11.1*	*24.4*	*15.5*

Methods: Nine consecutive patients treated for oligometastatic prostate cancer at the Radiotherapy Department of the University "Federico II" (Naples, Italia) between July 2018 and February 2020 were enrolled. One-Three fractions of SBRT with a total dose ranging between 18 and 30 Gy were administered. The characteristics of primary tumor and metastatic sites are described. Biochemical control (bRFS) and overall survival (OS), together with toxicitiy were evaluated.

Conclusions: Clinical and pathological characteristics of all patients are reported in Table 1. Nine patients received SBRT to 12 metastases (3 spine, 2 non-spine bone, and 7 lymph nodes); all patients were in the state of oligorecurrence. 7 patients had 1 metastasis, 1 had 2 metastases, and 1 had 3 metastases. The median gross target volume (GTV) was 3.76 cc and the median planning target volume (PTV) was 28.62 cc.

The median follow-up after RT was 11.5 months (2-24 months). No acute G≥2 toxicity was reported; one patient experienced G1 pelvic pain. Late toxicity was evaluated in 7 patients with follow-up >3 months. No late G≥2 toxicity was observed. Two patients experienced G1 rectal tenesmus, and G1 hematuria, respectively. The mean biochemical progression-free survival was 19 months. Mean OS was 22 months. A total of 7 patients received ADT: five patients before and two after SBRT. Another two patients were not given any ADT during the whole period of observation. Local control was obtained in all patients. Complete PSA response was observed in 6 patients. One patient died of diffuse disease progression. At the time of the analysis, eight patients were alive with no clinically evidence of progressive disease or biochemical failure.

Conclusions: SBRT in oligometastatic prostate cancer patients is an effective and well tolerated therapy and can help to achieve high local control in the area of the metastases. Further studies are needed to understand if this improved local control implies an advantage in survival and to select patients most likely to benefit from ablative therapy of oligometastatic disease.

P297

CLINICAL RESULTS OF LINAC-BASED STEREOTACTIC BODY RADIOTHERAPY FOR SPINAL METASTASES USING A DEDICATED CONTOURING AND PLANNING SYSTEM

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Aims: To report clinical results of spinal metastases SBRT using a dedicated software (Element Spine SRS®, Brainlab™).

Methods: The selection criteria were: diagnosis of spinal metastases (n ≤ 3), life expectancy >3 months, controlled primary tumor. The dedicated software Elements Spine SRS® was used to coregister the MRI-T1 sequences or PET-CT scans for target volume and the organ at risks definition, using dedicated anatomical atlas. Gross tumor volume (GTV) was defined as macroscopic lesion on T1-MRI or pathological uptake on PET-CT. Clinical target volume (CTV) was created by an expansion of the GTV according to international guidelines, including adjacent normal bone to avoid subclinical tumor spread. Planning target volume (PTV) was obtained by adding isotropic margin of 1 mm to the CTV. Different dose prescription ranged between 10-24 Gy in 1-3 fractions (fx). Toxicity and tumor response were evaluated with periodic PET-CT or MRI and clinical evaluations.

Results: From April 2018 to April 2020, 89 spinal metastases in 58 patients (median age 67 ys, range 43-85) were treated with Linac-based SBRT. The most common histologies were prostate in 50% and breast in 34.5% pts. The cervical spine was involved in 11.2% cases, thoracic spine in 59.6% and lumbar spine in 29.2% cases. Anatomical part of the vertebra affected was the vertebral body in 53 metastases (59.6%), peduncle in 9(10.1%), spinal process in 5(5.6%) and mixed vertebral sites in the residual 22(24.7%) cases. A total dose of 12 Gy/1-2 fx was prescribed in 4 pts as re-irradiation, 18 Gy/3 fx in 18 lesions (20.2%), 21 Gy/3 fx in 36 (40.5%), 24 Gy/3 fx in 29 lesions (32.6%). In 17 selected cases (radio-resistant histology and/or small GTV area) a simultaneous integrated boost to the GTV was proposed (range dose 24–27 Gy/3 fx). At a median follow-up of 6 months (range 3–25 months), local control rates at 6-months and 1-year were both 96.3%. No

acute or chronic adverse events ≥3 grade were reported at the follow-up. At the time of the analysis, 72 lesions were evaluable for response by PET-CT scans: complete metabolic response was observed in 23(32.4%) cases, partial response in 30(42.3%), stable disease in 17(23.9%) cases and only two cases of local progression was recorded at 5 months from SBRT.

Conclusions: Spine SBRT using this dedicated software is effective and well-tolerated, with high rate of early metabolic response. Longer follow-up is needed to assess late toxicity profile and outcomes.

P298

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR PATIENTS WITH PULMONARY OLIGOMETASTASES FROM GASTROINTESTINAL PRIMARY TUMORS

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Aims: To evaluate the efficacy and safety of using stereotactic body radiotherapy (SBRT) in pulmonary oligometastatic disease (OMD) from gastrointestinal (GI) primary tumors.

Methods: Patients with pulmonary OMD treated with SBRT from January 2016 to December 2018 were retrospectively evaluated. Primary endpoint was LC. Secondary endpoints were overall survival (OS), progression free survival (PFS) and toxicity. Uni- and multivariate analyses to assess variable correlations were conducted.

Results: A total of 37 patients and 59 lung metastases were evaluated. The median follow-up after SBRT was 23.0 months (range 6.3-50.4 months). The most common site of primary GI tumor was colorectal (64.9%). The median number of treated lesions for each course was 1 (range 1-4), and 3 (8.1%) patients were treated with a second course of SBRT after the first treatment. The median GTV and PTV volume were 2.0 cc (range 0.6-28.1 cc) and 10.7 cc (range 3.8-68.4 cc), respectively. The dose delivered ranged from 30 to 60 Gy in 3-8 fractions. A BED10 ≥ 100 Gy to the PTV was prescribed in 54 (91.5%) lesions. LC rate at 1/2 years was 89.7%/85.0%, and increased to 96.0%/91.0% for lesions treated with a biologically effective dose (BED10) ≥ 100 Gy (p = 0.03). RECIST response at 6 months was a strong predictor of LC (p = 0.002). OS rates were 94.6% (95% CI 87.6%-100%) and 84.6% (95% CI 72.9%-98.2%) at 1 and 2 years, respectively, and the comparable PFS rates were 45.5% (95% CI 31.3%-66.1%) and 32.7% (95% CI 19.9%-53.8%), respectively. A BED10 ≥ 100 Gy was a significant predictor of PFS (p = 0.027), but had not significant impact on OS (p = 0.33). The treatment was well-tolerated, no acute or late G≥3 toxicities were reported and no patients required SBRT interruption due to SBRT-related adverse events.

Conclusions: SBRT is an effective option for pulmonary OMD from GI malignancies. A BED10 ≥ 100 Gy and radiological response at 6 months can affect LC.

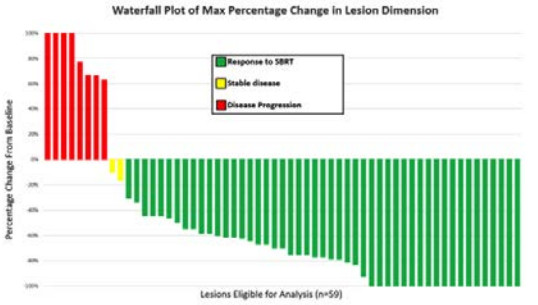

Figure 1. According to RECIST Criteria, 49 lesions (83.1%) had a partial/complete response after SBRT (at least 30% decrease in target lesion dimension from baseline), while 2 (3.3%) lesions had stable disease, for an overall crude local control rate of 86.4%. Local progression occurred in 8 (13.6%) lesions (> 20% increase of target lesion).

P299

FEASIBILITY AND IMPACT ON QUALITY OF LIFE OF RADIOTHERAPY IN DE NOVO OLIGOMETASTATIC PROSTATE CANCER PATIENTS.

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Aims: Patients (pts) with de novo oligometastatic prostate cancer (PC) increased over the years. Continued presence of the primary tumor might provide an uncontrolled source of cells and mediators with the capacity to seed and feed new distant metastasis. To date emerging evidences support feasibility and progression-free survival (PFS) benefits of radiotherapy on both primary tumor and metastatic lesions combined with systemic therapy (ST) based on hormonal therapy.

Methods: From October 2019 to April 2020 we treated 14 pts, average age 80,7 years (range 74 - 90 years) with de novo oligometastatic PC 12 out of 14 pts had 1 bone metastasis (BM) and 2 patient had 2 BM synchronously. The diagnosis occurred in 4 pts with Choline Positron emission tomography (PET) and Magnetic Resonance Imaging Whole Body (MRI WB), in 6 pts with PET and 4 pts with only MRI WB. All pts

underwent radiotherapy on both primary tumor and metastatic lesions combined with androgen deprivation therapy (ADT). Delivered doses were 8 Gy-37,5 Gy in 1-5 fractions on BM and 25 Gy-60 Gy in 5-20 fractions on prostate with Volumetric Modulated Arc Therapy (VMAT) technique with 1-2 arc in a daily fraction. Four pts were submitted to moderate hypofractionation and 10 pts were submitted to stereotactic radiotherapy. Different schedules were given according to age, Performance Status (PS) and disease site. The evaluation of the treatment response was recorded by analyzing the pre and post treatment imaging studies and sequential PSA value. Late toxicity was assessed through quarterly follow-ups.

Results: In our study we have recorded a reduction of PSA value in all pts treated ranged from 8.8% to 99.9% of the initial PSA value. After a 6-month follow-up 4 pts experienced a complete response (CR) on primary tumor and partial response (PR) on BM; eight pts had stability disease (SD) with a zero PSA slope; two pts had a slight increase in the PSA level. Only 1 pt reported urinary incontinence after RT the others G0 toxicity Common Terminology Criteria for Adverse Events (CTCAE). Only 2 pts have changed ST.

Conclusions: Radiation therapy on both primary tumor and metastatic lesions combined with ST, according to our experience, is safe and effectiveness. A multimodal approach (local and metastasis-directed therapy) could allow for outcomes improvement of oligometastatic de-novo PC patients and delay the change of ST line.

P300

STEREOTACTIC BODY RADIOTHERAPY FOR ADRENAL OLIGOMETASTASIS IN LUNG CANCER PATIENTS

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Purpose: To report our experience on stereotactic body radiotherapy (SBRT) in adrenal metastases from lung cancer.

Methods and materials: 37 oligometastatic lung cancer patients with 38 adrenal metastases submitted to SBRT were retrospectively analyzed. SBRT was delivered by volumetric-modulated arc therapy (V-MAT) or helical tomotherapy (HT). Primary study endpoint was local recurrence-free survival (LR-FS), while secondary endpoints were distant-progression free survival (d-PFS) and overall survival (OS).

Results: Median age was 67 years and primary tumor was NSCLC in 27 (73%) and SCLC in 10 (27%) patients. Adrenal metastases were in the left side in 66% cases. Median prescribed dose was 30 Gy in 5 fractions for a median biologically equivalent dose of 48 Gy (α/β ratio 10 Gy, BED10). The majority of patients (62%) received SBRT alone, a minority (38%) chemo-immune- or target- therapies. Median follow-up was 10.5 months, median OS 16 months and median d-PFS 3 months. 27 (70%) patients obtained a local control with a median LR-FS of 32 months. LR-FS was significantly related to BED10 with a better LC with BED10 $\geq$72 Gy, 1- and 2- year LR-FS rates were 54.1 ± 11.6% and 45 ± 12.7% versus 100% and 100% for BED $\leq$59.5 Gy and BED $\geq$72 Gy, respectively (p=0.05). There was no severe toxicity.

Conclusions: SBRT was effective and safe in lung cancer adrenal metastases. A dose-response relationship was found between BED10 >72 Gy and better local control. No significant toxicity was registered thanks to the respect of dose constraints and suspension of chemo- and target-therapies.

P301

STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PATIENTS WITH LYMPH NODE OLIGOMETASTASES: ANALYSIS ON THE IMPACT ON SYSTEMIC TREATMENT INTENSIFICATION

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Aims: Lymph nodes (LN) are common site of oligometastases and stereotactic body radiation therapy (SBRT) represents an effective ablative treatment. Aim of this study was to analyze a large cohort of nodal oligometastases treated with SBRT to identify impact on systemic therapy intensification, pattern of recurrence, and predictive factors.

Methods: We included patients with a maximum of 5 oligometastases. Concomitant treatments were allowed. Patients were treated with Volumetric Modulated Arc Therapy (VMAT) and end points were local control of treated metastases (LC), locoregional nodal control (LRNC), distant nodal control (DNC), distant metastases free survival (DMFS), overall survival (OS) and freedom from treatment intensification (FFTI).

Results: 418 LN were treated in 278 patients with 327 SBRT treatments. Patients were more commonly affected by colorectal (20.9%) and prostate cancer (17.99%). Most represented schedule was 45 Gy in 6 fractions, with a median BED10 of 78.75 Gy. After median follow-up of 15.1 months, LC at 1 and 2 years were 87.2% and 76.8%, respectively. Prostate primary tumor, small volume, oligorecurrence, and BED10 $\geq$ 75Gy were associated with higher LC. One and 2 years FFTI were 82.8% and 74.5%; in patients reporting intensification of systemic therapy, median time was 8.43 months, while for patients who

repeated SBRT, median FFTI was 14.6 months. Rates of LRNC at 1 and 2 years were 70.9% and 57.6%, and DNC were 82.0% and 77.9%.

Conclusion: With the present analysis, we confirmed on a large cohort the benefit from SBRT on lymph node oligometastases in multidisciplinary management. Combination of SBRT with new systemic therapies, including immunotherapy and targeted therapy, should be investigated to reduce the risk of progression out of the field of irradiation.

P302

SAFETY AND EFFICACY OF STEREOTACTIC RADIATION THERAPY IN OLIGOPROGRESSIVE RENAL CELL CARCINOMA

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Aims: Renal cell carcinoma (RCC) is the most frequent type of kidney tumor and its incidence is increasing every year. Clear cell is the most common histology, affecting 70% of the patients. About 30% of patients have recurrent disease and another 30% have stage IV at diagnosis. Patient with oligoprogressive disease after first line treatment (surgical or systemic) can benefit from stereotactic radiation therapy (SBRT) treatment, as suggested by National Comprehensive Cancer Network (NCCN) guidelines. SBRT allows for highly conformal radiation therapy while respecting adjacent organs at risk. This technique provides a good local control of the disease.

Methods: 21 patients with 31 metastases were treated from 2018 to 2020. Patients with a maximum of 3 metastases in the setting of oligopressive disease were subjected to stereotactic treatment. In every case the primary tumor has been surgically resected. All the SBRT treatments were delivered with a Varian True Beam LINAC with 6-FFF MV. The set up for the simulation CT and subsequent treatments was customized accordingly to the metastasis site. Every treatment was delivered with daily Image-Guided RT (IGRT) with Cone-Beam CT (CBCT). All adverse effects and toxicities were registered accordingly to the Common Terminology Criteria for Adverse Events v5 (CTCAE.5).

Results: The histology was RCC for 19 patients, only 2 patients had a different type of renal carcinoma. A total of 7 metastases (22%) were located in the lungs, 4 (13%) were in the lymph nodes, 3 (10%) in the bones, 4 (13%) in the adrenal glands, 10 (32%) in the brain and 3 (10%) in other organs. A single fraction was used to treat 5 metastases with a median dose of 20 Gray (range 16–26 Gy), 14 lesions were treated with 3 fractions (range 27-52.5 Gy) and 12 with 5 fractions (range 30-50 Gy). After treatments, one patient presented with pain G1. No acute toxicity more than grade 2 was recorded. No long-term side effects were observed. Median follow up was 6.5 months (range 2 to 30 months). Of 21 patients treated with SBRT, to this day only 1 (4.76%) had in-field progression. The follow-up is too brief to evaluate the time to change of systemic therapy.

Conclusions: Stereotactic body radiation therapy for RCC metastasis can be considered a safe approach and it provides effective local control of oligometastatic renal cell carcinoma. Ongoing international trials are still necessary to evaluate the impact on overall survival.

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HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR OLIGOMETASTATIC BREAST CANCER

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Aims: to analyze the long-term follow-up of patients treated with hypofractionated, stereotactic radiotherapy (HSRT) for oligometastases from breast cancer.

Methods: We retrospectively evaluated 25 *de novo* oligometastatic or oligorecurrent patients with 1–5 radiographically apparent metastatic lesions (in 1–3 organs) from primary breast cancer, who underwent hypofractionated stereotactic radiotherapy from 2010 to 2019 on a total of 36 metastatic lesions. The investigated outcomes were local control, progression-free survival and overall survival.

Results: The mean age was 61,8 years. The most common metastatic sites were brain (52.7%), lung (22.2%), liver (8.3%), lymph nodes (8.3%), and bone (8.3%). Seventeen (68%) had 1 involved organ and 16 (64%) had 1 lesion treated. The mean radiotherapy dose was 35,5 Gy (+/- 11 SD). Mean 4.6 BED was 120.6 Gy. 21 patients underwent radiotherapy during systemic therapy. The most common molecular subtypes were as follows: luminal A (40%) and triple positive (20%). The median follow-up was 26 months. Radiological response was obtained in the vast majority of patients. The local control at 1 and 2 years was 90.6% and 77.5% respectively. One year and two years progression free survival was 56.4% and 37.6%, but in patients with metastases other than brain PFS at 2 years was 52%. No major radionecrosis, pulmonary toxicity, chest pain or rib fracture occurred. Overall Survival (OS) at 1 and 2 years was 93.3% and 86.6%. In patients with metastases other than brain OS at 2 years was 100%.

Conclusions: A small subset of select breast cancer patients (luminal A and triple positive) with limited metastases treated with HSRT are long-term survivors. Local therapy with more effective systemic treatment will need deeper investigation.

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CAROTID BLOWOUT SYNDROME AFTER REIRRADIATION FOR HEAD AND NECK MALIGNANCIES: A COMPREHENSIVE SYSTEMATIC REVIEW FOR A PRAGMATIC MULTIDISCIPLINARY APPROACH

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[#]Affiliation at the time of the study.

Aim: Acute carotid blowout (CBO) represents the most feared complication for patients treated with reirradiation (reRT) for head and neck (HN) malignancies. Literature data are still scarce with a low level of evidence. Aim of this study is to provide a comprehensive systematic review of the literature including all aspects of the multidisciplinary strategy to reduce the risk of CBO in patient submitted to HN reRT.

Methods: The literature search was carried out, designed and conducted by three Radiation Oncologists and by an experienced medical librarian. MEDLINE, Embase, Scopus and Cochrane electronic databases were searched in up to September 2019. Inclusion criteria were: 1) CBO following reRT in the HN region, 2) description (patient-, tumor- or treatment-related risk factors, summarize in Figure 1), 3) clinical or radiological signs of threatened or impending CBO, and 4) CBO prevention strategies. Selected works were organized into four main categories: 1) pretreatment evaluation (patients'- and tumor-related risk factors), 2) dosimetric parameters (RT technique, accumulated radiation doses and fractionation) 3) early diagnosis (clinical symptoms and radiologic signs), and 4) treatment of threatened/impending CBO (interventional procedures aiming to prevent acute carotid hemorrhage).

Results: Thirty-five studies were selected for the analysis from five hundred seventy-seven records. Results of the present analysis highlighted that a multidisciplinary approach is mandatory to minimize the risk of acute CBO. Radiologists should precisely quantify the proximity of carotid arteries to the tumor mass and, during the follow-up, should report the presence of radiologic abnormalities. Radiation Oncologists should define the most adequate radiation technique and should plan a strict follow-up. Furthermore, skull base surgeons and interventional radiologist should be considered as core physicians fully involved in patients' management. Carotid stenting/occlusion could be evaluated before re-RT in high risk patients or during follow-up in case of threatened/impending CBO.

Conclusions: CBO remains the most feared side effect in patients treated with reRT for HN tumors. Several efforts should be spent to properly select patients candidate to this treatment, to use the best available radiation strategy, to early recognize the threatened and impending CBOrelated symptoms and sings in order to apply all preventive procedures and to avoid the occurrence of CBO.

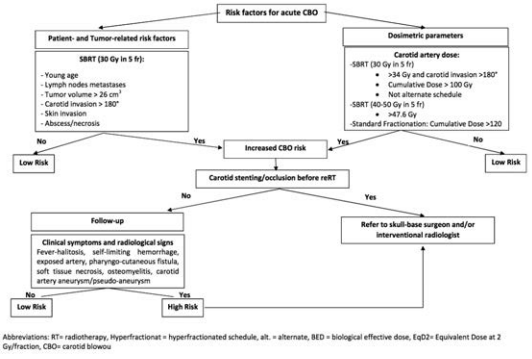

Figure 1. Patients and tumor risk factors for carotid blowout syndrome.

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STEREOTACTIC RADIOTHERAPY WITH SINGLE-ISOCENTER IN MULTIPLE BRAIN METASTASES: A MONO INSTITUTIONAL SERIE

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Aims: An obstacle of stereotactic radiotherapy (SR) in the management of numerous brain metastases is the longer treatment time using traditional radiotherapy. Single-isocenter multitarget (SIMT) SR is a novel technique that permits rapid therapy delivery to multiple metastases.

Methods: We identified 13 patients with advanced solid tumors (9 Non Small Cell Lung Cancer (NSCLC) -69.2%-,1 melanoma -7.7%-, 1 Merkel cancer -7.7%- and 2 breast cancer -15.4%-) with multiple brain metastases treated with SR in 3 fractions using SIMT technique at our institution. A two-month control MRI was performed after each treatment.

Results: We identified 13 patients with 71 brain metastases, between December 2018 and June 2020. Only 2 patients received whole brain radiotherapy before SIMT, one patient due to histology (small cell lung cancer) and another patient because he had more than 20 metastases at diagnosis. The other 11 patients performed only SR with single isocenter on single metastase or multiple metastases for a maximum of 5 lesions treated simultaneously. The prescription dose was 9 Gy for fraction with prescription to isodose of 80% to the isocenter. Lower doses were considered in case of organs at risk close to target or in case of previous treatment, however metastases number didn't influence the prescribed dose. All patients performed simultaneously systemic therapy. Response at two months MRI was: 2 (15.4%) had brain progression, 5 (38.5%) stable disease and 6 (46.2%) partial response.

Conclusions: SIMT radiotherapy delivered in 3 fractions offers good local control and absence of toxicity in the treatment of multiple brain metastases. This technique should be evaluated prospectively.

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ABLATIVE RADIOTHERAPY FOR OLIGOMETASTATIC PROSTATE CANCER

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Aims: The purpose of the study was to assess biochemical progression-free survival (PFS), local control (LC), hormone/systemic therapy-free survival and toxicity of stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer patients.

Methods: From 2017 to 2020, 37 lesions (12 bone and 25 lymph nodes) detected by Ga68-PSMA positron emission tomography (Ga68-PSMA PET), magnetic resonance (MR), computed tomography (CT) were treated in 29 patients (pts). Pts included were: oligometastatic at diagnosis (2 pts), oligorecurrent castration-sensitive (19 pts) and castration-resistant (6 pts) after primary surgical treatment, oligoprogressive under systemic therapy (2 pts). The clinical target volume (CTV) was contoured on a 1-mm CT scan and a planning target volume (PTV) margin of 3-mm was added. SBRT was delivered with a 6 MV photon volumetric modulated arc therapy-cone beam CT (VMAT-CBT) with a dose of 21 Gy in 3 fractions for bone and of 30 Gy in 5 fractions for nodal metastases. In 10/29 (34%) pts hormone therapy was combined with SBRT. We evaluated prostate serum antigen (PSA) level every 3 months after SBRT (PSA decrease >10% identified response, PSA increase > 10% identified progression). Kaplan-Meier methods were used to determine PFS (time from SBRT and biochemical progression) and LC (time from SBRT to the in-field progression detected by radiologic imaging). Toxicity was assessed using Radiation Therapy Oncology Group (RTOG) scale.

Results: Median follow-up was 21 months (range 3-33). At 3-months, biochemical response was observed in 20/29 pts (69%). At median follow-up of 17 months (range 6-33), 8/20 (40%) of the 3-months responders remained progression-free. Two-year PFS and LC rates were 37% and 70%, respectively. In-field progression occurred in 3/37 (8%) lesions. Androgen deprivation in oligorecurrent castration-sensitive (8/19 pts) and systemic therapy in oligorecurrent castration-resistant pts (4/6 pts) was delayed by an average of 11,6 months (range 3-28) after SBRT. No significant difference in PFS depending on type of lesion or concomitant hormone therapy was observed. None of the treated patients developed toxicity > Grade 2.

Conclusions: SBRT is a viable and safe treatment option for oligometastatic prostate cancer. This approach offers a good in-field tumor control and delay of both androgen deprivation and systemic therapy.

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REIRRADIATION: TWO IS BETTER THAN ONE – DOUBLE MEDIASTINAL REIRRADIATION IN OLIGOMETASTATIC AND HORMONE INDEPENDENT PATIENT

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Aims: In the era of oligometastatic cancer disease, therefore patient request strongly rises up, and so on the medical mission, to clearly improve quality of life in metastatic stage even. In last years, SBRT is increasingly acquiring new therapeutic opportunities that were unthinkable before, which could take the great match against cancer to another level. In this case we report two thoracic SBRT reirradiation on patient with recurrence metastatic prostate cancer.

Methods: A over 80-years-old man with a history of prostate cancer treated with radical prostatectomy, adjuvant Radiotherapy and androgen deprivation therapy , followed by SBRT on sequential lymph node recurrence sites, presented several relapses of thoracic disease. Out of hormonal therapy control, we treated every mediastinal metastatic repetition with SBRT for three times to the same/neighboring site. The prescribed doses for the 3 treatments were: 1) 30 Gy/ 15 fr delivered on mediastinal area and sequential plus a single fraction SBRT boost (8-10Gy) on PET-positive paratracheal and hilar nodes; 2) 40Gy/5fr on PET-positive right hilar nodes and 3) finally 30Gy delivered in 3 fraction (1fr/ week) on PET- positive right hilar, subcarenal and paratracheal nodes. The intervals between the 3

irradiations were 34 and 7 months, respectively.Linear accelerator-based SBRT was delivered via 2-3 non co-planar therapy arc (RapidArc) with 6 MV photons with Flattening filter-free beams.

Results: No acute and late toxicity was observed until the last follow up (46 months from the first treatment). A CT scan 2 months after the last RT treatment showed significant reduction of right ilar lesion (1.6 vs 2.9 cm) and no more evidence of other mediastinal pathologic nodes. The PSA value halved from 7.9 to 3.9 ng/ml. At the moment we have achieved excellent clinical control of a metastatic disease.

Conclusions: This case report suggests that multiple mediastinal/thoracic SBRT irradiations might be possible in selected cases, even in proximity of dose-limiting OAR, based on highly conformal radiation fields and advanced Image Guided Radiation Therapy. It requires high technologies and expertise from contouring and planning to delivery and setup verification. Nowadays, in the era of oligometastatic chronic disease, SBRT is an important treatment option that allows delivering high-BED doses that could strongly counteracts macroscopic evidence of diffused cancer helping systemic therapy as in this case or delaying begin of another chemotherapy treatment.

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LUNG OLIGO PROGRESSIVE DISEASE AFTER RADIOTHERAPY: PRIMUM NON NOCERE

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A standard treatment for patients with oligo progressive disease in lung who undergo radiotherapy and subsequently developed local progression, has not yet been established. Historically, thoracic reirradiation (ReRT) has been limited by toxicity concerns. Recent technological advances have made it possible using stereotactic radiation therapy (SRT), resulting in high local control (LC) and low toxicity, with a reduction in the dose to organs at risk (OAR) We here report on a colon-rectal cancer patient who received para-mediastinal ReRT. In January 2014, a 50-year-hold woman underwent laparoscopic extended left-hemicolectomy for moderately differentiated adenocarcinoma of sigmoid colon, pT3, pN0, M1 (lung and liver metastases), followed by chemotherapy. In February 2015, a right lower lung lobectomy was performed to remove adenocarcinomàs metastasis. The first radiotherapy treatment was delivered, in August 2016, to right mediastinal lymph node, near the ascending aorta, with a maximal extension of 37 mm and pathological uptake at 18□fluorodeoxyglucose positron emission tomography (18 FDG PET/CT). The total dose delivered was 50 Gy in 20 fractions, the treatment field included the right hemimediastinum. The followed 18 FDG PET/CT showed good response of disease with reduction of pathological uptake and lymph node size. In August 2019, a new 18 FDG PET/CT showed: a new suspected uptake in the left hip (then treated with hypofractionated SRT (40 Gy in 5 fractions) and an increase in volume and pathological uptake of previously treated right mediastinal lymph node (SUV 8.5 VS 2.9). At simulation CT patient was scanned with the Sentinel™ system in Free Breathing (FB) and in Deep Inspiration Breath Hold (DIBH). All structures were delineated in both the DIBH and FB CT, PTV was defined as the pathological mediastinal PET/TC uptake and in FB CT a PTV ITV has been defined using the co-registration with the CT DIBH. The prescribed dose was 30 Gy in 5 fractions. Essentially identical VMAT isocentric treatment plans were created for both DIBH and FB. Dose to heart, right lung and ascending aorta was reduced for all dose levels with comparable target coverage for DIBH compared to FB treatment To re-irradiate mediastinal lymph node we chosed DIBH technique, in order to minimize thoracic excursion and volume of treatment. The treatment was delivered with Versa HD by Elekta, FFF, CBCT and Catalyst™ system. Actually, 5 years after her initial radiotherapy and without any additional therapy after Re-RT, the patient is still alive without the presence of disease and without adverse effects. CT after 3,6 and 12 months after lung Re-RT don't show signs related to lung damages. The last revaluation 18 FDG PET/CT showed dimensional reduction of lung lesion without pathological uptake.

Table 1.

	DIBH	FB
Heart	Dmax 4.7 Gy	Dmax 7.4 Gy
Heart	Dmean 0.2 Gy	Dmean 0.3 Gy
Right Lung out PTV	Dmax 30.8 Gy	Dmax 29.4 Gy
Right Lung out PTV	Dmean 2.9 Gy	Dmean 4.2 Gy
Ascending aorta	Dmax 29.4 Gy	Dmax 30.6 Gy
PTV ITV		35,16 cm3
PTV	18.01 cm3	20.6 cm3

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HYPERFRACTIONED CHEMORADIOTHERAPY FOR LOCALLY RECURRENT ANAL CANCER IN A PATIENT PREVIOUSLY IRRADIATED TO THE PELVIS: A CASE REPORT

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Aims: Concomitant chemoradiotherapy (CRT) is

the primary treatment of choice for non-metastatic squamous cell carcinoma of the anus (SCCA). 10-30% of these patients will fail to achieve complete response and will undergo salvage surgery (abdomino-perineal resection, APR). Up to 44% of patients can experience locoregional recurrence after APR, which is associated with poor prognosis and impaired quality of life; in these cases re-irradiation (reRT) could play a role.

Methods: We present the case of a 62 year old man affected by SCCA (staged cT3N1) who underwent CRT with mitomycin-C and 5-fluorouracil. SIB technique RT was delivered with total dose up to 55 Gy followed by a 4 Gy brachytherapy boost. Due to progressive disease, APR was performed but was followed by local relapse for which standard CT was initiated. Local relapse progressed infiltrating pelvic structures and assumed characteristics of an abscess with cutaneous fistulization. An anti-PD1 agent was administered followed by further progression of disease, which now caused significant pain and blood and purulent secretion by the fistula. Palliative surgery was excluded. Taking into account the patient's will and following a collegial discussion, reRT was performed in the attempt to palliate symptoms; interval with previous CRT course was 32 months. Given the increased infectious risk, antibiotic therapy was administered during the whole RT course.

Results: 40.8 Gy were delivered to the pelvic disease (1.2 Gy twice daily with a minimum 6-hours interval) and concomitant CT was administered (weekly 5-fluorouracil and cisplatin). Treatment was well tolerated with only an acute gastro-intestinal grade 2 toxicity and rapid improvement of symptoms was reported. Two months after completion of treatment, a substantially decreased pain level was reported together with rare exudates. A CT scan revealed partial response. Systemic therapy with 5-fluorouracil and oxaliplatin was then initiated. All treatment options were collegially discussed and shared with the patient.

Conclusions: Hyperfractionated accelerated reRT with close clinical monitoring is a feasible treatment option for locally recurrent SCCA resistant to previous therapies, even when radical treatment is no longer desirable and there is increased infectious risk. Symptom control should be the main aim, however the chance of local control cannot be excluded. Multidisciplinary management and adequate patient counseling are recommended.

P310

SPECT/CT EVALUATION OF 99MTC-MACROAGGREGATED ALBUMIN UPTAKE IN HEPATOCELLULAR CARCINOMA (HCC) PATIENTS TREATED WITH SELECTIVE INTERNAL RADIATION THERAPY (SIRT): RESULTS OF A SINGLE CENTER

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Aims: Primary aim was, in patients (pts) undergoing SIRT, to compare 99mTc-labeled macroaggregated albumin distribution at hepatic artery perfusion scintigraphy and SPECT/CT (MAA scan) with 90Y-resin-microspheres PET/CT distribution. Secondary aim was to correlate scan results with treatment response.

Methods: A retrospective single center analysis was performed including pts who underwent MAA scan and 90Y-PET/CT, pre and post-SIRT respectively, between November 2016-October 2018, with available clinical/imaging follow-up (FU). We evaluated: a) absent/partial/complete distribution match between MAA and 90Y-resin-microspheres on target hepatic lesion and, when present, on neoplastic thrombosis; b) response to treatment (performing ceCT or MRI at least every three months after SIRT).

Results: Overall 49 pts with primary HCC were included (11F-38M; mean age: 65 ± 11years; range:39-88years). At least one previous treatment (surgery, chemotherapy, TACE/TAE or radiofrequency) was received by 20/49 pts. 1/49 PET post-SIRT was not available for technical issues. In 47/48 pts there was a good distribution match between MAA and 90Y-microspheres, with complete target lesion correspondence (in 3/48 pts target was only partially covered). Among the 27/48 pts with neoplastic thrombosis, 26/27 presented a complete MAA-90Ymicrospheres correspondence (in 2/27 pts thrombosis was only partially covered). Mean dose delivered to the tumor calculated with partition model-MIRD was 260Gy (range:53,8-679,8Gy) and mean dose to the whole liver was 9,3Gy (range:1,5-24,7Gy). Extra-hepatic activity in 90Y-PET was detected in 4/48 pts (1lung;1 gallbladder and bowel;1 gallbladder;1 gastro-duodenal spots). No significant complications were observed after SIRT procedure, except one case of pneumonia. Mean FU was 17.6months (range:1-39months). 5/49 pts were lost at FU. At last FU we recorded: complete response (CR) in 9/44 pts (20,5%), partial response (PR) in 1/44 (2,3%), stable disease (SD) in 17/44 (38,6%) and progressive disease (PD) in 17/44(38,6%). Overall, 3 cases presented with target CR+thrombosis SD whereas a single case target CR+thrombosis PD.

Conclusions: Our results confirm that a careful MAA scan evaluation reliably reflects 90Y-resin-microspheres distribution and impacts on SIRT response. Further analyses are ongoing in order to establish a pos-

sible prognostic value in terms of progression free survival and to search for potential imaging predictive factors of treatment response.

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IMPACT OF 18F-FDG PET/CT ON THE MANAGEMENT OF WELL DIFFERENTIATED THYROID CANCER (DTC) PERSISTENCE/RECURRENCE IN THE SUSPECT OF RADIO-IODINE REFRACTORY DISEASE (RAI-R-DTC)

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Aims: There is still lack of data in literature about the real 18FDG-PET/CT impact on treatment management in advanced and aggressive thyroid cancers. The first aim of our study was to retrospectively assess the impact of 18F-FDG PET/CT and secondly to confirm the prognostic role of clinical and semi-quantitative metabolic 18F-FDG PET/CT parameters in comparison with scientific literature.

Methods: A monocentric retrospective/observational study was performed from a database of 208 pts treated in our Center, from January 2011-July 2019, for local/metastatic DTC with several RAI courses. Fifty-three pts underwent 18FDG-PET/CT scan after the second RAI course because of strong suspect of RAI-R-DTC (negative Rx-WBS scan and/or high thyroglobulin levels). Clinical, laboratory and imaging data were collected. Metabolic response was defined according to PERCIST criteria. SUVmax, SUVmean, MTV, TLG were calculated. Kruskal-Wallis,Chi-Square-Pearson tests and Cox regression were used to compare metabolic/clinical parameters and PFS.

Results: In our sample (mean age: 52±19.9years; 31F-22M) 20/53 (38%) pts had negative RxWBS and positive PET/CT scan, 7/53 (13%) pts had positive RxWBS and PET/CT scans, 24/53 (45%) negative RxWBS and PET/CT scan and 2/53 (4%) positive RxWBS and negative PET/CT scan. Therapeutic approaches addressed after PET/CT positivity were external-beam-radiation therapy in 4/27(15%) pts, surgery in 4/27(15%), further RAI course in 2/27(7.4%), surgery+EBRT in 1/27(4%) and observation in 16/27(59%) pts. PERCIST response was evaluated in 14/27 FDG/PET positive scans. Median FU and median PFS were 5.8±3.9 years and 38±21.8 months respectively. At the last FU, 13/53 (24.5%) pts had persistence of structural disease, 25/53 (47%) persistence of biochemical disease and 15/53 (28%) excellent response. Significant associations were found between clinical response assessment and therapeutic approach (p=0.01) and between PFS and metabolic response (p=0.02). Linear correlation between MTV and TLG and suppressed-Tg was found. At Cox-Regression multivariate analysis only MTV (p=0.034 HR 1.100 CI95% 1.007-1.202) and PERCIST response (p=0.004 HR 2.434 CI95% 1.322-4.481) were independently associated to persistent disease.

Conclusions: Our analysis suggest that 18F-FDG-PET/CT may drive the clinical management of RAI-R-DTC, particularly to avoid further ineffective/toxic RAI administrations.

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RADIOIODINE THERAPY (RAIT) GUIDED BY 124I-PET/CT IMAGING IN METASTATIC DIFFERENTIATED THYROID CANCER (DTC): LONG-TERM FOLLOW-UP OF PATIENTS RECRUITED IN A PROSPECTIVE TRIAL

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Aims: Although RAIT was used for over 80 years in the metastatic-DTC management, number, frequency and optimal administrated 131I activity remain matter of debate. 124I-PET/CT can be a useful tool to identify lesions still iodine-avid with higher detection rate compared to post-treatment I-131scan (RxWBS) and to perform personalized dosimetry to the lesions, particularly in the case of potentially curative RAIT. The aim of this study is to confirm with long-term follow-up (FU) data the utility of 124I-PET/CT in RAIT planning of metastatic-DTC.

Methods: We collected long-term FU data of 30 patients (pts) affected by metastatic DTC and recruited in a prospective trial from July 2011-July 2013, who underwent to a personalized RAIT after performing 124I-PET/CT. Clinical/laboratory data were collected every 6/12months. In the case of strong suspect of relapse, contrast-enhanced-TC and/or 18FDG-PET/CT were also performed. Response to therapy was assessed according to ATA2015 guidelines.

Results: Mean FU was 73.5 months (range:108-17). All pts received prior RAIT, with an average adminis-

tered 131I activity of 9195.5MBq(range:1110-25900). 15/30(50%) pts had negative 124I-PET/CT and RxWBS scans;11/15 pts received 3700MBq while 4/15 pts refused treatment. At last FU, 4/15 pts had indeterminate response (IR), one pt had biochemical persistence (BP), 7/15 pts had structural persistence (SP), one pt died for disease not-related causes and 2/15 pts were lost at FU. 15/30(50%) pts had positive 124I-PET/CT and RxWBS scans but in 2/15 pts dosimetry was not performed because of the influence of intestinal activity. All those pts received an 131I activity of at least 7400MBq. Overall, dosimetry was performed to 34 lesions. In 5/13(38%) pts lesions received less than the target dose of 80Gy(average dose:14.25Gy;range:1.47-60.50); at last FU 2/5 pts had SP and 3/5 pts died for progression disease. In 2/15(15%) pts the majority of lesions received less than 80Gy and at last FU one pt had SP and one had IR. In 6/13(46%) pts lesions received more than 80Gy (average dose:393Gy; range:163.73-1283.12); at last FU 2/5 pts had SP, 2/5 pts had an excellent response, one pt died for disease not-related causes and one pt was lost at FU.

Conclusions: 124I-PET/CT imaging may drive the choice of optimal 131I administered activity; long-term FU data confirmed that pts who received more than 80 Gy to the lesions have a better response disease than those who received lower activities.

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MULTIDISCIPLINARY DIAGNOSTIC AND THERAPEUTIC PATHWAY IN A PATIENT AFFECTED BY OESOPHAGEAL NEOPLASM WITH UNUSUAL CLINICAL PRESENTATION

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Aims: present multidisciplinary diagnostic and therapeutic pathway in a patient affected by oesophageal neoplasm with unusual clinical presentation.

Methods: in November 2019 came to our observation to evaluate possible Radiotherapy to the lung a 66-year-old man, affected by SCLC extended (probable proximal oesophagus metastasis); he was submitted to Cisplatin and Etoposide based chemotherapy at a territorial Medical Oncology Unit. In April 2019, due to the appearance of worsening dysphonia, odynophagia and left earache, was undertaken to an ENT assessment by FLS, which has shown a severe hypomobility of left true vocal cord, without any anatomical alteration. A neck and chest CT scan confirmed asymmetry of the laryngeal space as for retraction of the vocal cords, and multiple roundish parenchymal lung lesions, considered as secondary lesions. He was then submitted (July 2019) to EGD with biopsy, with evidence of sessile lesion at 15 cm from the upper dental arch: according to the histological and immunohistochemical features (TTF1+, CD56+, p63-, CD20-, Ki67 close to 100%), also due to clinical description provided in the request, the lesion was diagnosed as SCLC metastasis. A 18FDG CT-PET scan showed pathological uptakes of the cervical oesophagus and upper left paratracheal lymphnodes (SUV 7–6.30), well as multiple lung injuries below the limits of diagnostic significance. Thus, the patient initiated the first-line chemotherapy in progress. Once he was submitted at our assessment, attention has been paid to the unusual clinical presentation and the pulmonary diagnostic uncertainty (metastasis vs. primary lung cancer), and then, in agreement with fellow Medical Oncologists of our Institution, it was decided to reassess the patient at the end of chemotherapy with CT and CT-PET scans. In February 2020, the reassessment CT scan documented the substantial stability of clinical frame, whereas 18FDG CT-PET showed the numerical but not metabolic increase of the pulmonary lesions, and the increased uptake of cervical oesophagus and left paratracheal lymph nodes (SUV 10 vs. 7). A surgical evaluation, performed at another Institution, excluded surgery due to pulmonary injuries. The patient complained of worsening of odynophagia, irradiated to left side of the neck, and left earache. Then, considering the lack of response to the standard therapeutic regimen for SCLC and the lung spread of disease, in agreement with the fellow Medical Oncologists and Pathologists of our and other Institutions, it was decided to re-evaluate the diagnostic-therapeutic pathway: after a review of literature, it was agreed to assess feasibility of a radiometabolic treatment Somatostatin analogues based, requiring a CT-PET scan with Gallio-peptides and a re-evaluation of histological preparations at an Institution of excellence in the diagnosis of neuroendocrine tumours, accredited ENETS. CT-PET scan Gallio-peptides based was negative for the presence of lesions expressing Somatostatin receptors, while the pathological frame was defined, based on the immunohistochemical profile (widespread detection of CKAE1/AE3, chromogranin A, synaptophysin, CD56, TTF-1, negative CDX-2 and Somatostatin receptors 2 and 5, high proliferation index ki67 - Mib1 of about 90%), as a coherent finding with poorly differentiated NEC with small cell aspects. Following consultation with the fellow Nuclear Medical specialists, there was no indication of Metabolic Radiotherapy. Therefore, because of the clinical framework, it was decided to propose a palliative Radiation therapy for pain relief to the proximal oesophagus and left paratracheal region, to a dose of 30

Gy, at 3 Gy a day.

Results: the patient, after expressing informed consent, started Radiotherapy to the proximal oesophageal region; however, due to a sudden worsening of the general conditions, after only 2 fractions, he was hospitalized in Geriatrics, with severe hyponatremia and hypokaliemia; the tests performed diagnosed systemic infection by Rickettsia Prowazekii; therefore, he was subjected to high-dose antibiotic therapy, at the end of which, having noted the clinical improvement, he resumed Radiotherapy, terminated at the expected dose, with good tolerance. In particular, the patient reported, already during the Radiotherapy, the disappearance of the odynophagia and the feeling of oesophageal encumbrance. It will be planned a reassessment CT scan 40 days after the end of treatment, to decide the next therapeutic pathway.

Conclusions: doubt about the diagnostic framework and the starting therapeutic process, reinforced by the lack of response to first-line chemotherapy, stimulated the multidisciplinary clinical reassessment, also involving colleagues of Institutions of excellence in the management of neuroendocrine tumours, in order to achieve a definitive diagnosis and the appropriate therapeutic approach. However, the results of the reassessment, due to the biological nature of the disease, did not allow a specific therapeutic solution. Palliative Radiotherapy was terminated without any toxicity and with almost immediate clinical benefit. The appropriateness of a second-line pharmacological approach will be evaluated collectively, according to the result of a CT scan, which will perform at 40 days from the end of radiotherapy.

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FATAL ACUTE RADIATION INDUCED LUNG INJURY (RILI) AND COVID-19 INTERSTITIAL PNEUMONIA: A SINGLE MODEL FOR TWO COMPARED CASE REPORTS

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Aims: Acute sporadic RILI is a dramatic and rare event occurring during thoracic radiotherapy (RT). Severe dyspnea, fatal acute respiratory failure due to acute distress respiratory syndrome (ARDS), outfield radiographic bilateral findings are the main features as found in COVID-19 (CO-19) pneumonia. The model of RILI has been well known and could be applied in CO-19 pneumonia understanding to contribute to its management. Herein a comparison of a case of RILI with a case of CO-19 pneumonia to assess a similarity.

Methods: Clinical records, laboratory data and CT images of two patients died for ARDS were evaluated and compared. The RT patient (RTpt) had a lung cancer treated with limited field adjuvant RT 50 Gy on right hilum who died from ARDS one-month RT off. The pneumonia patient (COpt) died from ARDS due to CO-19 infection.

Results: By clinical records in both cases fever, cough, severe dyspnea, and oxygen saturation < 70% requiring C-PaP and ventilation were reported. Anemia, neutrophilic leukocytosis, high levels of D-Dimer, fibrinogen and IL-6 were recorded. In the RTpt, the CT images described pleural effusion in right lung with air bronchogram, massive bilateral alveolar thickening and diffuse ground-glass opacities to a white lung. In the COpt a partial white lung with diffuse bilateral ground-glass opacities, interstitial thickening, and air bronchogram, were found. In RILI, by autopsy in irradiated patients, alveolar disruption with microvascular hemorrhage and hyaline membranes have been observed due to fibrin deposits and serous fluid. Pneumocytes exfoliation, platelets clots with microthrombi and loads of giant macrophages and neutrophils are recorded. All these findings have been widely described in post-mortem autopsies of CO-19 pneumonia patients too.

Conclusion: By this comparison, hypothesis of a similarity to RILI model could be a reasonable explanation of CO-19 pneumonia. As the RT, virus disrupts epithelial and endothelial integrity leading to edema, recruitment of leukocytes, resident activated platelets, immature mesenchymal and endothelial cells, neoangiogenesis, and a cascade of a self-sustaining cycle of inflammation which mimic the RILI process. Assuming this similarity, novel therapies as suggested in RILI could be applied to manage the viral pneumonia (Sivelestat sodium, anti-COX 2, nebulized Heparin, mesenchymal stem cells therapy, low tidal volume ventilation).

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DISCOMFORTS AND NEW CHANCES IN RADIATION ONCOLOGY UNIT DURING COVID-19 PANDEMIA: OUR EXPERIENCE

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Aims: Coronavirus disease 2019 (CO-19) is a declared global pandemic which has required strict containment rules to minimize community transmissions mainly in high-risk individuals such as those older than 65 years or having chronic comorbidities and cancer patients. To protect cancer patients from infection and ensure them a treatment continuity, a new health care policy have been adopted in our hospital. A completely separated logistic path has been defined which has provided several discomforts for our patients but new opportunities in our clinical practice.

Methods: Due to the location of the Territorial Covid Centre in our hospital, to preserve treated cancer patients from CO-19 infections, the Heamatology and Oncology Units have been displaced far away from the Moscati Hospital where the Radiotherapy (RT) Unit is placed. This has led to drastic changes in the cancer

therapeutic approach, emergencies managements and chemotherapy delivery in concurrent radiotherapy treated patients.

Results: Among discomforts, diagnostic imaging, laboratory tests, medical visits have been delayed while the periodical scheduled multidisciplinary team discussions have been stopped. Emergencies in RT have required mandatory hospitalizations far from the RT Unit, uncomfortable transports in unfit patients and time expensive palliative short-course radiation treatments (a full day for the whole treatment). By the patient's point of view this has been felt as a poor quality of cure indicator. Among new opportunities, short course RT treatments like a single fraction in a single day have been improved while the entire medical management of the concurrent chemotherapy delivery has been entrusted completely to our clinical practice. A refresh training course for nurses and chemotherapy management guidelines have been implemented. In agreement with medical oncologists a dedicated medical room has been organized in RT Unit to visit the patient, schedule laboratory tests, program CVC positioning and management, prescribe and delivery chemotherapy and supportive therapies. This policy has been felt cost, time spending effective and safe by the cancer irradiated community as an improved quality of care indicator.

Conclusion: Disasters as CO-19 pandemia has impacted heavy the healthy policy worldwide. Many efforts have been tried to minimize discomforts and infection risks in cancer patients. By our point of view, this event has provided a big chance to radiation oncologist to treat cancer patients as a whole.

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PNEUMONITIS OUTSIDE THE RADIATION PORTS: A COMPLEX DIAGNOSTIC DILEMMA IN THE SUSPECT OF COVID-19 PNEUMONIA

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Aims: Respiratory involvement, as mild flulike illness to potentially lethal acute respiratory distress syndrome or fulminant pneumonia is the main clinical manifestation of COVID-19 (CO-19) in adults. Chest computed tomography (CT) scan has a 98% sensitivity in CO-19 pneumonia diagnosis. Features show atypical pictorial fashions that make difficult images reporting by radiologists in case of those post radiation pneumonia features outside the radiation ports as could be in radiation therapy (RT)-Boop or Hypersensivity syndrome.

Methods: Two radiologists of CO-unit (R1) and two conventional radiologists (R2) were asked to interpret the images findings of 3 CT chest scan series belonging to 3 cancer patients treated with thoracic conventional RT within mean 3 months before CO pandemia. No data on previous RT were provided. The history of febrile episodes in a flulike syndrome was the only known information. Patient (pt) A was a 60 years (yrs) female treated with 3D conformal adjuvant RT on right breast with 50 Gy; pt B was a smoker 66 yrs old man who had been treated with adjuvant RT 50 Gy on right hilum for lung cancer; patient C was a 70 yrs old man treated with 50 Gy adjuvant RT on right mediastinum for lung cancer.

Results: In case A CT showed findings of nodular opacities with diffuse bilateral pattern and air bronchograms. The case B a bilateral and diffuse ground glass opacities within a whited-out lung picture associated to ARDS symptoms were found. In the C case images recorded a single posterior peripheral air-space infiltrate with a vessel and bronchus signs inside a slight reticular pattern area. All radiologists agree with the diagnosis of CO-19 pneumonia features with different patterns due to the different severity of the disease. After known the anamnesis of a previous chest RT, the R1 still doubted on diagnosis of CO-19 pneumonia. R2 changed the diagnosis in post-RT findings. In case A the diagnosis was RT-Boop syndrome; in case B, the diagnosis of hypersensitivity pneumonia was done; in case C the new diagnosis was focal RT-Boop. The swabs were negative in all of them.

Conclusions: In CO-19 pneumonia, chest CT findings vary in different patients and stages with a pictorial fashion difficult to differentiate from atypical findings related to post RT pneumonitis outside the RT ports. In CO-19 pandemia, sharing information with radiologists is mandatory to reduce interobserver variability in reporting a right pneumonitis diagnosis.

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ADOPTED PROCEDURES FOR COVID-19 EMERGENCY

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Aims: Departments' Directors undertook actions to prevent SARS CoV-2 infection for patients (pts) and healthcare personnel.

Methods: Epidemiological data define Covid-19 like a very contagious infection transmittable by droplets and touch. The infection is potentially lethal in particular in aged persons affected by other diseases. Our Structure of Radiotherapy (RT) treats or performs medical examinations or TC Simulations for about 100 pts/die. Most of these pts are in Chemotherapy or just finished it. So, they are often immunosuppressed.

Results: From February 23nd we done these indications: healthcare personnel holidays of were suspended. All pts and companions were triaged about symptoms

like fever or flue. In case of presence of these symptoms the pts or the companions are directly sent to general practitioner. An unique companion may stay in waiting room only if essential. Crowds are not allowed in the waiting room. All pts, companions and healthcare personnel must use surgical mask and gloves. Care is recommended for hygiene rules (washing hands, intensification of disinfection of tables and other furniture). In March 2 nd, after the DPCM of first of March, we reduced the presence in Hospital of pts without very urgent problems. We procrastinate the control visit for pts with stable or completely cured disease. These pts were monitored by phone. We analyzed the planned RT treatments of March and April: for pts over 70 years we evaluated the risk to get sick by Covid-19 or a delayed cure of tumor. For pts affected by tumors at good prognosis, controlled disease or with slow cellular kinetics, we decide, in accord with the pt, to procrastinate the treatment, anyway maintaining the guide lines timing. Moreover RT in single fraction is employed in all palliative pts. We increased the timing for each first RT visit and we recommended pts in RT therapy to be on time to avoid overcrowding in the waiting room. We did some conversations with all the heath care personnel of Structure to calm and suggest methods of prevention of infection. We positioned on the doors some information signs about the procedures to perform.

Conclusions: At the moment, no pts in RT treatment developed Covid-19 infection, but some of Physicians, Technician and Physics were infected. After the quarantine all the infected health care personnel went back to work.

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SHARING OPINIONS ON BREAST CANCER RADIATION THERAPY DURING COVID 19 PANDEMIC

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Aims: During COVID 19 pandemic, a significant role of Radiation Oncologist has been reducing exposure of patients to virus without compromising their oncological outcome.International proposals (e.g. Clinical Oncology 32 (2020) 279e281)also based just on trials,indicated to help radiotherapists in the treatment of breast cancer can be element of sharing and discussion.

Methods: We have done a reflection around two proposals. 1. Omit RT for patients 65 years and over (or younger with relevant co-morbidities) with invasive breast cancer that are up to 30mm with clear margins, grade 1-2, oestrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative and node negative who are planned for treatment with endocrine therapy. 2. Boost RT omitted to reduce fractions and/or complexity in the vast majority of patients unless they 40 years old and under, or over 40 years with significant risk factors for local relapse. One of risk factors is the presence of involved resection margins where further surgery is not possible.

Results: Omitting RT in favourable invasive breast cancer or in ductal carcinoma *in situ* (DCIS) can depend on individual risk and benefit. One of references is represented by PRIME II trial.[1] Anyway, moderate hypofractionation could be always used for whole breast treatments (40 Gy in 15 fractions over 3 weeks). Breast Cancer AIRO Guidelines (BCAG) described simultaneous integrated boost (SIB)[2,3] as time-sparing and with a radiobiologic advantage for the hypofractionated dose. In literature[3] it's been showed a low profile of late and acute toxicity. Also omitting boost is a possibility in BCAG for low risk level of patients, because boost has no proven survival advantage. Another way can be the hypofractionated sequential boost. BCAG recommended 10 Gy in 4 fractions.[4] In our practice during COVID 19 pandemic we have respected AIRO indications, both choosing hypofractionation regimen in whole breast treatment and omitting boost in low risk level of patients.

Conclusions: Risk and benefits should be discussed with patients to facilitate shared decision-making in the difficult and modified riskbenefit situation of a pandemic.Then radiotherapists should consider both an interdisciplinary approach and all the possibilities offered by the guidelines.

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P319

ANXIETY AND DEPRESSION IN PATIENTS UNDERGOING RADIOTHERAPY DURING OF THE COVID-19 PANDEMIC: THE EXPERIENCE OF UNIVERSITY OF TOR VERGATA

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Aims: The purpose of this longitudinal observational study is to evaluate emotional state of the patients who underwent to radiation therapy (RT) during of the COVID-19 pandemic.

Methods: Eligibility criteria were: any oncological disease, age ≥ 18 years, absence of concomitant psychiatric diseases, no limitation to answer to questionnaire, RT treatment more than 10 fraction. All patients signed the Informed Consent. The emotional state was evaluated by to Hospital Anxiety and Depression Scale (HADS). Patients were assessed as baseline (T0) and at

the end (T1) of radiation therapy. HADS Italian version (HADS-A subscribe to anxiety and the HADS-d subscribe to depression), is a valid and reliable self-assessment scale that measures hospital anxiety and depression. Provides clinically significant results as a psychological screening tool and can assess the severity of symptoms and the onset of anxiety and depression disorders in patients with disease. The tool it is easy to score and provides suggested intervention for clear cut-off points, which indicate the severity of the mood disorder (0-7 Normal; 8-11 Borderline case; >11 Abnormal case). In addition, two questions were proposed to describe how concerned they were about their health and how much of the COVID-19 emergency. Each question was rated on a four-point scale (0= not at all; 1 = a little bit; 2= quite a bit; 3= very much; 4= most).

Results: A total of (N=44) patients were treated with RT between 17 March 2020 and 31 May 2020, 17 males (39%) and 27 (61%) females, median age of 63 years. At the beginning of radiation therapy and in the complete covid-19 pandemic (T0), 32% of patients had mild anxiety levels with 14% expressing severe levels of depression and 54% he had no emotional distress. At the end of the radiotherapy treatment (T1) 25% of patients had mild anxiety levels with 14% expressing severe levels of depression and 61% he had no emotional distress. A Sankey diagram was performed in order to assess variations from time T0 to T1 about anxiety, depression, health and COVID-19 (Figure 1).

Conclusions: Our data show that a substantial number of patients had moderate to severe anxiety, while not many patients had severe depression. This can potentially have a negative impact on outcomes, as suggested in previous studies. Data on more patient will be available because the study is actually on-going.

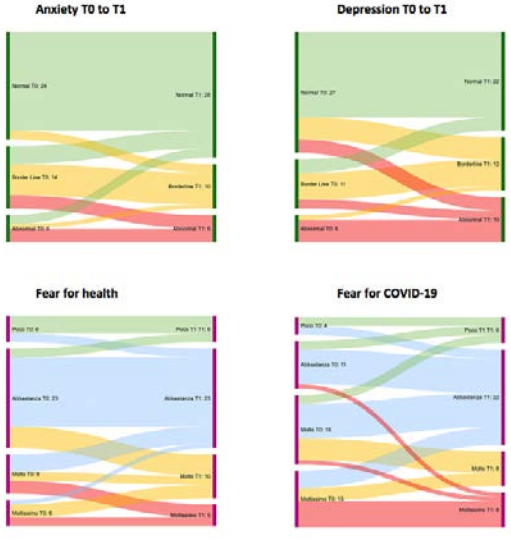

Figure 1. Sankey diagram for anxiety, depression, fear for health and for COVID-19.

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SARS-COV-2 PANDEMIC AND RADIOTHERAPY: PSYCHOLOGICAL IMPLICATIONS DURING THE LOCKDOWN

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Aims: Aim of study was to evaluate the cognitive, emotional and physical state of the patients who started RT a week (wk) before the Lockdown, leading and ending their treatment during quarantine.

Methods: Patients were assessed at 3time points: at the RT beginning (corresponding with 1 wk before Lockdown, T0), during RT (1 wk after Lockdown, T1)and at the RT ending (during Lockdown, T2). Attachment Style Questionnaire (AQS) and Brief Cope (BC) were applied at the first psychological interview to define the style of attachment within interpersonal relationships and the type of coping activated in response to stress. To evaluate anxiety, depression and distress, Hospital Anxiety Depression Scale (HADS) and Distress Thermometer (DT) were used. The analysis of the adaptation process involves different dimensions: personality characteristics, psychosocial elements, cognitive and emotional processing of the event, paying attention to the patient's history. The levels of security and insecurity in current relationships and the management strategies put in place to deal with stressful conditions were examined.

Results: 22 patients were evaluated. They underwent daily RT at a single Institution for a median time of treatment of 5 wks (range 3-6wks). 18 were female and 4 were male; the median age was 49 years (range 34-73yrs). The breast cancer was the most represented pathology (12 cases), followed by gastrointestinal, gynecological, prostate and head-neck cancers (3, 3, 2, 2 cases respectively). The AQS was reported for 5 items (Confidence, Uneasiness in intimate relationships, Secondary relationships, Worry for ralationship, Need approval) with a median value of each score, respectively of 27 (range 19-36), 42 (range 27-53), 10 (range 7-19), 22 (range 17-37), 28 (range 20-52). Regarding BC, 16 patients showed an propositive approach, while 6 an avoidant approach. The ratings of anxiety, depression and distress at T0-T1-T2 were represented in Figure 1. In general, respect baseline, all considered aspects increased during Lockdown associated with daily RT and tended to decrease with the end of the treatment. All patients completed their RT without delays.

Conclusions: This study shows that quarantine restrictions generated an increase in anxiety, depression and distress at a time already stressful due to the need to receive RT for cancer. Cognitive flexibility and emotional stability is a protective factor and allows the

adaptation of the person in conditions of stress (Cancer) and perception of risk (COVID-19).

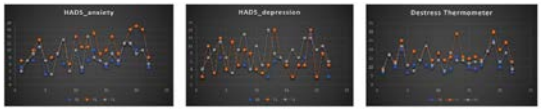

Figure 1. Ratings of anxiety, depression and distress at T0, T1 and T2.

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THE REORGANIZATION OF A RADIATION THERAPY (RT) DEPARTMENT TO REDUCE THE RISK OF CONTAGION DURING EMERGENCY COVID 19: OUR EXPERIENCE

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Aims: To perform a new organization of the activity of the RT Department during the COVID-19 emergency in order to reduce the risk of Sars-Cov2 infection among health workers and patients.

Methods: During the Sars-Cov2 pandemic several measures were taken to counter the spread of the virus within hospitals. In our RT Department in March and April 2020 non-urgent follow-up visits were postponed after contacting patients by phone, evaluating the tests performed and scheduling new exams when necessary. Obviously treatment sessions continued regularly even if some patients asked to postpone the start of the treatment or in some cases not to carry it out for fear of infection. In fact, during the most critical months of the epidemic, treatments decreased by about 10%. From March 26 to May 4, in order to reduce the risk of contagion, we decided to divide all the staff of the RT department into two homogeneus groups each of them consisted of: 3 doctors, 4 technicians, 2 nurses, and a physicist. The two working groups alternated two days in two days without ever meeting each other. Moreover, extending working hours from 8.00 a.m. to 8.00 p.m.. we could reduce the presence of patients in the waiting room by treating the patients of one of the two linacs in the morning and those of the other one in the afternoon. All staff members regularly used masks and gloves and the instrumentation in contact with the patient was sanitized after each treatment session. All patients underwent triage for Sars-Cov2 infection at the ward entrance and temperature measurement. All patients who experienced fever or respiratory symptoms were invited to stay home and, after recovery from the disease, underwent Sars-Cov2 test before resuming radiation treatment.

Results: It is difficult to clearly define the results of this project. However, we can note that during the most critical period of the emergency, no health worker from the RT department was infected. During this period, one patient undergoing treatment tested positive for Sars-Cov2. She had performed two treatment sessions coming into contact with the operators of both work groups but for a very limited time. All the health workers who came into contact with her were tested and resulted negative.

Conclusions: This project, although limited in time, allowed us to reduce the risk of contagion among patients and health workers but also to partially relieve the psychological stress of the operators related to the emergency COVID 19.

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MANAGEMENT OF A RADIATION ONCOLOGY DEPARTMENT DURING THE COVID-19 GLOBAL EMERGENCY TO REDUCE EPIDEMIC IMPACT ON PATIENTS AND HEALTHCARE: THE EXPERIENCE OF TOR VERGATA UNIVERSITY

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Aims: Radiation Oncology Departments have to guarantee treatments during the Sars Cov-2 epidemic. Some preventive measures have been adopted and suggested by AIRO; herein we analyze results about those actions applied by the UOC of Radiation Oncolgy of Tor Vergata University Hospital.

Methods: To guarantee patients and healthcare personnel safety from Sars Cov-2 infection restrictive measures were taken. Since 17 March 20 was set up triage, DPI, prioritization of cases, procedural protocol, routine and work shifts. Screening activity are divided into two phases T0 and T1. Patients were screened before entering in the UOC of the Radiation Oncology Department (T0): body temperature was measured with a thermoscan and a questionnaire about the presence of symptoms related to Covid-19 and possible contact with Covid-19 positive people was compiled. Patients with suspect symptoms were clinically evaluated before being admitted or not admitted. After 14 days patients were called back to ascertain possible appearance of any symptom referable to Sars Cov-2 infection (T1).

Results: Two hundred fifty-five patients were admitted to RT department (T0) and called back after 14 days (T1). At T0 5/255 patients (2%) patients were not admitted because of the high body temperature (BT >37.5°C), and were readmitted after monitoring. Among all patients at T0, 3/255 (1.17%) patients had contact with Covid-19 positive people, 44/255 (17.2%) had confounder symptoms due to habits (13/255), chemotherapy 22/255 (8.6%) and disease 9/255 (3.5%). The most frequent symptoms were asthenia 5.5% and cough 5.1%. At T1 232/255 (81%) were available with 3/232 (1.3%) people (2 patients and a relative) turned out to be Covid-19 positive at T1. Among the two

COVID positive patients, in one case it appears between simulation and treatment start, and the patient was admitted after 2 consecutive negative swabs, while another developed symptoms and was admitted in the Hospital. Finally at T1 one patient declared a relative with COVID infection. All 5 patients not admitted to the Department had no symptoms nor fever at T1.

Conclusions: we observed a very low incidence of COVID positive patients, and thanks to the recall we could monitor the evolution of patients conditions and ensure the safety of all the patients and the heath care personnel.

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PLASTIC-FREE RADIOTHERAPY FOR PELVIC CANCERS DURING COVID-19 PANDEMIC

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Aims: The benefit of a bladder filling protocol in order to reduce treatment toxicities in pelvic radiation therapy (RT) is well documented in the literature and adopted in daily clinical practice. In our Institute, during COVID-19 pandemic, the bottles of water used by the patients, according to government regulations, have been considered potentially infected and dangerous to dispose, no more recyclable and then throw away as biological waste. The first aim of this project was to improve security for patients and hospital staff, limiting the single-use plastics in RT waiting rooms. Second aim was to ensure the full adherence of the patients to bladder filling protocol in our Institute.

Methods: Our institutional bladder filling protocol provides that patients drink 750 cc of water, half an hour before each RT fraction, in the waiting RT rooms, in order to adapt their urination stimulus with waiting times. From May 2020 a specifically graduated and reusable water bottle was handed to each patient with pelvic cancer during first RT evaluation. The same bottle was used by the single patient during all the treatment. The bottles were donated by a non-profit association in support of our RT Unit (Associazione Onlus "Il Tratturo: Una Strada per la Vita").

Results: The project is still ongoing. Although the exiguous number of evaluated patients, in our experience, the compliance to our institutional protocol resulted improved. In fact, adopting graduated (750 cc) bottles, a lower bladder filling variation has been found in Image Guided RT controls by Cone Beam Computed Tomography (CBCT). Moreover, this project contributed to reduce the risk of contagion, since none of patients or hospital staff got COVID-19 infection during this period. Finally, the amount of biological waste has been diminished. Indeed, with an average of 20 patients daily treated on pelvis in our Center, a reduction of 40 daily, 200 weekly and 800 monthly single-use bottle of water in our Institute is estimated.

Conclusions: This project highlights the importance of support from non-profit associations for a global care of cancer patients. Since this project was introduced in our Unit was noticed a more uniform adherence to the bladder filling protocols and a greater reproducibility of patient set-up during pelvic treatment. The use of recyclable water bottles resulted in a safer habit for patients and RT staff during COVID-19 pandemic, offering also a more ecological solution.

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DOES THE COVID-19 PANDEMIC IMPACT ON RADIATION ONCOLOGY PRACTICE? AN OVERVIEW OF PUBLISHED REPORTS

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Aims: Worldwide, the COVID-19 pandemic seems to significantly impact on cancer care – both in diagnostic-therapeutic pathways and in follow up strategies – due to emergency-related conditions. To synthetize the observed changes in multiple fields of Radiation Oncology (RO), we report an overview of clinical experiences and practical proposals which were published since the beginning of the emergency period of COVID-19 pandemic

Methods: On 30 May 2020 a Pubmed search via PICO was performed using the following terms: P(cancer patients and Covid) and I (radiotherapy). No restrictions for publication type were chosen.

Results: A total of 52 titles was selected. Papers reporting national and international recommendations for clinical practice are 14; 13 papers report on practical experiences of single centers; one is a survey and 23 other analyses (risk-adapted proposals and strategies, triage and management in RO centers, physical considerations, etc). Globally, 14 papers report on multiple neoplasms, while the following studies report on tumors of specific districts: 3 breast, 3 gastrointestinal, 4 genitourinary, 3 gynecological, 2 head and neck, 3 lung/thorax cancer, 2 skin/sarcoma, 1 ocular, 3 hemaological neoplasms; one study focused on pediatric neoplasms, while one on older patients. One paper presents the rational of low dose lung radiotherapy for COVID-19 pneumonia. In summary, the use of RADS (Remote, Avoid, Defer, Shorten) principles is suggested, taking into account the necessity of personalized cancer treatments. The evaluation of patient-specific risk factors and a multidisciplinary therapeutic approach are crucial. Grouping/separating patients and optimizing the resources are important strategies to reduce risk of infection, as well as offering a pshycological support to patients and staff.

Conclusion: We observed an exponential increase in the COVID-19 publications, also including literature in RO fields. Globally, the principal endpoint of published

works was to support the balance between the risk of oncological disease progression and ill from COVID-19. Remote visits are often conducted to limit face-to-face contact. Radiotherapy avoidance could be considered only in selected cases - exclusively if the evidence suggests there will be too little advantages, or if an alternative effective treatment is available. Defer radiotherapy could be proposed if clinically appropriate. The use of hypofractionated regimens is encouraged in selected cases.

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A CLOSE LOOK AT 2-MONTH BREAST CANCER TREATMENTS IN A NON-COVID RADIOTHERAPY FACILITY IN LOMBARDY DURING THE PANDEMIC PEAK

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Aim: During the Covid-19 pandemic, the Regional Health Council did not include our Institute in the list of Covid Hospitals, creating instead a cancer HUB. We aimed to analyze the workflow of breast cancer (BC) radiotherapy (RT) in our Institute by comparing a specific time interval in 2020 and 2019.

Methods: Patients (pts) candidate to adjuvant RT in two-month interval comprising March and April 2020 were compared to those treated in the same period of 2019. Data included RT type and schedules, RT discontinuities, acute toxicity and suspicious symptoms. This study was part of a research notified to our Ethical Committee (nr 725). Median intervals were calculate and ANOVA test was performed to evaluate statistical significance.

Results: In March-April 2020, 175 BC pts were scheduled for RT. Of them, 19 eventually turned to the nearest RT centers for Covid-19 related issues and 2 forewent RT (1 declined RT and 1 had disease progression). One hundred and fifty-four remained in the wait list, registering a 16% increase compared to the same period in 2019. A comparison of key points between the two time frames is summarized in the Table 1. The increased pts volume was due to a greater influx of women coming from across Lombardy, even if the proportion of pts residing outside Lombardy remained quite high (67 in 2019 and 57 in 2020), despite restrictions of mobility. RT schedules did not basically change, being already centered on hypofractionation. Regarding the type of treatment, there was a slight increase in delivering partial breast irradiation. Chest wall re-irradiation increased in 2020, explaining the higher use of conventional fractionation, as per our re-treatment policy. A statistically significant increase of the median time (28 days in 2019 vs 31 days in 2020) between the end of chemotherapy (CHT) and the RT commence for all pts, including high risk patients, was observed, but it was clinically negligible. No relevant difference was found in the time interval between surgery and the beginning of RT for low and high risk pts. It should be noted that some high-risk pts received RT concomitantly with CHT in 2019, while in 2020 all pts completed systemic therapy before starting RT.

Conclusion: The workload of BC treatment remained basically unchanged in the study period, despite concerns and difficulties due to the pandemic. Hubs allowed the continuation of oncologic treatments, while mitigating the strain on frontline Covid Hospitals.

Table 1.

	March – April 2019	%	March – April 2020	%	Δ%
N of scheduled pts	137		175		+28
N pts treated	133		136		+2.2
N of treatments*	134		136		
Patients median age**	56 (48 – 63)		56 (49 -64)		
RT Type					
WBRT with boost	73	54.9	68	50.0	-4.9
WBRT without boost	1	0.8	5	3.7	+2.9
Fast-like RT	4	3.0	3	2.2	-0.8
Loco regional with boost	12	9.0	9	6.6	-2.4
Loco regional without boost	34	25.6	36	26.5	+0.9
APBI	5	3.8	6	4.4	+0.7
PBI re-irradiation	2	1.5	5	3.7	+2.2
Chest wall re-irradiation	1	0.8	4	2.9	+2.2
Palliative	2	1.5	0	0.0	-1.5
Fractionation schedule					
15 fractions	117	87.3	117	86.0	-1.3
25 fractions	1	0.7	7	5.1	+4.4
8 fractions	6	4.5	5	3.7	-0.8
5 fractions	5	3.7	2	1.5	-2.3
13 fractions	2	1.5	4	2.9	+1.4
20 fractions	3	2.2	1	0.7	-1.5
Patients' location					
Lombardy	66	49.6	84	61.8	+12.0
Other regions	67	50.4	52	38.2	-12.0
RT discontinuity or shift					
N of discontinuities	17	12.4	33	18.9	+6.4
Simulation CT shift	0	0.0	11	33.3	+33.3
Logistical difficulties	0	0.0	4	12.1	+12.1
Covid concerns	na	0.0	6	18.2	+18.2
Timing CHT- RT	0	0.0	1	3.0	+3.0
RT commence shift	8	47.1	10	30.3	-16.8
Personal reasons	2	11.8	1	3.0	-8.7
Timing issues	6	35.3	3	9.1	-26.2
Excess CHT toxicity	0	0.0	1	3.0	+3.0
Covid concerns	na	0.0	3	9.1	+9.1
Covid-like symptoms	na	0.0	2	6.1	+6.1
RT breaks	9	52.9	12	36.4	-16.6
Aspecific symptoms	2	11.8	2	6.1	-5.7
Excess RT toxicity	7	41.2	4	12.1	-29.1
Covid-like symptoms	na	0.0	6	18.2	+18.2
Adjuvant CHT					
Yes	34	25.6	41	30.1	+4.5
No	99	74.4	95	69.9	-4.5
Neoadjuvant CHT					
Yes	12	9.0	17	12.5	+3.5
Cancer Histology					
invasive	125	93.3	128	94.1	+0.8
in situ	8	6.0	7	5.1	-0.8
other	1	0.7	1	0.7	0.0
Endocrine therapy					
Yes	113	85.0	109	80.1	-4.8
Transtuzumab maintenance	15	11.3	11	8.1	-3.2
Acute Toxicity RTOG					
G0	16	11.9	8	5.9	-6.1
G1	94	70.1	93	68.4	-1.8
G2	19	14.2	33	24.3	+10.1
G3	5	3.7	2	1.5	-2.3
	March - April 2019		**March - April 2020**		***p*-value**
*Days between CHT and RT***	28 (19 - 33)		31 (22 - 39)		**< 0.05**
*Days between surgery and RT for low risk patients***	67 (56 - 80.7)		74 (66 - 96)		0.21
*Days between surgery and RT for high risk patients***	72 (65 - 88)		81 (71 - 96)		0.6
*Days between CHT and RT for high risk patients***	28(17 - 34)		31 (21 - 39)		**< 0.05**

*one bilateral breast treatment

**data are reported as median interval and corresponding interquartile range

High risk patients included: age <40, triple negative, Her 2 positive, inflammatory cancer, nodal positive, residual disease after neoadjuvant chemotherapy.

Low risk patients included: stage I/II, age under 65, luminal tumors, grade 1-2. absent LVI.

List of abbreviations: APBI = accelerated partial breast irradiation; BC= breast cancer; CHT = chemotherapy; CT = computed tomography; N = number; PBI = partial breast irradiation; RT = radiotherapy; RTOG = radiation therapy oncology group scale; WBRT = whole breast radiotherapy.

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INCIDENTAL SARS-COV-2 DIAGNOSIS WITH CONE BEAM CT

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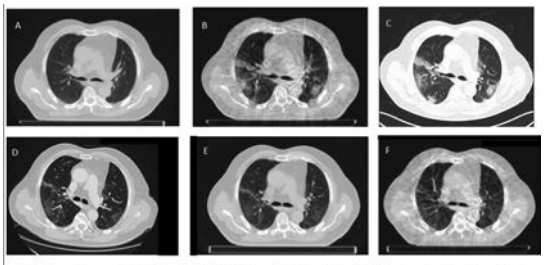
Aims: At the beginning of 2020 the Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) pandemic spread in Italy. The incidence was very high in the northern part of the Country, lowered along the Italian boot as well as the mortality. We report a case of a man with a suspected diagnosis of SARS-CoV-2 at Cone Beam Computed Tomography (CBCT) performed just before the first stereotactic treatment fraction.



A) CT simulation on 6th March 2020; **B)** CBCT on 18th March 2020; **C)** High resolution CT on 18th March 2020 at Hospital admission; **D)** High resolution CT on 29th April 2020 about forty days after negative SARS-CoV-2 test; **E)** Re-simulation CT on 8th May 2020; **F)** CBCT on 18th May 2020 at the beginning of stereotactic radiation treatment.

Figure 1.

Methods: We report a case of a 68 years old man in good clinical state, with recent diagnose of solitary heteroplastic lesion of left superior pulmonary lobe occurred during cancer follow-up. Indeed, the patient reported a history of contralateral adenocarcinoma undergone to pulmonary lobectomy (in 2016), moderate respiratory failure, diabetes mellitus, hypertension. On 6th March in stable conditions, he underwent CT-PET simulation. On 18th March, the patient came back to our hospital in order to perform the first fraction of the scheduled stereotactic radiation therapy treatment. Before his entrance he was apyretic and declared no SARS-CoV-2 related symptoms. The CBCT, performed before the first fraction to check the patient setup, showed a dramatic clinical picture with bilateral extensive Ground Glass Opacities (GGOs) and interstitial thickening. These radiologic findings were without any counterpart in the previous CT scan performed at the time of simulation. At a new interrogation, the patient told that for some days between simulation and 18th March he had presented some episodes of diarrhoea and, in the last days, a kind of dry cough and the onset of a very slight fatigue. We measured his pO2 96%. Few hours later a high-quality CT chest scan confirmed the previous suspected radiologic clinical picture and a SARS-CoV-2 test was positive. He was admitted at hospital suffering of weakness, slight dyspnoea at rest and pO2 90%. He underwent medical treatment based on Hydroxychloroquine with Darunavir plus Cobicistat. After an initial phase of worsening, severe dyspnoea at rest with O2-Therapy, clinical conditions improved. Two SARS-CoV-2 tests, on 5th an 8th April, were negative and he was discharged on 14th April eupnoeic and with no medical therapy. From 18th to 22nd May the patient was able to undergo his stereotactic radiation treatment.

Results and Conclusion: CBCT can be effective in early detection of asymptomatic or paucisymptomatic COVID-19 lung disease as shown in this clinical case and in two articles published at the time of this paper submission.

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FRAMELESS LINAC-BASED STEREOTACTIC RADIOSURGERY (SRS) FOR BRAIN METASTASES: ANALYSIS OF INTRAFRACTION SET UP UNCERTAINTIES OF A HOMEMADE MOUTH-BITE MASK FIXATION BY MEANS OF CBCT AND HEXAPOD

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Aims: To assess the accuracy of patient intrafraction errors of a frameless stereotactic linac-based radiosurgery (SRS) for brain metastases using a homemade mouth-bite thermoplastic mask in combination with with cone-beam computed tomography (CBCT) and six-degrees of freedom couchtop (Hexapod).

Methods: A retrospective cohort study was conducted selecting patients who had undergone SRS with Versa HD Linac in the Covid-19 emergency period (february 2020 to june 2020). Delays in the delivery of SRS dedicated frameless masks led to the development of homemade thermoplastic masks combined with tongue depressors as mouth-bites. An isotropic margin of 2 mm was added to the GTV to generate a PTV. A CBCT obtained immediately before SRS was used to evaluate the accuracy of intrafraction set up in the mask by comparing the isocenter position to the isocenter position established in the planning CT.The six-degrees of freedom Elektàs Hexapod Evo Couchtop system allowed to correct both translational and rotational errors for an accurate patient's repositioning. During the treatment session of the last 8 patients a post treatment CBCT was also performed to evaluate intra fraction motion. A fast treatment delivery was accomplished using 6 MV FFF beams.

Results: Thirteen patients have been selected: ten of them were treated in a single fraction, one in 3 fractions and two in 5 fractions amounting to 23 analysed fractions. The pre treatment errors were on average within

2 mm [1 – 6 mm] and 1° [0° - 2.6°] in all axes. In 8 fractions, after the correction with Hexapod Evo Couchtop, post treatments CBCTs were also acquired,.The post treatment errors were on average within 0.5 mm and 0.3° in all axes, demonstrating an appropriate mask fixation and a insignificant intra fraction error. In one post treatment CBCT the error on Z axis was 2.2 mm, exceeding the PTV's margin expansion by 0.2 mm. The other values were all within PTV margins.

Conclusions: Our findings show that homemade mouth-bite thermoplastic masks combined with six-degrees of freedom Hexapod Evo Couchtop, CBCT and fast FFF treatment delivery guarantee minimal intra fraction uncertainties in intracranial SRS for brain metastases, thus confirming the accuracy of PTV margins.

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REORGANIZATION OF A RADIATION ONCOLOGY UNIT FOR ADULT CANCER PATIENTS ACCESS DURING COVID-19 PANDEMIC LOCKDOWN: A SINGLE ISTITUTIONAL EXPERIENCE

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Aims: To contain the outbreak of COVID-19 in Radiation Oncology Unit during quarantine period (phase I) in Italy.

Methods: Adult patients with primary or metastatic solid cancer continued to have access to our Radiotherapy (RT) Unit for cancer care during quarantine period. Preventive adopted measures against the spread of the virus were: (i) telephonic triage 24 hours before patients first access in RT Unit (1st evaluation), CT-scan simulation, and 1st RT fraction; (ii) mandatory nasopharingeal swab for hospitalized patients and for patients from the most affected areas (eg San Marino); (iii) body temperature measurement at the entrance to the center; (iv) weekly triage during treatment visits; (v) to educate patients verbally and with brochures not to touch the nose-eyes-mouth area, to wear a face mask, to wash hands often with water and/or hydroalcoholic gel; (vi) no entry to accompanying persons unless deemed medically necessary; (vii) telephone follow-up calls; (viii) use of protective devices for all health care workers (change of the face mask every 4 hours or more often if clinically required, use of the FFP2 mask for patients considered at higher risk as ENT cancer, double gloves, transparent plexiglass protective visor, disposable gowns, shoe covers); (ix) medical team division into 2 groups that alternate at work every 2 weeks (to ensure care continuity in case of worker contagion and/or create a separated team dedicated to RT of positive patients).

Results: From 9th March to 3rd May 2020 a total of 100 patients (M:F=53:47; median age 71 years, range: 42-88 years) had access to our RT Unit for oncological care. Seventy-eight of the 100 patients (78%) were treated with external RT during quarantine period. Considering age as potential risk factor of severe COVID-19 illness, the majority of treated patients (61.5%) were ≥65 years, with 15.4% of older patients ≥80 years. No patient or health care worker have developed the disease.

Conclusions: The careful application of preventive measures reduce the probability of COVID-19 contagion and spread, especially among old and fragile people with cancer potentially considered at greater risk for COVID-19 complications.

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COVID-19 PANDEMIC AND RADIOTHERAPY: SURVEY ABOUT IMPACT ON WORK AND PERSONAL LIFE OF LOMBARDY RESIDENTS

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Aims: Since 20th February 2020, Lombardy has been one of the most involved areas worldwide by COVID-19 pandemic. Consequently, the healthcare system has been overwhelmed by the emergency, and so did the radiation therapy (RT) facilities. The aim of this study is to evaluate work and psychological impact of COVID-19 from the Lombardy RT residents' point of view.

Methods: An online questionnaire (22 multiple-choice questions) via Microsoft Forms was administered on 30th May 2020 to Lombardy RT residents. The survey was composed of general queries (gender, age, year of residency and housing situation) and sections dedicated to working activity and psychological area. All of the subjects gave their consent to the use of data anonymously for scientific purposes.

Results: Eighteen Lombardy RT residents responded to the survey. In most cases hospitals were converted in a hub for oncology (67%) and in 22% of cases the healthcare staff was deployed to COVID-19 departments or triage activities. 28% of residents underwent a nasal swab and/or were quarantined, after finding suspicious symptoms or contact with positives. Moreover, screening programs (nasal swab and/or serological tests) have been performed for all healthcare personnel. Fifteen residents (83%) reported a low or moderate increase of the workload. Eleven residents (60%) did not find any difference in terms of work distress, while a worsening was highlighted in 5 cases (30%) and only 2 residents reported a reduction. In any case, the majority has never considered the possibility of stopping work due to excessive stress. Almost all the residents experienced self-or relative-referred apprehension. Everyone reported having missed extra-working social

relationships. The majority of the sample noted worsening sleep quality and difficulty concentrating (72%). Nonetheless, no residents declared to have requested from psychological support.

Conclusions: Our survey represents an initial evaluation of COVID-19 impact on Lombardy RT residents' life. Overall, the residents reacted well and adapted to new workplace scenario greatly contributing to the management of COVID-19 outbreak, although some health risks and wellbeing challenges have been reported. An extension of the survey to all Italian RT residents endorsed by Italian Association of Radiotherapy and Clinical Oncology "AIRO giovani" will allow an evaluation of COVID-19 impact on a national level, also permitting to highlight any inter-regional differences.

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COVID RISK ASSESSMENT AND MANAGEMENT PROCESS IN RADIATION ONCOLOGY

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Objective: Optimization of radiotherapy work-flow during the Covid-19 pandemic to minimise or prevent the exposure of vulnerable patients and healthcare workers to the infection and ensuring full functioning of radiation activity and oncological outcome for the patients and the safety of everyone.

Materials and method: To limit the risk for patients and employers a screening protocol was implemented and radiotherapy work flow was optimized. A check-up point carried out by nurses at the radiation department entrance to measure the temperature and interview about suspected symptoms and possible contacts with Covid-19-positive patients has been the first level of screening. All patients were asked to enter alone or with just one accompanying care-giver if necessary, forwear a surgical mask, perform hand hygiene and respect interpersonal distance measures. Hypofractionated schedule and delaying of adjuvant treatment were adopted when possible. Hormone therapy or medical therapy was started or implemented if feasible by phone as well as. All appointments were scheduled by phone and follow-up visits were postponed when not necessary. The staff protection levels consisted in strict hand hygiene, disposable surgical masks and gloves, interpersonal distance measures and activation of smart working when possible. Web multidisciplinary meetings were carried out. All department zones were ventilated and disinfected twice daily. Any surfaces touched by patients were disinfected with 75% of ethanol after any scheduled treatment to avoid cross contamination of patients and personnel. Patients were asked to colour mandalas to reducing their stress level and these colourful pictures were then hanged on the walls of the department.

Results: During six-weeks of radiation oncology activity no Covid-19 infection occurred in our patients and staff. The number of patients and treatments during the lock-down did not differ from the one of the same period of the previous year. So far the Covid-19 prevention and protection measures adopted in our department have been efficient and ensured the safety and the regular clinical operativity at our radiotherapy centre.

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MANAGEMENT OF RADIOTHERAPY DEPARTMENT DURING COVID-19 PANDEMIC

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From Mar to July 202, the Covid-19 pandemic had caused around 240,000 cases and 35,000 deaths in Italy. Our hospital, the Dimiccoli was listed as "NO COVID HOSPITAL", meaning that no department was dedicated to treatment of Covid-19 cases. The general access to the hospital was reduced to one main entrance. Before access, patients (pts) followed the procedures: - measure of body temperature - inquired for symptoms of fever and respiratory disorders - inquired for contact with Covid-19 positive people - compiled auto-certification module of health - disinfect hands with hydroalcoholic solution - wear surgical mask and gloves The entrance to the Radiotherapy department was reserved only to patients for radiotherapy-related consultation and/or treatment. Only one caregiver was admitted for non-sufficient patients. They had to follow the same strict procedures listed above. Also pts treated for cranial and head-and-neck cancer required to wear the surgical mask under the thermoplastic mask. In order to minimise time in the waiting room, we invited people to strictly respect their medical examination schedule. Moreover, we developed an informed consent form about the risk of cross-contamination during treatments. The staff received training about COVID-19 prevention and protection: ffp2 masks, visors, gloves, boots and waterproof suits, disinfection procedures of treatment bed and pts immobilizations devices. We preferred shorter treatment regimens with hypofractionated radiotherapy (RT) for breast, brain and bones metastases, in order to reduce treatment time without compromising the local control. It is important to not delay or skip RT treatments. The 9th of April, a 66-year-old woman receiving treatment at our department (at her 28th out of 30 daily session of RT on the scalp for skin cancer) informed us that her husband resulted COVID-19 positive after his hospitalization for diarrhoea. She was immediately tested for Covid-19 and quarantined separately from her husband. Waiting for the test result, her RT was interrupted, and all health workers who got in her proximity were also quarantined. Luckily, her Covid-19 test resulted negative. A second test repeated after 15 days also confirmed negative. In this case the RT had almost been completed. However, it is important to screen for Covid-19 before planning treatment. Until today, fortunately, there has been no other case of Covid-19 positive pts or visitor in our RT department.

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RADIOTHERAPY DURING COVID-19 PANDEMIC. HOW TO CREATE A NO FLY ZONE: A NORTHERN ITALY EXPERIENCE

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Aim: SARS COV-2 pandemic represents a troubling health emergency but also a main challenge for the clinical governance of the system. Discontinuation of radiation treatments is not desirable and potentially life-threatening, On the other hand, accesses to hospital expose cancer patients to an increased risk of COVID-19 infection. We report our extended protocol, draft to manage clinical activities in our radiotherapy department, by minimizing contagion risks.

Methods: We used telephonic screening to assess the need for patient admission. A telephonic triage was performed to identify the presence of COVID-19 infection risk factors or symptoms. New treatments were stratified according to priority codes. A reserved entrance to radiotherapy department was assured for patients and staff. Surgical disposable mask was required for patients and caregivers. The activities were distributed during the whole workday, avoiding overlap to reduce aggregation.

Results: From 1st February 2020 to 31 March 2020, we reported an increase in the number of first medical examinations and treatments, compared to the same period of the previous year. Outpatients first medical examinations have been spread over the 12 working hours. No COVID-19 cases were detected.

Conclusions: During COVID-19 pandemic, we introduced procedures that allowed us to ensure the continuity in oncological cares, with limited risks of infection for patients and staff.

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BACK TO (NEW) NORMALITY - A CODRAL/AIRO-L SURVEY ON CANCER RADIOTHERAPY IN LOMBARDY DURING PHASE 2

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On behalf of the CODRALBoard of Directors of Radiation Oncology Departments in Lombardy network and of the AIRO Italian Association of Radiotherapy and Clinical Oncology Lombardia

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Introduction: Italy experienced one of the world's

deadliest COVID-19 outbreak, and Lombardy accounted for approximately half of all Italian deaths. A previously published study[1] investigated how Radiotherapy (RT) Departments in Lombardy faced the emergency during the so-called Italian phase 1 (P1) (8th March - 3rd May 2020). The present work, endorsed by CODRAL and AIRO Lombardy (AIRO-L), is based on a survey aiming to assess how RT Departments in Lombardy have faced up the recovery during the Italian phase 2 (P2) (4th May 2020 – 17th June 2020) of the pandemic.

Table 1. COVID-19 cases among Lombardy RT staff.

	Rad Oncol		RTT		Nurses		Admin		Physicists		All	
	N	%	N	%	N	%	N	%	N	%	N	%
Total*	170	100.0	193	100.0	80	100.0	35	100.0	76	100.0	554	100.0
Suspect	26	15.3	31	16.1	17	21.3	3	8.6	3	3.9	80	14.4
Tested**	24	14.1	19	9.8	14	17.5	1	2.9	2	1.3	59	10.6
Positive**	16	9.4	18	9.3	13	16.3	1	2.9	2	2.6	50	9.0

Legend

The sum of all suspected cases, tested cases with swab, positive cases after swab, out of the total number of units of staff, are reported for each working category - namely radiation oncologists including specialists and residents (rad oncol), radiotherapy technicians (RTT), nurses, administrative staff (admin) and medical physicists (physicists) – and overall (all).

NB Data not available for 2 units of personnel in 4 centres and in 4 units of personnel in 1 centre. Table reports the sum of all units of personnel across the 21 centres which reported positive cases for each working category in absolute values (N) and in percentage of total staff (%).

* total number of Rad Oncol/RTT/Nurses/Admin/Physicists in Lombardy RT centres

** swab test was performed

Materials and Methods: An online questionnaire was developed by the Governing Council of CODRAL and AIRO-L by readapting its P1 counterpart (queries were restructured according to the current epidemiologic and legislative scenario). The final version was anonymously sent, via Google Forms, to all CODRAL Directors on the 10th of June 2020. The questionnaire focused on two major key points and aimed at assessing to what extent the clinical and outpatient activities have been restored and at investigating the contagion data (patients, staff) and anti-contagion measures put in place during P2Results: At the due date, all 33 contacted RT facilities (100%) responded to the survey. Despite the scale of the pandemic in Lombardy, results show that during P1 14 (42.4%) centres managed to continue the activity (< 10% reduction in workload). During P2, 10 (30.3%) centres fully recovered and 14 (42.4%) reported an increase. Nonetheless, 6 (18.2%) still declared no changes with respect to P1 and, interestingly, 3 (9.1%) reduced activities. Concerning the management of personnel, during P2 virtually all centres (29, 87.9%) made available class II/III filtering facepieces (FFP2/FFP3) to healthcare staff. Overall, 21 centres (63.6%) reported suspected or positive cases within workers, especially those in contact with patients (Table 1), since the beginning of the pandemic. One or more staff units were in quarantine in 19 (57.6%) and 6 (18.2%) centres during P1 and P2, respectively. In the two phases, about two thirds centres registered positive or suspected cases among patients.

Conclusion: The P1 study showed how RT departments in Lombardy had rapidly coped with the COVID-19 disruption. The present P2 study demonstrated a return to normal or even higher clinical activity in most Lombardy RT centres, accompanied by improved staff, patient and ambient anti-contagion protection.

Reference

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P334

FOLLOW-UP MANAGEMENT IN PATIENTS TREATED WITH RADIOTHERAPY FOR HEAD-NECK CANCER (HNC) IN A SINGLE CENTER DURING COVID-19 PANDEMIC

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Aims: SARS-CoV-2 infection was declared a global pandemic by WHO; in Italy by May 26th 231000 cases were confirmed with 32955 deaths. HNC cancer patients (pts) represent a high-risk group for COVID-19, especially if comorbidities are present and older age. The pandemic severely changed pt's management, not only in terms of diagnosis and treatment but also regarding follow-up(FU). Here we present how FU and post-treatment toxicity evaluation were carried out during the lockdown in order to guarantee HN pts' continuity of care.

Methods: HNC pts underwent a phone interview where they provided information about their nutrition, pain control and presence of skin toxicity, mucositis, xerostomia and dysgeusia; where available, a digital copy of instrumental exams report was viewed, otherwise the patient read it during the call. Dematerialized prescriptions for blood test or instrumental exams were sent by e-mail, making arrangements to prioritize most urgent requests. If necessary , accesses to the unit occurred with individual protection devices after nursing triage with body temperature check and a brief medical history collection.

Results: Between 3thMarch and 7th May, 51 pts with HNC cancer were called on the phone. 15 pts took contact more than once (2-4 times) based on clinical necessities. 2 pts were received in our unit for a toxicity evaluation due to low compliance and lack of caregivers (1pt) or anxious state (1pt). Treatment to obtain better pain control and ease post-radiation therapy toxicity were prescribed in 11 pts. About 70% of total re-evaluation instrumental exams were postponed, especially for adjuvant treatments, while therapies with radical intent were considered high priority. 2(4%) tumour relapses and 1 suspected local relapse were detected during lockdown. No pts reported COVID-related symptoms. The most notable problems during the observation period was toxicities control like mycotic infection, malnourishment and FU of elderly pts. Only 8 pts were contacted by mail due to younger age. All pts were agreed with FU methods during the lockdown.

Conclusions: Elderly HNC pts required particular attention in accessing health structures due to higher probabilities of negative event in case of SARS-CoV-2

infection. COVID-19 pandemic drastically changed risk/benefit ratio for health structures' access in terms of FU, anyway a high standard of care could be maintained in order to investigate disease progression or suspicious symptoms.

P335

RADIOTHERAPY IN SOUTHERN ITALY AT THE TIME OF COVID-19: A MONOCENTRIC EXPERIENCE

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Aim: To share the experience of our Radiation Therapy department in Southern Italy in the management of the steady state of the COVID19 pandemic.

Methods. The patients and department staff's safety required a strictly plan to minimize the risk of infection between operators whose absence would have made impossible to carry out the radiotherapy (RT) treatments. The head of the RT unit and members of the Hospital Crisis Unit had put in place a series of measures to manage the emergency.

Results. A "clean" team has been established consisting of 2 doctors, 2 radiation therapists and 1 nurse who were kept out of the RT unit for 2 weeks on rotation. Several separate work areas were made in order to reduce the direct contacts between the staff. Each staff member had to wear personal protective equipment if close contact with patients is required. We also extended our time of activity, to further distance the treatments, reducing the risk of crowding in the patients' waiting areas. Before confirming a RT consult or a follow up visit, a phone clinical and epidemiological screening is performed by nurses through a questionnaire regarding the presence of respiratory symptoms or eventual social contacts with COVID-19 positive people. Once the patients arrive in our hospital, a triage point at the entrance to the hospital perform a second screening as well as a temperature check; moreover, if the patient was suspected or confirmed to be positive to COVID-19, dedicated routes inside the structure were identified to avoid contact with other patients. In order to reduce the patients flux we conducted most of the programmed follow up visit (96%) by phone and/or telematic media. Confronting the time period before the pandemic between the 3rd January and 22th February with the acute pandemic period between the 9th March and 19th April, we registered a 30% reduction of first clinical evaluation, but only a 5% reduction of follow up visits and a 4% reduction of number of treatment fractions.

Conclusions. This management experience of a RT unit in Southern Italy could be an useful example for the next future. In fact, in the steady state of infection many Centres may face epidemiologically contagious numbers similar to those that we currently have in our region. These numbers require the maintenance of the alert and precautionary measures which in our case seem to have worked.

P336

RADIOTHERAPY MANAGEMENT OF GLIOBLASTOMA (GBM) DURING COVID 19 PANDEMIC: PRACTICAL VADEMECUM OF THE AVAILABLE EVIDENCE

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Aims: Pandemic COVID 19 requires remodeling of clinical activities and an optimization of resources; particular care towards cancer frail patients, which appear to have an estimated twofold increased risk of contracting SARS-CoV-2 than the general population. Patients with Central Nervous System (CNS) primitive tumors frequently require radiation treatment and chemotherapy, often also in association. Objective is to offer clinicians pocket usable guidelines to address management of patients with Central Nervous System (CNS) cancers during pandemic SARS coV-2. Focus was placed on strategies to reduce hospitalization time, to achieve the best possible balance between the two different issues: the risk of cancer progression and the risk of infectious disease; to reasonably offer the best oncological treatment.

Methods: We aim to develop a practical framework by which to evaluate Glioblastoma Multiforme (GBM), the most frequent neoplasia of CNS, radiotherapy management decision during COVID19 pandemic, based on current evidence. We assessed systematic reviews, national guidelines, results from randomized clinical trials, and treatment arms in randomized trials. Studies were required to be published in English between January 2000 and May 2020. This literature search was performed using MEDLINE via PubMed only. Dual screening of the literature for inclusion was performed by SL and MG to minimize the risk of selection bias.

Results: Treatment continued despite the current COVID 19 pandemic state. Minimization of infection risk is achievable without compromise oncological outcomes, privileging ipo-fractionated regimens and home-manageable oncologic drugs. The hypofractionated treatment in particular would seem to achieve the best possible balance between the risk of exposition while still guaranteeing the effectiveness of the treatment. Moreover, the treatment options should be considered on a case-by-case basis.

Conclusions: Cancer patients are those most exposed to COVID-19 infection, with risk of showing deteriorating conditions and poor outcomes. Treatment

continued despite the current pandemic state. Patient care plans should be guided by best available evidence to optimize outcomes while maintaining a safe environment in the setting of this pandemic. Finally, this framework could apply only to patients not infected with COVID-19.

P337

PROTECTION AND ACCESS TO CARE FOR CANCER PATIENTS DURING THE COVID-19 PANDEMIC: HIGH RELIABILITY ORGANIZATION IN THE EXPERIENCE OF RADIATION ONCOLOGY OF AREZZO - VALDARNO

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Aims: To guarantee access to care and continuity of radiotherapy (RT) during Covid pandemic to fragile patients such as cancer patients (CP), who have greater susceptibility to the infection itself and greater mortality.

Methods: Emerging data, national and regional legislation have entailed the need to revise or create some new procedures for CP on RT, focusing to both the dimension of "curing" and of "caring". High Reliability Organization (HRO) model has been the clear roadmap to move forward for safe and reliable care during pandemic.

Results: To ensure access to care while minimizing risk of infection, most of the RT treatments were moved from the Radiation Unit of Covid Hospital of Arezzo to the no Covid Hospital of Valdarno (pivotal role of Hospital Network of ASL Toscana Sud Est). The appropriateness of oncological treatments was re-evaluated and tailored on a person-centered perspective, to weigh risks (also in terms of Covid-19) and benefits (classification of oncologic risk of the disease and priority). Alternative therapeutic strategies to reduce access to the Facility (like active surveillance, endocrine therapy, oral chemotherapy, hypofractionated RT) were considered. Doctor-patient interaction via telemedicine was experimented to support CP, to minimize number of visits and risk of exposure. When telemedicine was not appropriate to healthcare needs, CP had fractional access to the waiting room with social distancing and use of Personal Protective Equipment. Health education and information about the Radiation Unit protocol against the spread of Covid-19 and psychological support were given to CP. Facility procedure for nasopharyngeal swabs for the detection of SARS-CoV-2 (in CP hospitalized in Day Hospital regimen) was developed. Access to the Radiation Unit was restricted to CP, with limited access for careers and volunteers. Moreover, Multidisciplinary Oncology Groups discussed clinical cases by videoconference. Innovative training resources on Covid-19 and CP were created and uploaded to ASL Toscana Sud Est Intranet.

Conclusions: Pandemic has defined a "window for opportunity", in which new procedures in response to Covid-19 represented positive changes that should be maintained and implemented (safety and reliability of personalized interventions, multidisciplinary teamwork, resilience and psychological wellbeing of both patients and medical professionals, development of Information and Communications Technology for telemedicine).

P338

BURNOUT RISK OF HEALTHCARE WORKERS WITH CANCER PATIENTS DURING THE COVID-19 OUTBREAK

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Aim: Since the WHO declaring of novel coronavirus (COVID-19) outbreak a pandemic on 11th March, the virus has reached more than three millions of cases and 250.000 deaths all over the world. At the same time, COVID-19 is having a devastating psychological impact on healthcare workers. This work aims to evaluate the risk of burnout among healthcare workers (HW) in radiation therapy department.

Methods: We included all the HW in Radiation Therapy Department in two time points (in May 2019) and during the COVID-19 outbreak (in April 2020). All the HW were asked to fulfill Psychological General Well- Being Index (PGWBI test) and Maslach test. The tests were anonymous and included nurses, radiotherapists, physicists, and radiation oncologists. We calculated the differences in scales for the timepoints with the Anova test.

Results: Thirty healthcare workers were included for the present analysis. PGWBI median score was 73 (mean 72.24, range 31-110), whereas the median Maslach scores were 32 for the Emotional Exhaustion (EE), 12 for the Depersonalization (D), and 31 for the lack of Personal Accomplishment (PA). PGWBI's total score was significantly correlated with the COVID-19 outbreak (p:0,021), whereas two of the subscales of Maslach test were significantly reduced during the COVID-19 outbreak.

Conclusions: HW are at a significant risk of burnout syndrome in this difficult period. These measurements could be useful as a baseline to start medical humanities programs to decrease these scores.

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CLINICAL EVALUATION OF COVID-19 IGM AND IGG RAPID TEST IN CANCER PATIENTS

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Aims: Italy is one of the most affected Countries in the world by the severe acute respiratory syndrome coronavirus 2 (SARS-COv-2) causing the Coronavirus disease of 2019 (Covid-19). Cancer patients are more subsceptible to viral infection and to contract severe form of Covid-19 because of their immune compromised status caused by the malignancy and antineoplastic therapies. Thus, a triage protocol aimed to avoid SARS-COv-2 outbreak in a radiation oncology department is warranted. The purpose of this study was to evaluate the clinical utility of rapid colloidal gold immunochromatography assay (RCGIA) for screening of patients in a Radiation Oncology department.

Methods: All patients who underwent radiotherapy or follow-up examination at the Radiation Oncology department of the University Federico II from April 2020 to 22 June 2020 were enrolled. For each participant, exposure history, clinical symptoms, oxygen saturation and body-temperature were collected, repeated once a week for in treatment patients. For each participants, finger-stick capillary blood was collected and SARS-CoV-2 IgG-IgM combined antibodies test (LeccurateTM kit, KHBR kit) was performed. Nasopharyngeal and oropharyngeal swab samples were collected in the same day for patients who tested positive or patients with at least one symptom and positive exposure history and sent to referral laboratory for RT-PCR test. If the RT-PCR result was negative, a repeated blood samples collection and, where appropriate, PCR test would be performed after two weeks.

Results: In the study period a total of 304 cancer patients (114 treated, including 29 cranial/head-and-neck patients, 52 thoracic patients, and 33 abdominal/pelvic patients, 190 follow up visits) were checked. Nine patients (3%) tested positive at RCGIA: 5 for IgG, 2 for IgM, 2 for IgM and IgG. The clinical characteristics of the 9 suspected COVID-19 cases were reported in Table 1. All these patients resulted negative at RT-PCR test on swab sample; seven repeated blood sample collection after two weeks and tested negative. Suspected patients experienced a radiotherapy interruption of an average of 4,6 days due to COVID-19 related investigation.

Conclusions: No patients had suspicious symptoms in the observation period, and no one actually developed Covid -19; thus our study is not informative about the ability of RCGIA to detect efficiently SARS-COv-2 infection. However, our study poses some concern about the rate of false positive of RCGIA. Further studies will be necessary to assess the utility of RCGIA to prevent infection outbreak in oncological environment.

Table 1. Clinical characteristics of all patients.

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9
Age	72	53	58	70	77	69	72	48	49
Sex	M	M	M	F	F	F	F	F	F
Treatment site	Head and neck	Pelvis	Head and neck	Thorax	Thorax	Thorax	Thorax	Thorax	Pelvis
Reason for access	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Follow-up	Follow-up
Positive antibodies	IgM	IgG	IgM	IgG	IgM/IgG	IgM/IgG	IgG	IgG	IgG
Interruption days	5	5	8	5	3	3	3	/	/
Repeated blood test	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No

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RADIOTHERAPY RESIDENTS' SMART APPROACH TO COVID-19: ANSWER THE PHONE, IT'S A QUESTION OF SAFETY!

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Aims: To report our experience as residents in dealing with the SARS-CoV-2 pandemic in the setting of Radiation Oncology (RTO) Unit 1 and 2 of the "Fondazione IRCCS-Istituto Nazionale dei Tumori" of Milan.

Methods: From April 2020 adult patients (pts) who accessed our RTO ward underwent a personalized telephonic triage created by 11 residents from 3 different universities (Milano-Statale, Milano-Bicocca, Napoli-Federico II). Pts were called in 4 different settings: simulation CT (sim CT), treatment start (TS), first outpatient visit (FOV) and follow up visit (FUV). The triage consisted of a brief questionnaire focusing on pts' symptoms and possible chain of at-risk contacts both in domestic and extra-domestic settings, for example visits in other hospitals and general practitioner (GP) in a span of time of 3 weeks.

Results: From the 7th of April to the 10th of June 2020, 712 pts were administered the triage questionnaire with 944 calls in total: 208/944 (22%) FOV, 274/944 (29%) sim CT, 255/944 (27%) TS and 207/944 (22%) FUV. None of the pts had a previous nasopharyngeal swab. The pts with characteristics symptoms were

116/712 (16%): in details 23/116 (20%) pts with fever ≥ 37.5°C, 46/116 (40%) pts with dry cough, 47/116 (40%) pts with dyspnoea. Pts who had previous access to other hospitals and/or GP were 246/712 (34%) while 7/712 (1%) pts reported living with symptomatic people. Only 17/712 (2%) pts were found to be at high risk for SARS-CoV-2 and they were not granted access to our department until further medical examination. To ascertain a possible infection, 4/17 (24%) pts underwent nasopharyngeal swabs and 7/17 (41%) were screened with a specific chest CT scan. All the swabs turned out negative while one chest CT was deemed suspicious but with a following negative swab. The remaining 6/17 (35%) pts were lost in follow up.

Conclusions: In the middle of the SARS-CoV-2 pandemic, our telephonic triage proved to be a helpful additional tool in rapidly selecting and isolating possible new asymptomatic cases beyond the institutional access controls. This enabled the other pts to undergo the scheduled radiotherapy treatment safely and without harmful delay, and the staff to pursue fearlessly their routine.

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IMPACT OF COVID-19 PANDEMIC IN THE CLINICAL MANAGEMENT OF CANCER PATIENTS UNDERGOING RADIOTHERAPY: MULTICENTRIC STUDY

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Aims: The current SARS-COV-2 pandemic (COVID-19) may affect the correct management of cancer patients, resulting in treatment delay and suspension. The aim of our study is to evaluate the impact of COVID-19 on patterns of care in a multicentric cohort of patients treated with radiotherapy (RT).

Material and Methods: A retrospective review of data from 5 institutions in Northern Italy and Sicily was carried out. Patients undergoing testing for clinical suspicion of COVID-19 between January 2020 and June 2020 were included in our cohort. Descriptive statistic was applied to summarize results.

Results: Forty-three patients were included, mostly requiring RT for Head and Neck cancer (n=7, 17%), Breast cancer (n=8, 19%), and cancer-related symptoms palliation (n=13, 30%). Clinical suspicion of COVID-19 was based on abnormal findings at lung simulation, in-treatment, or follow-up imaging (n=18, 41%), evocative semiology (n=10, 23%), or both (n=15, 36%). Isolation measures were enforced in all suspected cases until diagnosis was invalidated by specific testing. However, hospital admission due to interstitial pneumonitis was required for 20 patients (46%), that was ultimately fatal in 6 cases (14%). RT postponement and suspension > 48 hours were required in 7 (16%) and 20 patients (46%) respectively: among the latter, treatment was resumed after recovery in 11 patients (25%) and prematurely closed in 9 (21%). Treatment continuation was allowed in one case despite positive COVID-19 testing after implementation of personal protective equipment (PPE). COVID-19 diagnosis was confirmed by nasopharyngeal swab (NPS) testing in 51% (n=22) of cases; further confirmation by broncho-alveolar lavage (BAL) was required in 2 patients (5%).

Conclusions: Clinical suspicion of COVID-19 in cancer patients who are candidate or undergo RT may result in significant treatment breaks and delays that may negatively affect outcome. COVID-19 diagnosis was confirmed by NPS testing in 51% of patients referred for non-specific radiologic or clinical signs. Detection of lung abnormalities at treatment-related imaging occurred in 77% of cases and may help identification of initial lung involvement in asymptomatic patients.

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PHONE CALL TRIAGE FOR PATIENTS ADMISSION IN A RADIOTHERAPY DEPARTMENT DURING COVID 19 PANDEMIC

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Aims: The SARSCoV-2 caused coronavirus disease 2019 (COVID-19) is an epidemic which originated in China and spread around the world rapidly becoming a pandemic. A prompt identification of infected patients, together with all the prevention measures, is fundamental to manage the risk of Covid-19 in our Radiotherapy department and to prevent a diffusion in the new unexpected outbreak of the virus both during the peak and the mitigation phase.

Methods: Between March 2020 and July 2020, all patients who accessed Radiotherapy (RT) department received a telephone triage the day before entering our ward. The telephone questionnaire, based on SERESMI form, included questions about Covid-19 symptoms and an interview on possible contacts with positive patients.

Results: 679 patients received the telephone triage. One patient (0.14%) patient with an operated breast cancer was postponed for 2 weeks for rhinorrhea in the absence of further symptoms and attributable to an antihistamine-responsive allergy. It was not necessary to perform nasopharyngeal swab. One patient (0.14%) with lung tumor candidated for concomitant chemoradiation treatment reported contact with a swab positive patient; despite being asymptomatic, two negative nasopharyngeal swabs were performed before simulation computed tomography (CT) scan for radiotherapy treatment. All the other patients (677/679; 99.7%) received RT as planned; Only 15/679 patients (2.2%) referred asthenia which was present before diagnosis. No patients were found to be positive during and after treatment.

Conclusion: Covid 19 prevalence was limited in our Center. However, telephone triage remains an effective method of preventing the entry of symptomatics into the oncological department.

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PSYCHOLOGICAL IMPACT OF THE COVID 19 PANDEMIC IN CANCER PATIENTS: A CROSS SECTIONAL OBSERVATIONAL STUDY

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Aims: On 30 January 2020,WHO declared the outbreak of coronavirus disease 2019(COVID19).As cancer patients are already considered at increased risk of persistent depressive and anxiety disorders, the aim of this study was to evaluate psycological impact of the COVID19 pandemic in these patients. Psychological counseling services were offered to patients who showed anxiety and stress above selected cut off levels.

Methods: This study was approved by Institutional Ethical Commitee. All consecutive adult cancer outpatients who had access to our Department between April and May 2020 were prospectively enrolled in this study and therefore received structured and validated ad-hoc questionnaires. Emotional distress was measured by means of visual scale. The structured questionnaire consisted of questions covering several areas such as knowledge and concerns about COVID19, the psychological impact of the COVID19 outbreak and mental health.Validated self-assessment questionnaires for the evaluation of psychological functioning and resilience skills were: 1) Connor-Davidson Resilience Scale (CD-RISC-25) investigating five factors of resilience; 2) Beck Depression Inventory-II (BDI-II) consisting of 21 items evaluating the severity of depression;3)State and Trait Anxiety Inventory(STAI-TRAIT-Y) investigating the anxiety-trait and anxiety-state.

Table 1.

QUESTIONNAIRE	MEAN SCORE	STANDARD DEVIATION
Physical concern (score 8 to 40; higher score indicates worse levels of Physical concern)	22.57	16.15-28.99
Emotionality (score 6 to 30; higher score indicates worse levels of Emotionality)	14.33	8.41-20.25
Distress (score 0 to 10; higher score indicates worse levels of Distress)	3.34	0.68-6
CD-RISC-25 (score 8 to 40; higher score indicates better resilience)	33.48	27.58-39.38
BDI-II (score 0 to ≥30; higher score indicates worse levels of Depression)	8.81	1.09-16.53
STAI-Y (higher score indicates worse levels of Anxiety)	38.68	28.66-48.7
TRAIT-Y (higher score indicates worse levels of Anxiety)	36.56	26.81-46.8

Results: A total of 208 of 210 patients completed the survey with a participation rate of 99%.40% were male and 60% were female; 35.6% patients were employed and 20.8% patients got graduation. Most of patients (79.3%) were in treatment and 20.7% in follow up.70 patients (42.7%) received palliation treatment and 94 (57.3%) curative treatment. Questionnaires scores were summarized in Table1. Higher levels of depression were detected only in 3.4% of patients,while the majority of patients(78.6%) did not present any form of depression. Emotional distress was observed in 36.9% of patients. Higher physical concern was more common in treatment patients compared with follow-up patients (mean score 23.01 vs 20.9, p=0.05), as well as distress level(3.5 vs 2.6,p=0.022). Anxiety during COVID19 worsened in all patients (p=0.001). Psycological counselling was offered in 62 patients(29.8%).

Conclusion: During COVID19,depression and emotionality were limited in our patients.Physical concern,as expected due to the cancer diagnosis,was present in this cohort of patients and was higher in treatment compared with follow up patients.COVID19 worsens Trait-Anxiety in all patients.

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RADIOTHERAPY DURING COVID-19 PANDEMIC: EXPERIENCE FROM CATANZARO, ITALY

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Aims: We report our experience about the organization of the activity of a radiotherapy service during pandemic period. Protocols and procedures have been adopted with the aim of minimizing risk of infection

between patients and all radiation oncology professionals and allowed the continuity in oncology cares.

Methods: All the activities of our department were distributed during the whole workday, avoiding overlap. All patients (pts) planned to access in the our radiotherapy center (radiation treatment, simulation CT, follow-up and first medical visit) were contacted by phone the day before the scheduled appointment (telephone-triage). A triage point at the entrance to the hospital performs a second screening, as well as temperature check. All patients were located in specific waiting rooms with the chairs are spaced with the aim to maintain a minimum distance of 1 m. The dispensers with sanitizers for hand hygiene have been distributed in waiting rooms and treatment rooms. Where possible, entry of accompanying persons were restricted. According to the recommendations of the Ministry of Health and Civil Protection for cancer patients and on the basis of WHO recommendations, each members of staff and all patients cancers had to wear the surgical mask even in the absence of verified or suspected symptoms. In case of contact with Covid-19 positive patient, all operators were instructed to wear sterile disposable gowns, surgical and FFP2 masks, goggles, double gloves, clogs and over-shoes. Furthermore, all staff working in the radiotherapy department, underwent Covid-19 tests and none have tested positive. From 1st March 2020 to 30 June 2020, were treated 380 pts (breast 94, prostate 80, head neck 58, gastrointestinal 40, lung 37, bone metastases 37, brain 25 and skin 9) compared to 387 pts treated in the same period of the previous year.

Results: During Covid-19 pandemic we did not see a reduction in radiotherapy treatments but a decrease in follow-up visits. No COVID cases were detected between all operators and pts.

Conclusions: The procedures and protocols adopted in our center have guaranteed the continuity of treatment of cancer patients without any infection among healthcare professionals or patients.

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COVID-19 OUTBREAK: IMPLEMENTATION OF MONO-INSTITUTIONAL RADIOTHERAPY PROTOCOLS

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Aims: Oncology patients (pts) are at risk of severe forms of COVID-19 disease. During pandemia, Radiotherapy Units had to ensure cancer treatments continuity and to avoid risk of contagion of pts and health professionals. In our Hospital Center, several Units were closed because of many COVID-19 cases detecting (in particular, Oncological Unit). We considered the need of available guidelines for the optimal management of our activities during this new emergency, employing specific protocols.

Methods: Italian Association of Radiotherapy and Clinical Oncology (AIRO), American Society for Radiation Oncology (ASTRO) and European Society for Radiotherapy & Oncology (ESTRO) recommendations were rewieved. Italian Institute of Health Guidelines and Mazzini Hospital Management Directives were also taken into account to provide a specific Radiotherapy Unit document for COVID-19 emergency. Radiation Oncologists, Technicians and Nurses contributed to the drafting of the paragraphs relating of their own activity.

Results: We elaborated two protocols, one for the radiotherapic management of NON-COVID-19 pts and one for not deferable treatment of COVID-19 pts. We focused on 4 main issues: reorganization of activities, oro-nasopharyngeal swab tests for pts and staff (in terms of timing and indication), hygiene practices improvement, personal protective equipment (PPE) use. Documents were rewieved and approved by the Risk Management Unit. Protocols were easily and rapidly implemented in our clinical practice, so treatment and clinical visit schedules were modified to reduce overcrowding and follow-up visits were differed after phone interview. All radiotherapy staff was subjected to oro-nasopharyngeal swab tests every 20 days (even if asymptomatics) or before, if symptomatics or at risk of contagion. Pts received swab before CT-simulation; body temperature and oxygen saturation were assessed before the daily radiotherapy session. Pts were instructed by nurses about personal hygiene rules and the use of PPE. According to hospital directives, environmental sanitation and intervention were applied. We achieve treatment continuity, without delays or interruptions. No COVID-19 cases were diagnosed between pts, medical and paramedical workers.

Conclusions: In our experience, institutional protocols implemented during COVID-19 emergency allowed to mantain continuity of radiotherapy, balancig the need of oncological cares while limiting the spread of contagion for staff and pts.

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THE MANAGEMENT OF CLINICAL AND RADIOLOGICAL EXAMINATION IN THORACIC ONCOLOGY DURING COVID-19 EMERGENCY

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Aims: The global COVID-19 pandemic has brought huge challenges to the clinical practice of thoracic oncology. Patients with lung malignancy showed an increased risk worldwide of presenting symptomatology and serious complications. A large number of both clinical and radiological evaluation had been cancelled to ensure the availability of resources dedicated to the infectious emergency. We want to evaluate the flow of

patients and the proper timing performing radiological examination in lung cancer patients.

Methods: We analyzed the flow data relating to outpatient appointments of patients with lung cancer come to our center, comparing a 60-day period of the infectious emergency with the same time frame in 2019. We also assessed the delay for the staging and restaging radiological procedures due to the peak of the infections. The cut-off to defined a significant delay was established to be greater than 14 days.

Results: Outpatient appointments from the 15th of March and the 15th of May were 136 in 2019 and 187 in 2020. In 2019, 79.4% of outpatient visits were revaluation or follow-up, while 20.6% were first examinations. In 2020, 77% were revaluation or follow-up visits while 23% were first examinations. A total of 151 radiological examinations were performed in 2020. Only 11 of these (7,3%) were delayed. The mean delay for the radiological investigations was 4.8 days, with a standard deviation of 10.3 days.

Conclusions: Data demonstrate an overlap of number and type of visit between the same time frame, with higher absolute values in 2020. Despite the difficulties due to the restrictions caused by the COVID-19, our hospital has been able to guarantee both the diagnostic and the clinical activity. The scheduled medical appointments were performed with acceptable delays.

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COVID-19 IMPACT IN RADIOTHERAPY PRACTICE: A MONOINSTITUTIONAL EXPERIENCE

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Aims: During last months, medical clinical activities have been dramatically modified by the COVID-19 emergency, especially in Milan, one of the most affected cities by the pandemic. Cancer patients (pts) have been reported to be at higher risk of COVID-19 complications and deaths. Our aim is to evaluate the impact of COVID-19 to radiotherapy (RT) practice in a hub cancer center.

Methods: A retrospective data collection of pts with suspected COVID-19 infection, identified by pathognomonic symptoms feedback at triage realized at the entrance of RT Division. Inclusion criteria were: 1) diagnosis of oncological disease; 2) COVID-19 related symptoms reported from 01.03.2020 to 31.05.2020; 3) signed written informed consent for the use of personal data for scientific purposes (research project identifier: UID 2349).

Results: Thirty-two pts matched inclusion criteria, 20 women and 12 men. The cohort was heterogeneous for gender, age, Karnofsky Performance Status (KPS), tumor site and stage. Median age was 68 (range 42 – 94). Most of pts had KPS 100 (18/32), while 12/32 had KPS 90 and only 2/32 had KPS 80. Tumor sites were: 9 breast, 6 head and neck, 6 gynecological, 3 NSCLC, 3 prostate, 1 non-Hodgkin lymphoma, 1 neuroendocrine, 1 high-grade sarcoma, 1 rectum and 1 double site (rectum and breast). Thirteen pts had metastatic disease. Fifteen pts reported fever, 4 presented dyspnea, 4 complained of ageusia and anosmia and 1 developed conjunctivitis. Twenty-five pts underwent nasal swab, with 7 positive results. Among the latter, 5 were men, median age was 66 (range 50 – 83), the most had KPS 100 (4/7) and reported symptoms were dyspnea (4/7), anosmia and ageusia (3/7) and flu syndrome (1/7). From our cohort, 4 cases of pneumonia were diagnosed with CT scan imaging: 3 were related to COVID-19 infection, while the forth was evaluated as an RT adverse event. From the entire series, 4 pts died, one for other causes not COVID-19 nor cancer related, while 3 pts died during hospitalization in intensive care unit for complications of COVID-19 infection.

Conclusions: Our small series suggests that COVID-19 infection is frequent in oncological setting in the outbreak area. COVID-19 related symptoms are hardly distinguishable from cancer disease manifestations and treatments side effects. The real challenge for the future will be to understand pandemic consequences in cancer natural history and try to better manage its clinical impact.

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USE OF MYONCARE APP DEDICATED FOR REMOTE FOLLOW-UP DURING PANDEMIA

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During the lock down period due to the Covid-19 pandemia at our department, efforts were made to limit access to our consultation rooms to patients with non-deferrable problems such as therapies or doubts of disease progression. the other patients on follow-up appointment were contacted by phone. These patients sent the clinical reports of the planned checkup by e-mail or by fax. If the medical history or one of the tests were found to be doubtful for progression or toxicities due to serious side effects from therapy, the patient was invited to a face to face control and/or to undergo to further investigations. In this period of quarantine the use of MyOncare app was particularly helped. MyOncare consists of two elements, 1. portal (myoncare Portal) used primarily by physicians and 2. mobile application used primarily by patients (myoncare App). In combination, these platform elements give access to a modular set of containerized microservices (myoncare Services). As a patient-centered digital health platform, myoncare enables care providers to provide efficient,

remote, personalized and needs-oriented patient and activity levels analytics by indication, appointment management, medication plan, telemedicine (chat, video and picture).. The physicians who use myoncare to support their routine care are responsible for validating and localizing the careplans and assigning those to each patient or patient group. The oncare system use was limited to 103 the patients who had previously accepted and activated the service: 35 pts with breast cancer, 29 with prostate cancer, 16 with head neck cancer, 23 with bone met.. Through this software, it was possible to administer questionnaires to the patient that highlighted the clinical aspect of the disease trend through the patient's subjective evaluation of the symptomathology. This method was especially useful in monitoring symptoms such as pain or side effects of therapies in a more objective way. In the period between 1/3/2020 and 31/5/2020, 377 contacts were involved in the reference period; these patients had undergone radiotherapy in the last 5 years with various cancers and indications (curative, palliative and adjuvant). Of these 69 (18%) were subsequently summoned to define the modifies clinical situation. It has been found that the patients have not only appreciated the concern, but also the attention not to "force" the person at risk of contagion.

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RADIOTHERAPY ORGANIZATION IN PANDEMIC ERA: THE EXPERIENCE OF RADIATION ONCOLOGY DEPARTMENT OF THE AZIENDA OSPEDALIERO-UNIVERSITARIA PISANA (AOUP)

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Aims: On March 2020, due to the spread of COVID-19 infection, the Italian Government decided to put the country under a complete lockdown and all public hospitals tackled the emergency with radical changes in wards organization. Our center is located in the north-west Tuscany were the infection rate was superior than in the other regional zones and we ran into the local difficulty of handling the emergency ensuring the prosecution of radiotherapy treatments. The aim of this paper is to describe the approach of The (AOUP) and the issues raised during Pandemic.

Methods: The main problem of Pisa Radiation Oncology Unit, was how to continue activity while protecting patients (pts), families and medical staff from COVID-19. Our team, according to Hospital directives, assembled measures that allowed us to better face the emergency.

Results: Despite the measures assembled to face the emergency, many critical issues emerged during this pandemic. First, in our department we had insufficient spaces to guarantee social distancing and we had not specific room for Covid-19 suspected or positive pts. Moreover a lack of DPI occurred. The planning appointment of treatments was delayed to allow sanitize radiotherapy equipments between each pts and to avoid gathering of people so fewer pts were treated throughout the day with an increase of waiting lists. One of the difficulties we had during this pandemic was also to differentiate COVID-19 infection symptoms from those related to the tumor and to the treatments themselves. Finally, many pts refused to perform instrumental examinations, CT, surgery and RT for fear of a contagion; therefore our task was to convince pts not to desert the treatment sessions.

Conclusions: This experience has shown multiple critical issues in the national and regional health organization, even due to the past funding cuts for health. Although at the moment the Italian health emergency is being resolved, we have to make some basic precautions routinely and we must continue to learn and adapt ready to future health emergencies.

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COVID 19 EXPERIENCE IN A DIAGNOSTIC AND RADIOTHERAPY CENTER

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Aim: The Covid emergency in a radiotherapy unit has not been and is not easy to manage as it has to guarantee continued assistance to oncological patients, a population with an immunological profile that classifies them as particularly fragile. Even private health structures, to face this emergency, had to convert and adopt prevention and protection measures. The purpose of this work is to illustrate how a private health center has promptly and incisively changed its modus operandi to protect patients and staff.

Methods: On the 13TH of March when there were 272 positive cases in Campania, the Center decided to radically change its way of working, in light of the exponential and worrying increase of cases in Italy. In fact, since the 16th of March , to ensure the social distancing of at least 1 meter between the people involved, it has been decided to reduce the activity of the diagnostic unit by 60%, allowing the entry into the structure of a limited number of patients. The following precautionary measures have been activated: - Triage and thermo scanner at the entrance for each patient; - Purchase of IPD: the management of the center has purchased surgical masks, shoes, gloves and disinfectant for all patients, while for the staff, FFP2 masks, biological anti-contamination suits and visors; - sanitation of the premises once a week was guaranteed; - A shift of the healthcare staff every 15 days to ensure the continued assistance of cancer patients in the event of a possible infection; - In radiotherapy, normal care activities were guaranteed, postponing Follow up visits; - Where possible, following the AIRO guidelines, hypofractionated schemes have been used and radiotherapy treatments

for prostate or breast cancer have been postponed.

Results: By taking timely and very stringent measures, the center ensured a peaceful performance of the working activities not only of the employees but also of the patients. Nowadays no covid cases have been recorded neither among workers nor through patient-operator contact.

Figure 1.

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RADIOTHERAPY DURING COVID-19 PANDEMIC: EXPERIENCE OF THE REGGIO EMILIA HOSPITAL

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Aim: The COVID-19 pandemic is an international public health emergency declared by WHO on March 11th 2020. Emilia Romagna was one of the most coronavirus affected regions. In Reggio Emilia, epidemic reached its peak in the second half of March. Aim of this report is to describe the procedures and protocols used to provide safe and high quality radiotherapy care and protect patients and healthcare workers by potential viral exposure.

Methods: Reorganization patient circuit of first medical examinations and follow up were carried out. More extensive use of hypofractionated schedules, that was already the standard of care for various diseases in our department, was applied. Daily patients and staff triage, use of PPE, hand washing, environment sanitization, respect of social distancing and limitations for patients caregiver in the department, unless absolutely essentiall, were performed. Patients with suspected or confirmed COVID-19 were treated at the end of the day.

Results: Between February 15th and April 30th 2020, the major part of follow-up visits (replaced when possible by telephone screenings) and orthovoltage RT for skin cancer in elderly patients, were suspended. No reduction in the number of newly diagnosis examinations, and irradiations beyond the recommended time, declined or postponed treatments were reported. An increased number of treatments was carried out. Patients treated were overall 299 compared to 284 of the same period of 2018 (we couldn't compare with 2019 because one accelerator was temporarily unavailable). Using mild and deep hypofractionation we performed 2036 RT sessions, with a mean number of fractions per course of treatment of 6.8, compared to 3566 and 12.6 respectively in 2018. Of the 299 patients treated, 65 performed Real Time –PCR test because of suspected symptoms during or in 15 days after RT end. Three patients resulted COVID positive: 1 during, 2 after treatment, all recovered. Only one staff member was positive to serological test (swab negative).

Conclusions: Our data show that the adoption of a modified workflow, including a more extensive use of hypofractionation, allowed the maintenance of an effective RT service. The careful application of triage and protective measures permitted us to treat safely oncological patients, potentially at increased risk of infection, as demonstrated by the very low number of patients developing COVID- 19 infection during or in a short period after RT.

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THE LOCKDOWN PHASE I OF COVID-19 PANDEMIC IN OUR RADIOTHERAPY DEPARTMENT: A MONOINSTITUTIONAL EXPERIENCE

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Aims: From March 2020 to May 2020 in Italy there was a national lockdown (the Phase I) caused by COVID-19 pandemic. Since radiation oncology was considered a "life-saving" treatment, we ensured Radiotherapy (RT) activities during the phase I with a reorganization of our Radiotherapy Department. We reported our procedures during the lockdown phase.

Methods: During the COVID-19 phase I, we performed an internal procedure protocol, in order to ensure all our RT activities. According to Ministry of Health recommendation, oncological follow-up visits were interrupted: consequently, we planned phone contacts to patients, viewing laboratory and instrumental exams via telematics. Conversely, first RT visits, Simulation Computed Tomography (Simul CT) and RT treatments were regularly performed. Paths, spaces and all individual protective devices were organized, as well as measures of triage and management of suspected COVID-19 cases (Table 1).

Table 1. Planned actions implemented for radiotherapy activities in lockdown Phase I in the experience of Chieti Radiation Oncology Department.

	PLANNED ACTIONS DURING COVID-19 PANDEMIC LOCK-DOWN
	PHASE I: lockdown
1	Full maintenance of Radiotherapy treatments on both Linacs
2	Linacs disinfection at each workshift
3	Preference for hypofractionated schemes
4	Full maintenance of Simul CT and Dosimetry activities
5	Simul CT disinfection at each workshift
6	Staff: systematic hand washing before and after each clinical and technical procedure
7	Maintenance of a single clinic room for the first radiotherapy visits. Interruption of oncological follow-up clinic room with phone contact of patients and viewing of laboratory and instrumental exams via telematics. On urgency, patients are booked in the single clinic room active
8	Preparation of 2 dedicated areas outside the waiting rooms for family members and carers. Entry into the Radiation Oncology center reserved for one family member and only for the first radiotherapy visits or on urgent cases
9	Triage area with nursing staff: **a)** entry for 4 patients at a time with a distance of at least 1 meter; **b)** body temperature detection with Thermo Scan; **c)** finding of respiratory symptoms, dysgeusia and anosmia, ocular disorders (conjunctivitis); **d)** contacts with suspected COVID-19 by filling of the dedicated Hospital questionnaire; **e)** obligation of surgical mask for patients and carers
10	Management of suspected case in triage for patients, staff, carers and third parties: if temperature ≥37.5 ° repetition after 10 minutes and if confirmed, access to the center is not allowed. Evaluation for deferral of planned clinical or technical performance: in the case of deferral, the patient is rescheduled; in the case of non-deferral, the patient accesses the service by adopting all the safety criteria indicated in points 12 and 13
11	Alternate management of all staff in order to prevent potential multiple infections
12	Personal protective equipment. **a)** Visits: surgical mask and gloves; FFP2 mask with superimposed surgical mask in patients with respiratory symptoms; **b)** Simul CT and Linear Accelerators: FFP2 mask with superimposed surgical mask and single-use gloves; systematic hand disinfection; visor or protective glasses for Head and Neck and respiratory tumors and for patients with respiratory symptoms
13	Symptomatic and asymptomatic positive COVID-19 patient: medical evaluation for treatment interruption based on the clinical disease status, with monitoring of the clinical status and treatment recovery after 2 consecutive negative buffer, symptomatic absence and negative CT scan. In the case of treatment continuation because it cannot be deferred: preparation of separate paths; bunker disinfection before and after treatment; FFP2 masks with superimposed surgical mask; single-use gloves and gowns; visors or protective glasses and overshoes for staff; separate and disinfected room for dressing and undressing
14	Maintenance of Department meetings for discussion of clinical cases and ongoing scientific work with limited number of professionals and spacing measures
15	Maintaining of multidisciplinary Tumor Board meetings only by requesting consultations, e-mail correspondence, phone contacts and telematic platforms

Results: Comparing RT activity during the full lockdown phase I of the COVID-19 emergency (March-May 2020) respect to the same period of the 2019, no changes were observed regarding the number of services performed. First radiotherapy visits, Simul CT and RT treatments were 121, 135 and 170 in 2020 respect to 123, 137 and 151 in 2019. We preferred hypofractionation for breast, prostate and palliative treatments during the pandemic. Thanks to these taken measures, no cases of COVID-19 positivity were reported, as confirmed by negative results of staff buffers.

Conclusions: The number of services performed in the 2020, similar to that of the 2019, demonstrated as our RT activities have not been reduced during the COVID-19 pandemic. Treatments continuity, cancer patients and healthcare personnel safety were guaranteed. This planned protocol continued to be applied and it seems efficacious also in post-lockdown phase II with partial changes.

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NEOADJUVANT RADIOTHERAPY FOR INFLAMMATORY BREAST CANCER IN A COVID PATIENT: A CASE REPORT

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Aims: In March 2020 the outbreak of pandemic coronavirus SARS-CoV2 produced several challenges in oncological treatment. Recent AIRO Survey showed that more than 80% of the centres decided to interrupt or modify radiotherapy (RT) for some pathologies and in case of positive patients only a third of the centres decided not to stop the treatment. In this contest, in some cases the risk of cancer progression makes this issue controversial and therapy cannot be delayed. We report the case of a young woman with inflammatory breast cancer (IBC) not operable, found positive for SARS-Cov2 during the neoadjuvant RT course.

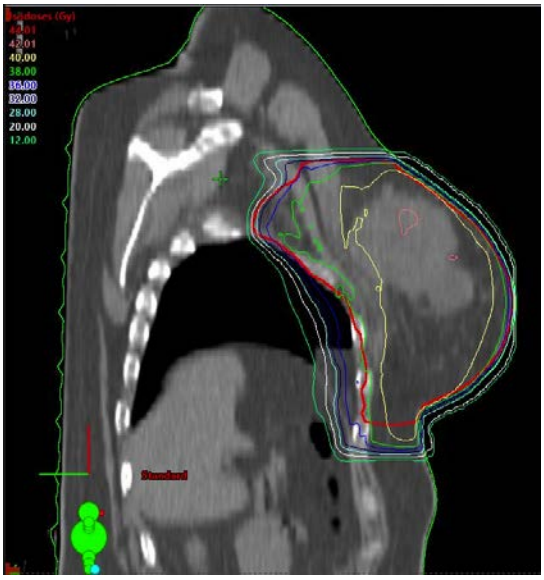

Figure 1.

Methods: A 40 years old female was diagnosed with triple negative invasive cancer cT4dN1M0 of the left breast. The patient received neoadjuvant chemotherapy (CT) with 4 cycle of Adriamycin+cyclophosphamide achieving a partial response and subsequently with weekly paclitaxel, with a local progression. Surgery was excluded for local extension and a switch to CT with carboplatin+paxlitaxel was performed. A further increasing of breast lesion was observed, therefore the multidisciplinary board decided to start a neoadjuvant RT. A total dose of 40 Gy in 15 fractions was prescribed to the left breast, including axillar pathological node and skin, with 3D conformal RT. After 3 fractions the

patient developed fever up to 38,5°C and diarrhea without any respiratory symptom. The naso-pharingeal swab revealed a SARS-CoV-2 infection, without any covid-related feature on the chest CT scan. Since the treatment was life-saving e and the patient presented mild sympthoms, it was decided not to interrupt it. The patient was hospitalized, RT session was scheduled at the end of the shift, using appropriate PPE for the staff, and after the treatment all the facilities were sanitized.

Results: Covid-19 remained mild, fever disappeared in 4 days and no other covid-related symptom was developed. RT was completed without any interruption and the treatment was well tolerated with only CTCAE skin G1 toxicity. No several side effect was documented. At the end of RT clinical evaluation showed a good partial response. After 25 days radical mastectomy was performed, revealing a pathological partial response ypT2N0.

Conclusions: Hypofractionated breast RT is well tolerated in a COVID patient with mild symptomatology, without worsening the course of the viral infection. Moreover, neoadjuvant RT in IBC is effective and could allow surgical approach in case of progression after CT.

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RADIOTHERAPY PROCEDURES PERFORMED DURING THE ITALIAN PHASE II OF COVID-19 PANDEMIC: A MONOINSTITUTIONAL EXPERIENCE

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Aims: In Italy, COVID-19 pandemic caused a national lockdown from March 2020 to May 2020. "Life-saving" treatments, as radiotherapy (RT), necessitated to be guaranteed to all cancer patients. Consequently, for ensuring both patients and staff safety and treatments continuity, a reorganization was performed in our Radiotherapy Department also in post-lockdown phase II. In this scenario, we report our institutional procedure realized in post-lockdown phase from May 2020 to today.

Methods: During the COVID-19 phase II, we defined a procedure protocol, ensuring workloads of the first and follow-up visits, radiotherapy planning, dedicated routes, measures for triage areas, management of suspected COVID-19 cases, personal protective equipment and management of environments (Table 1). Both for personnel and patients, temperature (required <37.5°C) was checked before entering the Department, as well as the obligation of wearing surgical masks. In the triage area 4 patients at a time were permitted to entry, with a distance of at least 1 meter; respiratory symptoms, dysgeusia and anosmia and ocular disorders, as conjunctivitis, were checked; a dedicated Hospital questionnaire on possible contacts with suspected COVID-19 patients was carried out to all patients. A strict hand hygiene with hydroalcoholic solutions and disposable gloves uses were mandatory to all staff, before and after each clinical and technical procedure.

Results: During the COVID-19 pandemic post-lockdown, no differences were identified with the same period (May-July 2019) of last year in terms of first and follow-up visits, Simulation Computed Tomography and RT treatments, preferring hypofractionated schemes for breast, prostate and palliation cancers. Ensuring triage management for patients and staff, we reported no cases of COVID-19 positivity neither in patients nor in professional.

Conclusions: Our results show as all protection and prevention measures performed in our Radiotherapy Department during COVID-19 outbreak seem to be able to guarantee treatments and prevent both patients and staff infection also in phase II COVID-19 pandemic.

Table 1. Planned actions implemented for radiotherapy activities in post-lockdown Phase II in the experience of Chieti Radiation Oncology Department.

	PLANNED ACTIONS DURING COVID-19 PANDEMIC LOCK-DOWN
	PHASE II: post-lockdown
1	Full maintenance of Radiotherapy treatments on both Linacs
2	Linacs disinfection at each workshift
3	Preference for hypofractionated schemes
4	Full maintenance of Simul CT and Dosimetry activities
5	Simul CT disinfection at each workshift
6	Staff: systematic hand washing before and after each clinical and technical procedure
7	Full recovery of the oncological follow-up clinic room clinic with double daily shift 8.00 am-1.00 pm and 2.00 pm-5.00 pm with spacing appointments of 1 patient every 45 minutes
8	Preparation of a single pre-waiting room area for family members and carers. Entry into the Radiation Oncology center reserved for one family member and only for the first radiotherapy visits or on urgent cases
9	Triage area with nursing staff: **a)** entry for 4 patients at a time with a distance of at least 1 meter; **b)** body temperature detection with Thermo can; **c)** finding of respiratory symptoms, ocular disorders (conjunctivitis), dysgeusia and anosmia; **d)** contacts with suspected COVID-19 by filling of the dedicated Hospital questionnaire; **e)** obligation of surgical mask for patients and carers
10	Management of suspected case in triage for patients, staff, carers and third parties: if temperature ≥37.5 ° repetition after 10 minutes and if confirmed, access to the center is not allowed. Evaluation for deferral of planned clinical or technical performance: in the case of deferral, the patient is rescheduled; in the case of non-deferral, the patient accesses the service by adopting all the safety criteria indicated in points 12 and 13
11	Personal protective equipment. **a)** Visits: surgical mask and gloves; FFP2 mask with superimposed surgical mask in patients with respiratory symptoms; **b)** Simul TC and Linear Accelerators: FFP2 mask with superimposed surgical mask and single-use gloves; systematic hand disinfection; visor or protective glasses for Head and Neck and respiratory tumors and for patients with respiratory symptoms
12	Symptomatic and asymptomatic positive COVID-19 patient: medical evaluation for treatment interruption based on the clinical disease status, with monitoring of the clinical status and treatment recovery after 2 consecutive negative buffer, symptomatic absence and negative CT scan. In the case of treatment continuation because it cannot be deferred: preparation of separate paths; bunker disinfection before and after treatment; FFP2 masks with superimposed surgical mask; single-use gloves and gowns; visors or protective glasses and overshoes for staff; separate and disinfected room for dressing and undressing
13	Full recovery of Department Meetings without contingent number of professionals but with maintenance of the safety distance of at least 1 meter
14	Full recovery of multidisciplinary Tumor Board meetings

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COULD CONTACT SKIN RADIOTHERAPY (BRACHYTHERAPY) BE AN OPPORTUNITY FOR THE TREATMENT OF SKIN CANCER PATIENTS DURING PANDEMIC? A MONO-INSTITUTIONAL EXPERIENCE

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Aim: In the context of the SARS-CoV-2 pandemic, it is of paramount importance to ensure the quality of cancer treatment as well as patients and health professionals' safety. Individual-based treatment option has to be considered in patients suffering from non-melanoma skin cancer (NMSC), who are more critical because typically older and frail due to comorbidities and functional performance. The aim of this study was to assess the feasibility and the safety of Contact Skin Radiation Therapy (CSRT) to treat NMSC during SARS-CoV-2 pandemic.

Methods: Patients affected by NMSC discussed at skin multidisciplinary tumor board (S-MDTB) from February the 21st to May the 4th (Phase 1 Italian Pandemic – Emergency period) were retrospectively analyzed. The patient's stratification and triage following internal recommendations were performed before starting treatment. CSRT was delivered in 8 fractions of 5 Gy twice a day, with a total dose of 40 Gy. Treatment success indicators, such as treatment acceptance and completion were identified to evaluate the feasibility of CSRT. After the treatment, a psychological assessment regarding patient's safety perception was performed.

Results: Six patients were treated and included in the analysis. Histological examination documented three patients affected by basal cell carcinoma (BCC) and three by squamous cell carcinoma (SCC). No high-grade acute toxicities occurred during treatment. No patients nor healthcare personnel developed SARS-Cov-2 infection. Psychological assessment results in 100% of the patient's compliance.

Conclusion: CSRT represents a non-invasive, safe, and feasible treatment option even during the pandemic emergency period. Hypofractionation would be an option to reduce overall treatment time and, consequently, infective risk exposition.

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STEREOTACTIC RADIOTHERAPY, RADIOSURGERY AND HYPOFRACTIONATED RADIOTHERAPY: EXTENDING INDICATIONS DURING THE COVID-19 PANDEMIC BY AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) AND EUROPEAN SOCIETY FOR RADIATION ONCOLOGY (ESTRO) RECOMMENDATIONS

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Aims: To estimate the effect of extended use of Stereotactic Radiotherapy, Radiosurgery and Hypofractionated Radiotherapy according to American Society for Radiation Oncology (ASTRO) and European Society for Radiation Oncology (ESTRO) recommendations, to limit number of accesses to the Radiation Oncology Unit of Arezzo - Valdarno.

Methods: We retrospectively reviewed 641 patients treated with radiotherapy (RT) in 2018 at the Radiation Oncology Unit of Arezzo, registered in our management information system (Mosaiq®-Elekta®). Patient characteristics, clinical/pathological stage of disease, risk – benefit balance (with alternative therapeutic option or possible omission of RT) were all evaluated and new RT dose and number of fractions were re-assigned to each treated patient according to ASTRO/ESTRO indications about Stereotactic Radiotherapy (SRT), Radiosurgery (SRS) and Hypofractionated Radiotherapy (HRT) during COVID pandemic. For each site of disease, we carefully selected dose and number of fractions, preferring those reported in randomized controlled trials suggested by ASTRO/ESTRO panel, with calculation of the biological equivalent dose (BED) and organs at risk constraints. Fractionation index (FI) was calculated by dividing the total number of fractions by the total number of patients, for both treatments delivered in 2018 and treatments obtained according to ASTRO/ESTRO recommendations.

Results: In 2018, 10548 fractions of RT were delivered, which would have corresponded to 6463 fractions if ASTRO/ESTRO indications had been used. According to our findings, extending indications of SRT, SRS and HRT would have reduced number of fractions, and therefore number of patients accesses to our Facility, by 38,7%. FI was 16.4 sessions per patient in 2018, that would have decreased to 10.1 with ASTRO/ESTRO criteria for SRT, SRS and HRT, an extremely low average compared to standard fractionation.

Conclusions: Using ASTRO/ESTRO indications for SRT, SRS and HRT means reducing the need for

patients to attend a Radiation Oncology Unit to the lowest possible levels during COVID pandemic, thus minimising exposure and risk of contagion without omitting/reducing the effectiveness of RT treatments.

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MEET ME AT THE TRIAGE: RADIOTHERAPY RESIDENTS' MOST THOUGHT-PROVOKING APPROACH TO THE PANDEMIC.

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Aims: During emergencies is mandatory that teams work as cohesive entities. The Radiation Therapy and Oncology (RTO) Unit 1 and 2 of the "Fondazione IRCCS - Istituto Nazionale dei Tumori" (INT) of Milan are not involved in first aid but indeed the Covid-19 emergency is challenging our well-organized system. Our Department deals with oncological patients, who are the most exposed to the pandemic due to both the lack of immune defences, and to the daily accesses to the radiotherapy treatment. The current, never faced before, global crisis has sometimes improved communications. From the 7th of April to the 14th of July 2020, 11 residents from the Universities of Milano-Statale, Milano-Bicocca, Napoli-Federico II, all working at the RTO department of the INT did a daily phone triage to all adult patients to be admitted in the ward: bridges to build instead of bureaucracy walls are the goal of that experience. Those are welcomed not just in hard times, but especially in daily routine.

Methods: The clinical activity of the INT's RTO is organized in nine teams which usually work independently. Thus, the RTO residents of the INT work in specific clinical groups (i.e. Breast, Head and Neck, Sarcomas and Gynecology) strictly compartmentalized, mostly because of the planning of the shifts and the insurance coverage. During the pandemic, residents contacted patients regardless of the group they are involved.

Results: To date, RTO residents made 1675 phone calls. Thanks to the triage, they learnt precious skills in communication with frail patients, putting effectively them at their ease and giving to the staff the safety for working fearless from the COVID-19. The collaboration laid the groundwork for future networks in an international setting.

Conclusions: In this unlucky phase for the training, straining for lessons to be followed and time for study to be found, RTO residents managed the clinical activity well, even though the shared concern for the pandemic. The ongoing daily phone triage is giving pivotal clues to collaborate and to reduce administrative problems. As soon as the emergency phase is mitigated, the suggestion to share with Senior physicians and Professors could be a remodeling of the academic organization in the light of the proven better synchrony between different Universities.

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FIVE-FRACTIONS HYPOFRACTIONATED ADJUVANT WHOLE BREAST RADIOTHERAPY (WBRT) IN ELDERLY PATIENTS DURING COVID-19 PANDEMIC

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Aims: to evaluate treatment compliance and toxicity of 5-fractions hypofractionated WBRT in elderly patients with high risk factors for local recurrence reducing the number of access to hospital during Covid-19 pandemic according to recent guidelines.

Methods: inclusion criteria for hypofractionated regimen were: age ≥ 65 years, no severe comorbidities, ECOG performance status 0, node negative tumors, presence of unfavorable prognostic factors of local recurrence (mainly positive margins, poor adherence to adjuvant endocrine therapy, grade 3, unfavorable biological pattern, lobular histotype). Radiotherapy (RT) schedules included 28.5 Gy in once weekly fractions over 5 weeks or 26 Gy in 5 daily fractions over 1 week ± simultaneous integrated boost (SIB) to the tumor bed in patients with positive margins or grade 3 tumors (2.5 Gy in 5 fractions over 5 or 1 week). Treatment was delivered with tangential field-in-field 3DCRT or VMAT. Compliance and acute toxicity were assessed according to the CTCAE-v3 criteria. Breast erythema, moist desquamation, pain, breast lymphedema were evaluated before RT, during each fractions, at the end of RT and at 2 and 4 weeks after treatment.

Results: from March to June 2020 9 patients were enrolled. Breast volume was ≤ and >1000 cc respectively in 6 and 3 patients. Hypofractionated RT was overall well tolerated with slight acute toxicity. Five (55%) patients experienced grade 1 erythema not requiring topical steroid, moist desquamation was not observed. Two (22%) patients showed grade 2 breast edema, 5 (55%) patients had slight self-limiting breast pain not requiring drugs. Two (22%) patients experienced asthenia. No grade 3-4 side effects occurred.

Conclusions: COVID-19 pandemic changed risks and benefits from treatments particularly for older

patients with comorbidities. Recent guidelines recommended to reduce the number of access to the hospital, omitting RT for low risk patients, delaying RT and adopting hypofractionated regimen. After literature revision, 5-fractions hypofractionated schedule has been adopted also in our RT Unit for WBRT in elderly patients. Compliance was excellent with low incidence of side effects. All patients were very satisfied. This regimen improves the management of elderly patients undergoing WBRT during Covid-19 pandemic and this experience might be useful at the end of sanitary emergency for consolidate scientific research in this direction.

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USEFULNESS OF A NOMOGRAM TO PREDICT POSITIVE 68GA-PSMA-PET/CT IN PATIENTS WITH BIOCHEMICAL RECURRENCE FOR PROSTATE CANCER

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Aim: 68Ga-PSMA-PET/CT is nowadays emerging as the most valuable imaging to detect sites of progression in prostate cancer (PCa) patients with biochemical recurrence (BCR). Recently a nomogram has been proposed by Ceci et al (doi:10.1007/s00259-019-04505-2) with a cutoff of predictive positive value of 0.4.

Methods: Data about fifty-two 68Ga-PSMA-PET/TC and 48 PCa patients referring at our institution between November 2016 and May 2020 were analyzed. All 48 patients presented with BCR after radical treatment (radical prostatectomy and/or radiotherapy) with different clinical setting. The clinical nomogram able to predict the likelihood of positivity rate of 68Ga-PSMA-PET/CT was applied to all patients. Then the sensibility, specificity, predictive positive value (PPV) and predictive negative value (PNV) of the 52 68Ga-PSMA-PET/TC were evaluated based on three different cutoffs value, the one proposed for the nomogram of 0.4, 0.5 (median value of our population), and finally an arbitrary cutoff of 0.75.

Results: Overall in our cohort, median value of likelihood ratio of positivity was 0.5 (range, 0.1 – 0.9). With a cutoff of 0.4, 13 exams were positive and 10 negative (≤0.4), while with a likelihood of positivity rate >0.4, 21 were positive and 8 were negative. The sensitivity was 62%, specificity 55%, PPV 72% and PNV 43%. With a likelihood of positivity rate < 0.5 (26 imaging exams), 15 resulted positive and 11 resulted negative, while with a value of > 0.5 (26 imaging exams) 19 were positive and 7 were negative. The sensitivity was 52%, specificity 61%, PPV 73% and PNV 42%. Finally, for a likelihood positivity rate < 0.75, 20 PET/TC resulted positive, 16 negative and for a value > 0.75 14 PET were positive, and 2 were negative. The sensitivity, specificity, PPV and PNV were 41%, 89%, 87.5% and 44% respectively.

Conclusion: Based on our experience the proposed nomogram is a useful tool to predict 68Ga-PSMA-PET/CT positivity, with similar results if a likelihood of positivity rate was set at 0.4 or 0.5, while an increase to 84% for PPV was recorded setting a likelihood of positivity rate at 0.75.

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MORPHOLOGICAL (MR) AND FUNCTIONAL (WEIGHTED MAGNETIC RESONANCE IMAGING AND POSITRON EMISSION TOMOGRAPHY) IMAGING FOR CLINICAL RESPONSE EVALUATION AND FOLLOW-UP OF CERVICAL CANCER PATIENTS TREATED WITH CHEMORADIATION THERAPY

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Aims: Treatment options for locally advanced cervical cancer (LACC) differ according to tumor and nodal status, and comprehend external beam radiotherapy (EBRT) with concomitant cisplatin chemotherapy (CRT) followed by intrauterine brachytherapy. The choose of imaging modalities for treatment response evaluation of LACC patients treated with CRT plus brachytherapy (BRT) therapy is an interesting and debated argument. Indeed, both Diffusion-Weighted Magnetic Resonance Imaging (DWI-MRI) and Positron Emission Tomography (PET/CT) give information for tumor response and metastases. This study was conducted to evaluate the role of DWI to assess response during CRT and the accordance between morphological and functional Imaging (MRI and PET/TC).

Methods: From 2017 to 2020, twenty-three LACC patients were treated in our Centre and 11 were retrospectively evaluated for this analysis. They underwent EBRT with a total dose of 4500 cGy (180 cGy/die) to tumor and pelvic nodes, plus boost for a total dose of 5500 cGy (220 cGy/die) on FDG uptake lymphadenopathies. All patients underwent both DWI-MRI and PET-TC scans for staging and restaging and DWI-MRI at 4 weeks from the beginning of CRT, before starting BRT. Regions of interest (ROI) were drawn by a radiologist with specific experience in LACC diagnosis along the border of tumor on apparent diffusion coefficient (ADC) maps on the baseline and 4 weeks MRI. PET-TC and MRI were performed 3-6 months after the end of CRT for 2 years.

Results: The median follow up was 12.6 (3-31) months. MRI during CRT showed a morphological response and an ADC value increment in 100% of patients, none of them reported local recurrence. Follow-up MRI presented a tumor complete response in 6/11 patients (54%), while residual disease was

observed in 3/11 patients (27%). Two patients presented para-aortic lymph nodes progression (19%). These findings were confirmed by PET-TC scans in 91% of cases. One patient presented partial response at MRI respect to a metabolic complete response. All data are detailed in Table 1.

Conclusion: Early responses on DWI resulted predictive of local control in our small sample experience. To confirm the prognostic role of ADC an evaluation of non-responsive patients could be advisable. Moreover, a high accord between follow-up PET/TC and MRI was reported. Based on our results DWI MRI could be suggest for early detection response and only PET/TC for adequate follow-up.

Table 1. clinical and radiological characteristics of patients

		Early evaluation			Follow-up		
Patient	FIGO stage	Tumor size MRI before CRT (cm)	Tumor size MRI during CRT (cm)	ΔADC	MRI restaging response (RECIST criteria)	FDG PET response (EORTC criteria)	Follow-up (months)
1	IV	5,6x5,2x4,9	1,0	100	CR	CMR	31
2	IIB	4,6x3,8x4,3	0,8	1041	CR	CMR	21
3	IB2	4,2x3,3x5,0	0,7	100	CR	CMR	14
4	IVA	4,8x4x4,6	2,3x1,6	100	CR	CMR	12
5	IIIC	2,6x2,4x1,7	1,3x0,8	100	CR	CMR	11
6	IIIB	6x5,5x3	3,3x3,5	189,7	PR	PMR	2
7	IIIB	4,5 x 7,7 x 5	fibrosis	100	LP	LP	6
8	IIIA	6,7x3,4x5,8	2,5x1,5x4,5	2041	PR	PMR	8
9	IB3	6x7x4,8	3,5x 2,8x 2	2054	PR	CMR	5
10	IVA	5x4,5x5	2,6x2,4x1,8	45,9	LP	LP	23
11	IIB	4,6x3,5x2,2	1	949	CR	CMR	5

$\Delta ADC = \frac{ADC\ during - ADC\ baseline}{ADC\ baseline} x100$, *CRT: chemoradiotherapy, CR: complete response, CMR complete metabolic response, PR: partial response, PMR: partial metabolic response, SMD: stable metabolic disease, LP: para-aortic lymph nodes progression.*

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POST-OPERATIVE STEREOTACTIC RADIOTHERAPY OF BRAIN METASTASES: A MONOINSTITUTIONAL RETROSPECTIVE EVALUATION OF C LINICAL OUTCOMES

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Aims: This is a Mono-Institutional study with the aim to evaluate the outcomes of our patients underwent post-operative stereotactic radiotherapy (SRT) in place of whole-brain radiation therapy (WBRT) following resection of brain metastases.

Methods: From November 2018 to December 2019 8 patients underwent post-operative stereotactic radiosurgery at our Department for brain metastases. 3 patients had synchronous metastasis at the diagnosis. 5 patients had primitive lung cancer, 1 renal tumor, 1 surrenal cancer and 1 esophageal tumor. Dose to surgical cavity was 3000 cGy in 5 daily fractions delivered with VMAT/IGRT technique (Figure 1). CT simulation was performed with patients in supine position using head and neck immobilization system with individual thermoplastic mask.

Results: Treatment was well tolerated. 1 patient died for progression disease, another one died for a second gastric tumor; 2 patients had PD, 4 complete response. Average follow up time was 7 months (range 3-13). Every patient with dural/pial involvement at the time of surgery had distant intracranial failure.

Conclusion: Post-operative stereotactic radiotherapy (SRT) in place of whole-brain radiation therapy (WBRT) following resection of brain metastases is well tolerated in selected patients, with a good response to the treatment. Dural/pial involvement may portend a high risk for distant intracranial disease; therefore, it may be prudent to consider alternative approaches in these cases.

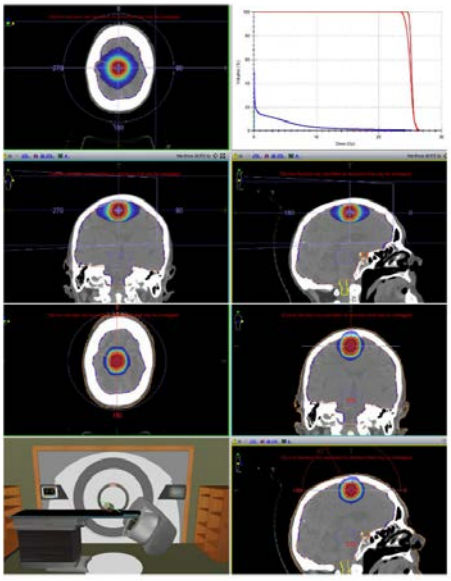

Figure 1. Dose distribution and DHV.

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LINAC-BASED STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER: A DOSIMETRIC ANALYSIS

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Aims: Extreme hypofractionation using Stereotactic body radiotherapy (SBRT) is an emerging therapeutic option for patients with localized prostate cancer due to tumor cells sensitivity to high dose per fraction. The

SBRT schedules of 7-7.5Gy x 5 fractions have already been tested in previous experiences, resulting feasible and well tolerated. In this work we compared two different modalities of dose prescription for FFF LINAC-based SBRT.

Methods: 28 low- and intermediate-risk prostate cancer patients suitable for image-guided SBRT were planned using two different dose prescription. Specific requirements were a prostate volume under 100 cc and an International Prostatic Symptoms Score (IPSS) in the range 0-7. All patients underwent simulation with full bladder and empty rectum, using vacuum bag device. The CTV encompassed the prostate (for low-risk patients) and the prostate plus seminal vescicles (for intermediate-risk). A CTV-to-PTV margin of 3 mm in all directions was applied. Bladder, rectum, femoral heads, penil bulb and bowel were contoured as Organs at Risk (OARs). The prescription dose was 35Gy in 5 fractions, requiring that 98% of PTV was covered by 80% or 90-95% isodose, respectively. All Volumetric Modulated Arc Therapy (VMAT) plans were created with Eclipse Treatment Planning Systems, using coplanar or non-coplanar complete arcs and 6X or 10 X FFF photons, with a maximum dose rate of 1400 or 2400 MU/min. For each patient the PTV D2% and Dmax, as well as Dmax for bladder and rectum, were comparend among treatment plans.

Results: For plans with 80% isodose prescription the PTV D2% was 42.5 Gy, Dmax 43.75 Gy. For plans with 90-95% isodose prescription the PTV Dmax was in the range 36-38 Gy. Dmax for bladder and rectum were in line with TG101 requirements for plan with 80% isodose prescription and under 35 Gy for plans with 90-95% isodose prescription.

Conclusion: Both the isodose prescription modalities achive excellent target coverage and OARs dose-sparing. Even if the gold standard for SBRT isodose prescription requires that 98% of PTV is covered by 80%, the expected advantage of a 90-95% isodose prescription is a sensitive reduction of Dmax within the PTV. This could translate into a probabilistic reduction of prostatic gland toxicity, especially in patients with high prostate volumes (range 80-100cc).

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EVALUATION OF INTER AND INTRAFRACTION SETUP ACCURACY OF THE BRAINLAB MASK FOR INTRACRANIAL STEREOTACTIC RADIOTHERAPY

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Purpose: The purpose of this study was to evaluate inter and intrafraction setup accuracy of the Brainlab stereotactic immobilization mask for intracranial stereotactic radiotherapy and to calculate a margin GTV–PTV to compensate the residual set up error.

Methods: We report data of 22 patients underwent intracranial stereotactic radiotherapy for secondary brain lesions. Radiotherapy treatment workflow included: planning CT with BrainLab mask, acquisition of contrast-enhanced magnetic resonance imaging, delineation of Gross Tumor Volume (GTV) on diagnostic MRI fused with planning-CT. GTV was expanded to 1 or 2 mm to generate Planning Target Volume. Before treatment delivery CBCT was acquired and co-registrated with planning-CT to correct set up errors. After set-up correction, ExacTrac X-ray imaging were obtained and registered with the DRRs to evaluate residual set-up errors. Bone matching algorithm was used to all registrations. According to our protocol the ExacTrac tolerance was set to rotation < 1° and translational shift < 1 mm. During treatment ExacTrac X-ray images were taken at each couch position. Mean and standard deviation of translational and rotational errors were calculated to obtain systematic and random errors.

Results: The interfraction systematic error registered with CBCT was 0.9 mm, 0.8 mm, 0.6 mm for vertical, longitudinal and lateral direction. About rotational, systematic errors was 0.89°, 0.60° and 0.63° for rotation, roll and pitch respectively. The random error was 0.9 mm, 1.2 mm and 0.7 mm for vertical, longitudinal and lateral shifts and 0.55°, 0.60°, 0.51° for rotation, roll and pitch. The intrafraction systematic error measured with ExacTrac X-ray imaging was 0.12 mm, 0.19 mm, 0.24 mm in the vertical, longitudinal and lateral directions, respectively. The systematic error in the rotation, roll and pitch was 0.21°, 0.09°, 0.23°. The random error was 0.24 mm, 0.33 mm, 0.31 mm for vertical, longitudinal and lateral shifts, and 0.24°, 0.18° and 0.26° for rotation, roll and pitch respectively. Applying Van Herk formula we calculated the set up margin which was inferior to 1 mm in all directions. Rotations were considered negligible assuming lesions with spherical shape and little volume.

Conclusion: Our CBCT data confirm the accuracy of BrainLab sterotactic mask in the interfraction error evaluation. Considering intrafraction errors evaluated with Exac Trac, we can assert that 1 mm GTV-PTV margin is adequate for treatment.

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STEREOTACTIC RADIOSURGERY IN THE TREATMENT OF INTRACRANIAL ARTERIOVENOUS MALFORMATIONS AFTER EMBOLIZATION WITH ONYX. A CASE REPORT

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Aims: Arteriovenous malformations (AVMs) are rare congenital vascular pathologies with high risk of intracerebral hemorrhage. Interventional treatment options include microsurgery, embolization and radiosurgery, as well as multimodal approaches. We reported a case report of a young woman, treated with radiosurgery for AVM recurrence after 16 months from onyx embolization.

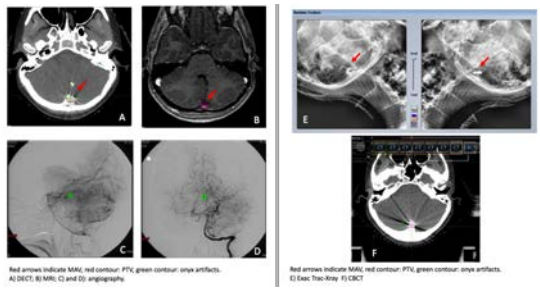

Figure 1.

Methods: A 23-year-old woman affected by left cerebellar AVM recurrence, underwent radiosurgery treatment. She was previously treated with endovascular embolization using "onyx", an embolic agent consisting of a mixture of tantalum that causes significant artifacts and dosimetric uncertainties due to its high density. A Dual Energy computed tomography (DECT) was acquired, as planning CT, allowing the reconstruction of synthetic mononoenergetic scans (40 keV-190 keV), to reduce high density material artifact and improve accuracy on CT density values. On the other side, MRI and angiography were used to define the target volume (Figure1 A-D) by radiation oncologist and neuroradiologist. Radiosurgery was performed on Varian True Beam STX with 6MV FFF beams, six non-coplanar arcs were optimized to avoid as much as possible onyx surrounding the AVM.

Results: A total dose of 22 Gy in a single fraction was delivered. The CBCT was acquired to correct set-up errors; moreover, for each couch position, ExacTrac X ray images were obtained to correct intrafraction errors, as well as to clear onyx visualization without artifact, unlike the CBCT (Figure 1 E-F). Treatment was well tolerated without acute toxicity.

Conclusions: Radiosurgery is a valid treatment option in case of MAV recurrence. We validated an internal protocol to improve MAV visualization after onyx embolization. This protocol includes: DECT, MRI and angiography for contouring and treatment planning, CBCT and Exac Trac X-ray for set-up evaluation before and during treatment.

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STERETACTIC BODY RADIATION THERAPY IN SINGLE FRACTION FOR BONE LESIONS IN OLIGOMETASTATIC/OLIGORECURRENT PROSTATE CANCER PATIENTS: A POOLED ANALYSIS OF A PHASE I TRIAL

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Aim. Aim of this pooled analysis was to report the toxicity profile and the rate of local control in oligometastatic/oligorecurrent prostate cancer patients treated with single fraction stereotactic radiotherapy (SRS) for bone metastases.

Methods. We retrospectively collected the clinical data of prostate cancer patients by who were enrolled in a prospective study in our institution (DESTROY-2) and treated with SRS on oligometastatic/oligorecurrent bone metastases. DESTROY-2 was based a SRS trial delivered by VMAT technique in patients with primary or metastatic tumours in various extra-cranial body sites. The toxicity profile, the Local control (LC), the Overall survival (OS) and the time elapsed between SRS and systemic therapy (hormonal or chemotherapy) start/change were analysed.

Results. Data on 36 patients harbouring 50 bone metastases treated with SRS at our institution between the 2010 and 2020 were collected. The clinical characteristics of patients and treated lesions are reported in the Table 1. Single fraction dose ranged between 12 Gy and 24 Gy. During treatment only one acute grade 2 toxicity (disphagya) was registered, while during follow up only one case of late grade 1 skin fibrosis and atrophy was registered. The median LC was 68 months (IC 95% 62-73 months), while 1-, 3- and 5-year LC was 100%, 96% and 89% respectively. The median OS was 66 months (IC 95%: 59-73 months), while 1-, 3- and 5-year actuarial OS was 100%, 95% and 85% respectively. The median time elapsed between SRS and systemic therapy (hormonal or chemotherapy) start/change was 36 months (IC 95%: 26-47 months) while 1-, 3- and 5-year actuarial time free from a new systemic therapy schedule was 82%, 47% and 28%, respectively.

Conclusions. In this scenario SRS, carrying out a low toxicity profile and an excellent LC rate, can be considered a safe and valuable option. Moreover, this

local treatment can delay the start or the changing of an eventual systemic therapy.

Table 1.

Mean age (years)	
72 (59-90)	
ECOG	N°
0	30 (85%)
1	4 (10%)
2	2 (5%)
Comorbidities	N°
Cardiovascular comorbidities	17 (46%)
Diabetes	2 (5%)
Renal failure	1 (2.5%)
Other tumor	3 (7.5%)
Pulmonary comorbidities	1 (2.5%)
Other	2 (5%)
New systemic therapy after SRS	N°
Hormonal therapy	26 (73%)
Chemotherapy	3 (7.5%)
Abiraterone	4 (10%)
Enzalutamide	1 (2.5%)
Site	N°
Hip bone	27 (54%)
Sternum	3 (6%)
Vertebrae	1 (2%)
Scapula	7 (14%)
Rib	8 (16%)
Femour	2 (4%)
Other	2 (4%)
Total Dose (Gy)	N°
12	2 (4%)
14	3 (6%)
16	3 (6%)
18	2 (4%)
20	3 (6%)
22	7 (14%)
24	30 (60%)
Mean PTV (cc)	
27,36 (0,9-458)	

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STEREOTACTIC BODY RADIOTHERAPY FOR BONE METASTASES IN PATIENTS WITH LIMITED METASTATIC BURDEN

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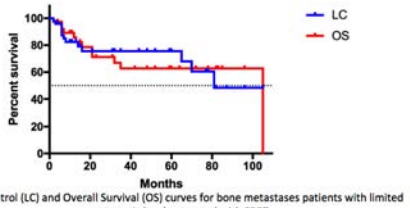
Aims: Stereotactic body radiotherapy (SBRT) is an emerging non-invasive technique for the treatment of limited metastatic diseases. Aim of the present study is to evaluate the outcomes and toxicity of SBRT for bone metastases in selected patients with limited metastatic disease.

Methods: Data from clinical records of patients treated in two Institutions from April 2009 to March 2020 with SBRT for bone metastases were retrospectively collected. Inclusion criteria were: controlled disease in the primary site, <5 sites of bone metastases, head-neck-thorax-abdomen CT scan, PET-CT and MRI to confirm the absence of metastatic spread to sites other than bones. Clinical outcomes in terms of local control (LC) and overall survival (OS) were analyzed with Kaplan-Meier methods. Patients were assessed by interval CT, PET-CT, MRI or bone scintigraphy by physicians' discretion. Pain failure (i.e., lack of response) was defined as worsening pain score (≥2 points on a 0-to-10 scale), an increase in morphine-equivalent opioid dose of 50% or more, reirradiation, or pathologic progression disease-related fracture. Toxicity was graded using Common Terminology Criteria for Adverse Event version 4.0.

Results: A total of 39 patients and 49 metastases resulted to be eligible for inclusion in the study. The median follow-up time was 51.5 months (range, 4-134). Primary tumour sites include prostate (24.5%), breast (22.4%), lung (16.3%), kidney (10.2%), head and neck (8.2%), myeloma (6.1%), pancreas (6.1%), cutaneous melanoma (4.1%) and colon (2%). All patients but 7 were under first line systemic therapy. The delivered median GTV biological effective dose (BED10) was 49.83Gy (range, 17.96-110.20Gy) and the prescribed median PTV BED10 was 23.10Gy (range, 14.40-50.40Gy). The median LC was 81 months. The 1-year LC was 82.43%, whereas the 2- and 5-year LC were both 75.53%. The median OS was 105 months. The 1-, 2- and 5-year OS were 85.50%, 71.14% and 62.77% respectively. Pain response rate (complete+partial) at 12 months was 70%. Radiation treatment was well tolerated and no adverse events were reported.

Conclusions: Our series shows that SBRT for bone metastases in highly selected patients with limited metastatic burden provides excellent LC and pain control, while being safe and well tolerated. Further larger prospective studies should be fostered to evaluate the actual benefits, including OS associated with SBRT for bone metastases in selected patients.



Local Control (LC) and Overall Survival (OS) curves for bone metastases patients with limited metastatic burden treated with SBRT

Figure 1.

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GAMMA-KNIFE RADIOSURGERY FOR BREAST CANCER BRAIN METASTASES: A RETROSPECTIVE SINGLE CENTER ANALYSIS

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Aims: This work reports a single institution experience of Leksell Gamma Knife® Perfexion™ radiosurgery (GKRS) in patients (pts) with brain metastases from breast cancer (BMBC).

Methods: We retrospectively reviewed the experience of our Radiation Oncology Unit between May 2013 and June 2020 with a patient minimum follow up of 6 months. The data collected included patient characteristics, GKRS parameters, radiological response according to RANO-BM (Response Assessment in Neuro Oncology-Brain Metastases) criteria, toxicity and outcome. The prognostic factors used were: diagnosis-specific graded prognostic assessment (DS-GPA), recursive partitioning analysis (RPA) and basic score for brain metastases (BSBM).

Table 1.

Pts characteristics	Number (53 - %)
Biological parameters primary tumor (PT)	
Luminal A	7 (13.2%)
Luminal B	14 (26.4%)
Her2 amplified	24 (45.3%)
Triple negative	8 (15.1%)
BRCA mutation status	
Yes	5 (9.4%)
Not	48 (90.6%)
Stage at PT diagnosis	
I	13 (24.5%)
II	20 (37.7%)
III	14 (26.4%)
IV	6 (11.4%)
Sites of metastases at IV stage diagnosis	
Bone	14
Liver	17
Lung	17
Brain	31
Other sites	5
Mean Overall Survival	69 months (95% CI 17.65 – 277,7)

Results: 62 GKRS treatments for 152 BMBC were delivered in 53 pts of which a man, patient characteristics are illustrated in Table 1. 18.9% (10 pts) underwent BMBC neurosurgery resection, 6 pts were HER-2 amplified. Median DS-GPA score, median RPA class and median BSBM were 3 (95% CI 2-4), 2 (95% CI 1-2) and 1 (95% CI 0-3) respectively. Median BMBC volume was 0.14 cc (95% CI 0.03-1.67), median of maximum dose of GKRS was 40 Gy (95% CI 19.1-51.9) with median isodose line (IDL) of 50% (95% CI 45-95). Supportive therapy had to be modulated due to the onset of neurological symptoms after GKRS treatment in 22 pts (41.5%), corticosteroids and anti-epileptic drugs in 16 pts (30.2%) and 6 pts (11.3%), respectively. After GKRS 14 (26.4%) radionecrosis cases were reported. Due to intracranial progression disease after GKRS, 12 pts (22.6%) underwent whole-brain radiation therapy (WBRT). Based on RANO-BM criteria, there were 17 (32.1%) cases of partial response/stable disease after GKRS. At the time-analysis 26 pts were alive.

Conclusions: In our experience, GKRS is a well tolerated treatment with a good disease local control in selected BMBC pts according to DS-GPA, RPA class and BSBM.

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GAMMAKNIFE RADIOSURGERY WITH ONE OR TWO SHOTS FOR TREATMENT OF BRAIN METASTASES: ASSESSMENT OF DOSIMETRIC PARAMETERS AND CLINICAL OUTCOME IN A SINGLE INSTITUTION EXPERIENCE

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Aims: Treatment of brain metastases (BMs) represents a significant healthcare problem in metastatic cancer patients due to their clinical relevance. Radiosurgery (RS) is one of the treatment options in selected patients with BMs and a major role is played by the GammaKnife radiosurgery (GKRS). In our study we collected data from patients treated with GKRS for brain metastases of maximum 1 cm and we analyzed if there was any difference in terms of dosimetric parameters and clinical outcome between treatments with one or two isocenters (shots).

Methods: We retrospectively collected demographic and disease features of 86 patients for a total of 282 BMs, treated with the Leksell Gamma Knife® Perfexion™ . Each lesion was treated using one or two shots with a diameter of 4 and/or 8 mm. Coverage, Gradient Index (GI) and Selectivity were recorded for each lesion. MRI was performed at 1, 3, 6 and 9 months from treatment and radiological response was evaluated according to the RANO (Response Assessment in Neuro Oncology) criteria.

Results: 210 (74.5%) BMs were treated with one shot and 72 (25.5%) with two shots. Mean metastases volume was 103.1 mm^3 (2.4-721 mm^3). Mean coverage

of plans was 99.9% (range: 92-100%) and 99.7% (range: 95-100%) with one shot and two shots, respectively. Mean selectivity was 0.25 (range: 0.001-0.63) in one isocenter plans and 0.35 (range: 0.07-0.78) in two isocenter plans. Mean gradient was 3.2 (range: 0.85-8.10) and 3.2 (range: 2.11-9.8) for one and two isocenters plans, respectively. We observed a statistically significative better coverage in one shot plans (0.9995 vs 0.9968, p=0.0001) but selectivity was significantly better with two shots (0.2494 vs 0.3546, p=0.0001). At one month the majority of BMs were controlled (96.4%). Patients with breast histology correlated with a poorer local control (p=0.0001) at 3 and 6 months MRI, while a GPA (Graded Prognostic Assessment) < 3 was predictive of local failure (p=0.018) at 9 months MRI. Patients treated with one shot had a better local control (absence of progressive disease) at one month (1.0% vs 11.6% p=0.0001) and six months (5.9% vs 20.7%, p=0.026) compared to BMs treated with two shots.

Conclusion: In our study, the use of a single shot resulted in a better coverage and a better outcome at one and three months in BMs with a diameter inferior to 1 cm. GPA score and histology are confirmed as important prognostic factors in patients with BMs.

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ROBOTIC STEREOTACTIC RADIOTHERAPY IN MULTIPLE BRAIN METASTASIS: EARLY RESULTS OF A MONO-INSTITUTIONAL EXPERIENCE

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Objective: To report our experience with single treatment plan robotic stereotactic radiotherapy (SRT) delivered with CyberKnife® (Accuray, Sunnyvale, CA) in pts with multiple(> 5) brain metastasis.

Methods: From March 2018 to July 2020 a total of 152 brain metastases in 17 pts (nine females and eight males) were treated with a single treatment plan SRT in our institution. Primary site of tumors was lung in seven pts, breast in four pts, melanoma in three pts, kidney in one patient, one patient had lung and breast cancer and another one had lung and prostate cancer. Five pts previously underwent Whole Brain Radiotherapy (WBRT). Gross target volume (GTV) and organs at risk (OAR) were defined after simulation computer tomography (CT) and contrast-enhanced T1-weighted MRI fusion. Planning target volume (PTV) was defined adding a margin of 1 mm to GTV. Toxicity was scored in accordance with the CTCAE scale. Assessment of response was obtained by Contrast-enhanced MRI every 3 months.

Results: Patient's median age was 53.5 (29-81) years and median Karnofsky Performance Status (KPS) was 90% (70-100). Median number of brain metastasis was 7 (6-25). Median GTV volume was 0,17 cm3 (0,02-17,45 cm3), and median PTV volume 0,53 cm3 (0,07-23.67 cm3). Median prescribed dose was 35 (21-37.5) Gy, at a median isodose of 78.5% (65%- 89%), in a median number of 4 fractions (1-5 fr). All fractions were delivered in consecutive days. All pts received preventive steroid therapy, median dose was 4 mg/day (2-16 mg). Median estimated treatment delivery time was 70 (41-114) minutes. Acute toxicity was observed in 1 patient and was limited to grade 1 neurological events represented by dizziness. At a median follow up of 7.38 months (1.25-44.25 months), seven pts patients presented local control and one patient had progression of the lesions. Four pts had intracranial progression due to new lesions. Nine pts were unavailable for follow up: in 3 pts the time from the end of the treatment was less than 3 months, 3 pts were dead for systemic progression and 3 pts were lost to follow-up. At the last follow up, 6 pts were dead, 1 with heart failure two weeks after the treatment, 1 with systemic progression and 4 with intracranial progression.

Conclusions: Our data showed that single plan robotic SRT is a promising option of treatment in pts with more than five brain metastases. The treatment is feasible with a low toxicity.

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THREE DIMENSIONAL DOSE VERIFICATION FOR STEREOTACTIC RADIOSURGERY TREATMENTS USING POLYMER GEL DOSIMETER IN A 3D PRINTED HEAD PHANTOM

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Aims: Standard quality assurance program for the evaluation of the dosimetric accuracy of stereotactic radiosurgery (SRS) treatments relies on discrete point dose measurements performed by diodes, ion chambers, TLDs arrays inserted in non-anthropomorphic phantoms. The aim of this study is to investigate the dosimetric accuracy of SRS treatments by using an innovative 3D dosimetric system consisting of a polymer gel dosimeter combined with a 3D printed head phantom.

Methods: An RTSafe Pseudo Patient head phantom 3D printed with bone equivalent material has been used. A CT scan of the phantom fully filled with water and its dedicated 3D cylindrical polymer gel dosimeter has been acquired for planning. An SRS treatment plan for a C-shaped planning treatment volume (PTV) proximal to the brainstem has been realized (Pinnacle TPS)

with a prescription dose of 10 Gy in single fraction to the PTV. The phantom has been irradiated (Varian TrueBeam STx linac) as it was a real patient. 24hs post irradiation the phantom has been scanned at (Magnetom TRIO Siemens) MRI scanner with 2D fast spin echo sequence with multiple echo times in order to obtain phantom T2 map. An independent dosimetric analysis has been performed in-house: rigid-registration (MIM software) was performed between the planning CT image and a gaussian blurred T2 map of the irradiated phantom; the TPS calculated (relative) dose was compared with the measured T2 map in terms of gamma index analysis (3D Slicer, Gel dosimetry toolkit). All the acquired raw images of the phantom and dose distribution were also separately processed by RTSafe for dosimetric report generation (Figure 1).

Results: Gamma analysis for the pre-treatment QA on a diodes array phantom (Delta4 phantom) showed 97.8% of measurement points passing the criteria of 5%/2mm agreement. RTSafe dosimetric analysis report indicates that the 3D gel phantom dose distribution within the expanded PTV (+7mm) agreed well with calculations with a 93.7% gamma passing rate using 5%/2mm criteria. For the in house dosimetric analysis 92.1% agreement was found for the 5%/2 mm criteria.

Conclusions: Gel dosimetry is able to face the challenge of verifying dose and spatial accuracy of SRS treatments with patient-modeled 3D-printed phantoms assuring quality delivery with high spatial resolution. Further investigation have to be performed to understand the impact of MRI field strength on the dosimetric analysis results and to automatize in house dosimetric analysis.

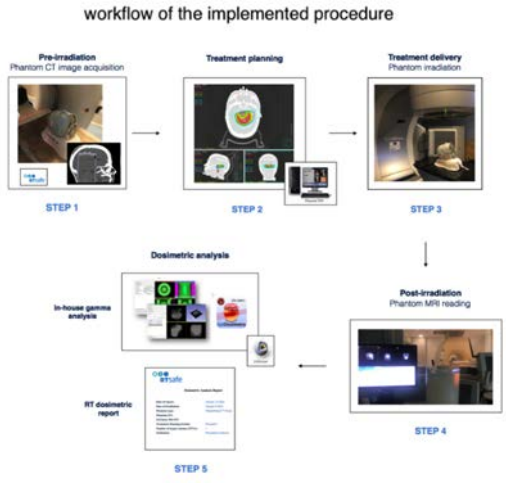

Figure 1.

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RADIOSURGERY FOR BENIGNANT CENTRAL NERVOUS SYSTEM DISEASE: DATA COLLECTION OF PRELIMINARY EXPERIENCE

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Aim: To evaluate acute/late side effects and early response of Linac-based Radiosurgery (SRS) for benignant Central Nervous System (CNS) Disease.

Method: Patients with benignant CNS disease suitable of SRS according to international guidelines were evaluated. In all cases, open-face masks dedicated for SRS were used for simulation and treatment. To correctly identify target, a fusion study of 1 mm-thickness CT simulation and diagnostic MRI was realized. PTV was defined by 1mm isotropic margin. FFF VMAT plans with 4 non-coplanar arcs were generated for each lesion. Prescription dose (Dp) was chosen based on pathology. Dp, normalization, optimization and Organs at Risk constrains were according to ICRU91 and in all cases they were respcted. During treatment, 3CBCT were performed (2before-1after SRS): first to revise setup treatment, second to confirm shifts and third to verify position at the end of SRS. For each treatment session, SGRT was applied to evaluate intrafraction variations, acquiring data in 3 different time points: before, end and during SRS, respectively.

Result: Between 10/2019-04/2020, 10 patients (6 female/4 male) underwent to SRS. Median age was 64years(range32-87). 7 were brain meningiomas (5 inoperable for location, including 2 cases of clivus disease, and 2 underwent surgery with histology of grade III), 2 were cavernomas in brainstem and 1 was inoperable MAV located in frontal-parietal area. For meningioma, Dp was 25 Gy in 5 fractions with isodose optimization of 80%; for cavernomas, Dp was 12 Gy in 1 fraction with isodose optimization of 75%; for MAV, Dp was 20 Gy in 1 fraction with isodose optimization of 75%. Median PTV was 8.25cc (range2-68). Median monitor units were 1458,05 (range1159.9-3621.2) with a mean overall treatment time of 2 minutes. At the end of treatment, no acute side effects were reported. At a median follow up (fu) of 5 months (range2-9) any late toxicities were described. During fu, MRI showed for meningiomas stable disease, for vascular disease partial thrombosis of lesions in absent of signs of recent bleeding.

Conclusion: The present findings in this preliminary experience highlight the feasibility, safety, and effectiveness of Linac-based SRS for benignant CNS disease, in line with the literature results mainly based on Gamma Knife experience. Future more large evaluation with long fu are warranted.

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PATTERN OF RECURRENCE/PROGRESSION IN NSCLC PATIENTS TREATED WITH STEREOTACTIC RADIOTHERAPY: A SINGLE CENTRE EXPERIENCE

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Aims: The aim was to evaluate the response to stereotactic radiotherapy on NSCLC lesions and the post-treatment recurrence pattern.

Methods: We performed a retrospective analysis of 57 treatments delivered to 50 patients from 2015 to 2019, by stereotactic radiotherapy on primary or relapsed lung lesion. SCLC and metastatic lesions were excluded. Fifty patients, 43 males and 7 females, with an average age of 77 (range 63-87 years) were included with minimum follow-up of 6 months. 28 lesions were NSCLC (15 adenocarcinoma, 12 squamous cell carcinoma, 1 non-differentiated carcinoma), 29 were non-typed lesions. 47/57 lesions (82%) had a peripheral location (distance> 2 cm from trachea/bronchus), while the remaining 10/57 (18%) had a central location (distance <2 cm from trachea/bronchus). Treatment response was assessed as "complete response" (CR), "partial response" (PR), "stable disease" (SD), "progression disease" (PD). In case of PD, locoregional and distant relapse patterns were considered. The locoregional relapse was classified as "in field" (InF), if it occurred within 90% of the isodose, "marginal" (M) if it was included in 50% of the isodose, "out of field" (OF) if it occurred outside 50% of the isodose.

Results: Mean total dose was 43.93 Gy (range 30-60 Gy) with mean daily fraction of 13 Gy (range 6-20 Gy) corresponding to a BED10 of 101.2 Gy (range 48-180 Gy). Mean follow-up was 21 months (range 6-51 months). During the follow-up, 29/57 (51%) RC, 5/57 (9%) SD, 2/57 PR (3%) and 21/57 (37%) relapses were observed, which were locoregional in 12/21 (57%) cases and at distance in 9/21 (43%) cases. Distant relapses occurred at an average of 8 months, median 7 months (range 4-14). Locoregional relapses occurred at an average of 15 months, median 11 months, (range 4-30) with the following pattern: 9/12 (75%) InF, 1/12 (8.3%) marginal, 2/12 (16.7%) OF. InF relapses were observed with a mean timing of 13 months, median 11 months (range 4-22). The cumulative patient survival at 12 and 24 months was 88% and 70% respectively, while disease-free survival was 78% and 66% respectively at 12 and 24 months. Survival free from InF of M relapse was 88% at 12 months and 82% at 24 months.

Conclusions: Despite the limitations of the study sample in terms of size, mean old age and follow-up time, considering cumulative survival and disease-free survival, stereotactic radiotherapy demonstrates good efficacy and good disease control with results in accord with literature data.

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GAMMA KNIFE STEREOTACTIC RADIOSURGERY FOR VESTIBULAR SCHWANNOMAS: A SINGLE INSTITUTION RETROSPECTIVE ANALYSIS

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Aim: Gamma Knife radiosurgery (GKRS) represent a well-established treatment modality for vestibular schwannomas, as alternative or in case of partial resection, as completion of surgery. Few studies have already been conducted to evaluate not only dose-response relationships for a highly effective tumor control but to toward optimizing long-term functional outcomes. The aim of the present retrospective is to evaluate the potential dose-rate effects following GKRS for vestibular schwannomas with respect to tumor control and preservation of functional hearing,

Methods: We retrospectively reviewed 60 patients treated at our institution Radiation Oncology Unit between 2013 and 2018 with GKRS for vestibular schwannomas. We collected baseline demographics characteristics, pretreatment symptoms and GKRS parameters. The cohort was divided into subgroups based on the prescription dose value. Outcomes included clinical and radiographic tumor control, hearing loss, and facial nerve dysfunction (FND).

Results: The study cohort included 60 patients with available follow-up of at least 2 years The average size of the treated neurinomas was approximately 2.57cc. 27% of patients underwent Gamma Knife after surgery, while 73% as primary treatment. 16% received a dose of 11 Gy, 11.6% a dose of 12 Gy, 50% of 12.5 Gy and then 23.3% a dose of 13Gy, all at 50% of idl. The patients were followed up with control MRI, clinical evaluations and audiometric tests at 3, 6 and 12 months, and then with half-yearly checks. No case was further treatment or surgery necessary. In most cases the lesions remained stable or decreased in volume. 2-yr control rates were 98% (95% CI: 95.6%-100%). The serviceable hearing preservation rate was 72.2%. Most patients experienced effective relief from prior headaches, tinnitus, balance issues and trigeminal nerve dysfunction, but not hearing loss.

Conclusion: Whereas GKRS provides effective tumor control , effective symptomatic relief for vestibular schwannomas, a dose-rate effects may impact post-treatment functional outcomes.

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PARMA HOSPITAL EXPERIENCE ABOUT HYPERARC TECHNIQUE

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Aims: Stereotactic Fractionated Radiotherapy (SFRT) is a treatment option in the management of brain metastases (BMs). However, the treatment of multiple BMs is challenge: frequency and severity of necrosis and neurological side effects strongly depend on the amount of healthy brain volume that was subjected to radiation. The aim of present study is to evaluate safety and effectiveness of SFRT for BMs, using a mono-isocenter non-coplanar solution: HyperArcTM Varian Medical System (HA). HA represents a potential step forward for linac-based SFRT of multiple BMs because assures a largely automated optimization process, thanks to dedicated algorithms1-2. In August 2019, the first patient was treated with HA in our center.

Table 1. Patient data, histology, volume treated and prescribed dose.

Patient #	Gender (M/F)	Age (y)	Histology	N. Lesions	Overall PTV (cm^3)	Dp (Gy)	N. fractions
1	F	62	Breast	4	11,9	27	3
2	F	50	Lung	1	4,9	24	3
3	M	59	Melanoma	6	11,4	24	3
4	M	60	Lung	2	9,2	24	3
5	F	65	Lung	2	1,2	24	3
6	M	69	Lung	2	4,2	24	3
7	F	60	Mesothelioma	1	10,6	27	3
8	F	87	Lung	3	9,6	27	3
9	F	46	Melanoma	1	0,4	24	3
10	F	67	Breast	3	10,2	24	3
11	F	62	Lung	2	4.6	27	3
12	F	63	Lung	2	2,1	27	3
13	M	58	Melanoma	8	12,2	24	3
14	F	30	Breast	2	12.3	24	3
15	F	61	Lung	5	1,9	24	3
16	M	60	Gastric Cancer	1	4,0	24	3
17	F	60	Mesothelioma	2	6,8	27	3
18	F	58	Lung	1	0,5	18	3
19	F	64	Lung	2	0.90	24	3
20	M	51	Lung	11	7,3	24	3
21	F	54	Lung	7	19,6	27	3
22	F	61	Melanoma	1	2,8	24	3
Median		59,4		3,1	6,9	24,7	
Standard deviation		10,3		2,7	5,1	2,1	
max		87,0		11,0	19,6	27,0	
min		30,0		1,0	0,4	18,0	

Materials and Methods: We performed a retrospective study of patients treated by HA for BMs. Patient data, treated volume and prescribed dose are summarized in Table 1. Patients underwent a CT simulation without contrast for RT planning with a thermoplastic mask (QFix®). An MRI-T1 sequences was used to delineate organs at risk and target volumes. GTV encompassed the macroscopic contrast enhancing lesion on T1-MRI. PTV was obtained expanding the GTV by an anisotropic margin of 1–2 mm in all directions. The fractionation scheme was chosen based on size and position of BMs, ranging between 24 Gy and 27 Gy in 3 fractions. Plan quality metrics included the volume of brain-minus-PTV (BmP) that receive no less than 12 Gy (V12Gy), the BmP mean dose (Dmean), the Paddick conformity index (CI) and the Paddick gradient index (GI) 3. At the end of treatment, all patients were clinically evaluated for acute neurological toxicity. A follow up MRI was acquired 2 months after the end of the SFRT. For each treated BM, complete response (CR), partial response (PR), stable disease (SD) or progression disease (PD) were defined by an expert neuroradiologist on MRI, according to the RANO criteria.

Table 2. Dose BmP_{mean}: mean dose brain-minus-PTV. VolBmP12: volume of brain-minus-PTV received 12 Gy. $C_{IPaddick}$: conformity index. $GI_{Paddick}$: gradient index. MU/fractions: monitor unit per fraction

Patient #	BmP D_{mean} (Gy)	BmP $V_{12\,Gy}$ (cm^3)	$CI_{Paddick}$	$GI_{Paddick}$	MU/fraction
1	3,1	31,8	0,87	3,60	2576
2	1,0	5,6	0,95	3,40	2625
3	3,5	34,7	0,90	3,80	3197
4	1,6	16,5	0,93	3,20	1679
5	1,0	5,4	0,66	5,70	2143
6	1,3	11,7	0,91	4,01	1915
7	1,3	19,5	0,95	2,74	2130
8	2,4	20,1	0,85	3,30	1968
9	1,7	2,0	0,96	5,07	2115
10	2,3	23,9	0,97	3,58	2080
11	1,8	13,5	0,87	3,35	2044
12	1,6	11,2	0,92	4,90	2027
13	3,7	45,9	0,77	4,30	3365
14	2,3	17,9	0,93	2,77	1946
15	2,4	13,8	0,79	6,52	2399
16	0,8	9,0	0,98	3,40	2528
17	1,5	22,3	0,90	3,60	1808
18	0,4	1,3	0,84	6,73	1310
19	0,6	4,0	0,97	5,39	2296
20	4,9	52,8	0,70	6,35	2581
21	5,4	92,4	0,78	5,30	2440
22	0,8	8,2	0,78	3,10	1971
Median	2,1	21,1	0,87	4,28	2234
Standard deviation	1,3	20,9	0,09	1,25	466
max	5,4	92,4	0,98	6,73	3365
min	0,4	1,3	0,66	2,74	1310

Results: from August 2019 to May 2020, 22 patients were treated (69 BMs). The treatment characteristics as well as the values of the plan quality metrics are reported in Table 2. Regarding to treatment response of brain lesions, CR, PR, SD and PD were respectively equal to 1%, 61%, 16% and 22%. Acute toxicities were mild: we had 6 events of G1 side effects.

Conclusion: our data show that SFRT with HA is safe, fast and useful tool both for planning and delivery. Dosimetric indices (GI, CI, mean dose and V12 brain-minus-PTV) were similar to those reported in literature.

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STEREOTACTIC RADIOTHERAPY FOR RE-IRRADIATION OF RELAPSED INTRACRANIC LESIONS

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Aims: Stereotactic Radiotherapy (SRT) is increasingly used for the treatment of recurrent primary brain tumors or metastases (mts) after previous radiotherapy (RT). We report the experience of our Institute.

Methods: From 1/2018 to 6/2020, 81 intracranial lesions in 19 patients (pts) were re-irradiated with robotic SRT (Cyberknife® - Accuray, Sunnyvale, CA)(CK). Five pts presented recurrent mts from breast cancer, 7 from NSCLC, 3 glioblastoma, 1 intracranial emangiopericytoma, 1 oligodendroglioma, 1 meningioma, 1 pituitary adenoma. Previous RT on the same volume were performed with: Gamma Knife radiosurgery in 5 pts, VMAT SRT in 3 pts, CK in 3 pts, whole-brain RT in 6 pts, post-operative IMRT in 1 pt, post-operative 3D-CRT in 3 pts. Median time from the previous RT was 14 (3-38.8)months. Five pts had ≥2 previous treatments. GTV was delineated on CT and contrast-enhanced T1-MRI. Median GTV size was 0.21 (0,02-36,7)cc. PTV was obtained adding an expansion of 1-3 mm to GTV. Median PTV size was 0.45 (0,07-62,3)cc. Median prescribed dose was 30 (21-35)Gy in 1-5 fractions (fr), at a median isodose of 78.5% (69-80%). Prophylactic corticosteroid therapy was prescribed to all pts and mannitol therapy to reduce intracranial pressure to 1 pt simultaneously treated on 21 lesions.

Results: Median follow-up after re-irradiation was 7.7 (2.3-30)months. SRT was delivered on a median number of 2 (1-21)lesions; 5 pts were treated on > 5 lesions simultaneously (6, 7, 9, 19, 21 respectively). Acute toxicity was G2 cefalea in 3 pts (GTV>1cc or >3 lesions), successful treated by increasing the dose of corticosteroids. Radionecrosis occurred in only one pt (GTV>1cc); he underwent 2 previous VMAT SRT (prescribed dose 30 Gy in 5 fr and 21 Gy in 3 fr) and was symptomatic for seizures, treated with corticosteroids and levetiracetam. Local control, evaluated with MRI (every 3 months) in 15 pts was: partial response (PR) in 7 pts, stable disease (SD) in 3 pts progressive disease (PD) in 5 pts. Four pts had less than 3 months follow-up. Eight pts were dead at the last follow up (1 systemic progression and 7 intracranial progression). Six months and 1 year OS were 47% and 26% respectively.

Conclusions: SRT for re-irradiation is feasible, with only 1 case of radionecrosis registered. The treatment is effective with SD or PR in 66% of pts. An accurate patient selection is warranted in order to avoid toxicity and a longer follow-up is needed to confirm the low radionecrosis rate.

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PRELIMINARY ANALYSIS OF CORRELATION BETWEEN RADIONECROSIS AND DOSIMETRIC FEATURES IN A COHORT OF PATIENT WITH BRAIN METASTASES TREATED WITH STEREOTACTIC RADIOTHERAPY

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Aims: The use of stereotactic radiotherapy (SRT) is a cornerstone for the treatment of brain metastases (BM). As the survival of patients with brain metastases is prolonged, patients could manifest late effects of SRT such as radiation necrosis (RN). Unfortunately, RN is hard to diagnose and manage, therefore the study aims to explore dosimetric features or index that could be correlated with RN.

Methods: We retrospectively analyse patients with BM treated with SRT in the 2 radiotherapy centres involved. The cohort was divided in 2 groups: the group of patients with RN and the group of patients without RN (control group). Patients were treated with different SRT schedule in terms of total and fraction dose. After the registration between the simulation CT and the MRI of RN diagnosis, a radiation oncologist and a radiologist contoured RN volume. We collected clinical and dosimetric data. Additionally, dosimetric indexes have been computed in order to assess the dosimetric distribution of the cohort. CIRTOG = volume encompassed the prescription isodose / target volume, Q= minimum dose given to the target / the prescription isodose. HI= maximum dose in the target / the prescription isodose. The gradient index , defined as the ratio of the volume of half the prescription isodose to the prescription isodose volume, has been extensively used over the last decade.

Results: We preliminary analysed 26 patients (pts) (15with RN and 11 without RN). Three pts received SRT in single fraction, 17 in 3 fractions and 2 in more than 3 fractions. Total dose was encompassed between 20 and 50Gy. In 12 pts the prescription isodose was 100% and 13 between 80 and 84%. Median time between SRT and MRI was 342 days (range:68-829). The mean PTV volume of the pts with RN was 4.05cc (range: 10.28cc-0.51cc). The mean PTV volume of the pts in the control group was 5.73cc (range: 20.31cc - 1.04cc). Higher RN volumes were found in pts (28.6%)

with a number of fraction equal to 3 and in pts (28.6%) with a prescribed dose per fraction of 8.5Gy The conformity index was able to identify the RN vs control pts' group, as shown in fig.. In particular pts with RN show a CI>1.4 or CI<0.9, instead control's group show a 1.1<CI<1.3 The other considered parameters are not able to identify the RN and control group separately.

Conclusions Even if the small sample size, this preliminary evaluation of pts with RN treated with SRT shows a trend of correlation between CI and RN. The enrolment is ongoing.

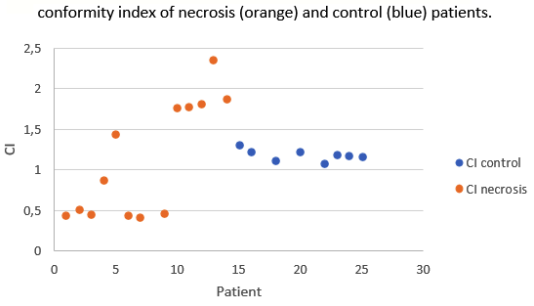

Figure 1.

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A MULTIDISCIPLINARY TUMOR CONSULTATION FOR PATIENTS WITH VESTIBULAR SCHWANNOMA: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: To facilitate the access for patients (pts) vestibular schwannoma (VS) to a multidisciplinary tumor (MDT) evaluation.

Methods: Pts with VS referred to our MDT consultation, involving a radiation oncologist, an otolaryngologist and a neurosurgeon. Clinical, radiological and full otoneurological data were collected. Audiological features were categorized according to the AAOHNS guidelines. The neoplasms were classified, according to the Koos criteria. The choice of the options (wait and scan, the microsurgery, the surgery, the stereotactic radiosurgery) depended on the pts' age, on the auditory function, on the dimensions, characteristics and growth over time of the tumor. Finally, two questionnaires were submitted to patients to investigate the number of doctors consulted before reaching our MDT, which therapeutic strategy has been recommended and the quality of life.

Table 1. Patients' characteristics at baseline.

Total patients	**72**
Sex M:F	**23 : 49**
Median age (Range)	**61 (25 - 85)**
Lesion side	**27 right, 44 left, 1 bilateral**
Staging according to Koos classification: • Stadio I • Stadio II • Stadio III • Stadio IV	**Pts number (%)** • 30 (42%) • 29 (40%) • 10 (14%) • 3 (4%)
Symptoms: • Tinnitus • Vertigo • Hearing loss • Asymptomatic	**Pts number (%)** • 44 (60%) • 31 (42%) • 30 (41%) Acute in 2 (3%) • 5 (7%)
Tone audiometric (PTA) threshold (AAOHNS) • Class A • Class B • Class C • Class D *Class A and B are considered as useful auditory capability*	**% di pazienti** • 21% • 26% • 13% • 40%

Results: From January 2018 to December 2019, 72 pts referred to our MDT consultation. Pts' characteristic at the first evaluation are reported in Table 1. The surgery was proposed in 11 pts (17%) (9 total resection and 2 partial); in 7 cases the basal auditory function was preserved. The stereotactic radiotherapy was proposed to 7 pts (11%), with a median age of 70 years, receiving a total dose of 18Gy in 3 consecutive fractions. The observation was preferred in 47 pts (72%). Two pts were treated in other hospitals, 2 were lost to follow-up and 3 chose therapies different from those proposed (radiotherapy and not surgery in 2 pts, surgery and not wait and scan in one patient). We observed a local control > 80% both with surgery and radiotherapy, with a better auditory preservation in case of stereotactic treatment (30-98% vs 30-50%). Neurological disfunction seems to be later with radiotherapy. According to the questionnaires, all patients were satisfied with the multidisciplinary consultation because of complete information. Before referring our centers patients consulted a median of three specialists with a proposed strategy of surgery in 35% of cases, radiosurgery in 40% and observation in 25%. The Quality of life resulted better in patient treated with radiotherapy.

Conclusions: The multidisciplinary assessment in presence with the patient allows to offer a complete informed vision of therapeutic options, to elaborate a

final recommendation, to follow-up our patients with their reported satisfaction.

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SRS / SBRT PLANS MADE WITH VMAT TECHNIQUE: A CT-BASED PRE-TREATMENT VERIFICATION CARRIED OUT BY THE ANATOMY ALGORITHM

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Aims: Volumetric Modulated Arc Therapy (VMAT) is a complex and precise procedure used to deliver a high dose of radiotherapy, The complexity of treatment makes it important to understand what the linac is doing during delivery especially for small fraction treatments planned such as a stereotactic radiosurgery (SRS) or a stereotactic body radiotherapy (SBRT), where the dosimetric errors in one fraction can potentially have a bigger impact compared to a conventional fractionation plan. Dosimetric inaccuracy on the VMAT SRS/SBRT plans was investigated using Gamma analysis method and the Delta4 Phantom+ (ScandiDos, Uppsala, Sweden) used in combination with a new implemented version of Anatomy algorithm that can assess the 3D Dose distribution on phantom and patient and perform a DVH analysis on the patient CT scan.

Materials and methods: A cohort of 10 SRS/SBRT patients with different prescriptions, target volumes and treatment sites were selected. VMAT plans, delivered on a Varian TrueBeam STx equipped with HD MLC using 6 FFF and 10FFF MV photon beams, were generated by Pinnacle3's SmartArc algorithm v.9.10 (Philips Fitchburg, USA) using local planning rules such as dose prescriptions and normalization, OARs sparing, and beam geometry in terms of multiple coplanar and non coplanar arcs to achieve the desired target objectives. Furthermore, on Delta Phantom+ the Anatomy tool was commissioned and the new TMM (Treatment plan dose with Measured Modification) dose reconstruction algorithm was tested to further estimate dose distribution errors. Each plan was measured on Delta 4 Phantom + and re-calculated using TMM algorithm.

Results: We investigated the difference between Anatomy TMM and Axial View tool by using Gamma Index evaluation, a DVH study in a discrete distribution perspective, and the dose profile PTV observation in terms of discrepancy (D) between measured and calculated distribution. Preliminary results showed a gamma index variation of -1,4%- 2% and a maximum variation of 4% related to OAR. Dose profiles study underlined a D = 14% finding a best accordance in Axial View algorithm. The accurate comparison between the DVH results showed an average variation equal to 4,5%.

Conclusions: The preliminary analysis showed a good agreement in terms of gamma index for the target and the OARs in homogeneous anatomical structures. Further investigations are undergoing in not small heterogeneities, where the variation can be statistically significant, probably due to the algorithm is based on the pencil beam.