XXIX Congresso

# AIRO2019

L'innovazione in Radioterapia
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## *Programme*

### NEW CHALLENGES FOR MODERN RADIOTHERAPY IN LONG-TERM SURVIVING PATIENTS: LATE TOXICITIES AND QUALITY OF LIFE

G.C. Iorio[1], S. Martini[1], 1V. De Luca[1], F. Arcadipane[2], S. Bartoncini[2], M. Levis[1], P. Franco[1], U. Ricardi[1]

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Radiotherapy (RT) is an effective anticancer agent. The current paradigm of research is to minimize radiation-induced toxicities, particularly late-effects compromising quality of life (QoL) and sequelae among long-term survivors,[1] while keeping optimal disease control rates.

Modern RT planning and delivery techniques represent the key to achieve this target. Herein, we discuss modern RT approaches in two different clinical settings:

- reducing the risk of cardiovascular disease and secondary cancers when treating young patients affected with mediastinal Lymphomas, particularly Hodgkin Lymphoma (HL);
- improving late toxicity profile in Head and Neck Cancer (HNC) patients.

Young patients with a long life expectancy are at higher risk of developing cardiovascular disease and secondary cancers after treatment for mediastinal HL. Historical long-term follow- up data showed that these survivors have an increased risk of late morbidity and mortality, primarily caused by cardiovascular disease and lung and breast cancer.[2] Nowadays, treatment for early-stage HL includes short course of multiagent chemotherapy followed by low-dose involved site RT.

Dosimetric benefits have been achieved with the introduction of different intensity modulated RT (IMRT) techniques (Butterfly-Volumetric Arc Therapy and Helical Tomotherapy).[3] Moreover, the employment of the Deep inspiration breath-hold (DIBH) technique, especially combined with IMRT, clearly showed the possibility to decrease the estimated mean doses to the whole heart and to its substructures (particularly coronary arteries and left ventricle) and, as well, to the lungs when compared with Free-Breathing.[4]

Promising results (but still preliminary) have also been reported when treating HL patients with intensity modulated Proton therapy.[5]

Focusing on HNC patients, technological RT upgrades led to lower acute and late toxicity profiles, with subsequent improved treatment compliance and quality of life (QoL).[6]

Of interest, promising results have been reported with the employment of multivariable normal tissue complication probability (NTCP) models for late swallowing dysfunction, 6 months after completion of treatment (swallowing sparing-IMRT).[7] Moreover, proton therapy, given the potential dosimetric advantages when compared with photons (Bragg Peak), represents a promising approach for HNC patients, potentially achieving a clinical benefit in terms of improved local tumor control and prevented/reduced radiation- induced side effects, considering the better sparing of critical organs (especially oral cavity and major salivary glands).[8,9] Results-based evidences from prospective randomized trials comparing IMRT and proton beam therapy are awaited.[10]

Further evidences are awaited regarding how to target optimal outcomes in terms of QoL and late toxicity profile in both HL and HNC patients.

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## REIRRADIATION IN CLINICAL ONCOLOGY: FROM RADIOBIOLOGICAL CONSIDERATIONS TO ASSOCIATION WITH NEW DRUGS

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In recent years, thanks to the development of more effective and fewer side effects radiation-systemic treatments, overall survival in cancer patients has increased considerably and the interest in radiation has grown. In order to make the oncological disease a chronic condition, the correct framing and treatment of the oligometastatic and oligoprogressive disease that often requires a second (or third) radio-oncological treatment, is becoming relevant. In fact, a therapeutic shift has progressively been observed from the purely palliative aim of reirradiations on painful bone metastases, for a curative purpose of retreatment on numerous districts and for all solid cancers. Re-irradiation is characterized by a narrow therapeutic window in which it is necessary to accurately weigh the dose to maximize efficacy and reduce toxicity, especially if the total cumulative dose of the various cycles is high. Reirradiation tends to pose even greater challenges and is therefore offered restrictively to highly selected patients on a case-by-case basis. Normal tissue dose limits are still an active area of investigation. However, examples of potentially useful indications have been published. Clinical and experimental studies suggest that specific normal tissues can tolerate a considerable radiation dose. From a technical point of view, in the case of reirradiation, an optimal dose conformation to the planning target volume is required. For radiobiological reasons - in order to reduce the risk of late effects - hyperfraction protocols should be applied to curative treatments. Alternatively, hypofractionated schedules to small volumes can be considered in a highly conformative and image-guided stereotactic approach. Furthermore, the treatment with protons and heavy ions, due to their peculiar physical and radiobiological characteristics, plays a key role in this context. The association with new drugs, immunotherapy and target therapy is a promising field of research, as recent evidence seems to show on the one hand an increase in efficacy due to a synergy of treatments, and on the other hand a reduction in toxicity.

## PRACTICE-CHANGING TRIALS IN RADIOTERAPIA ONCOLOGICA 2019

B.A. Jereczek-Fossa

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The medical knowledge is rapidly changing. New evidence is available based on the studies published in 2018-2019 and including radiotherapy. 18234 new reports on cancer radiotherapy are available at the 30th

June 2018 (since 1st January 2018). 650 reports regard clinical trials. Among the most significant studies are the following examples.

*Breast cancer*: Confirmation of the efficacy and safety of APBI for low-risk DCIS: APBI-IMRT-Florence phase 3 trial (NCT02104895). Becherini C et al. External accelerated partial breast irradiation for ductal carcinoma in situ: long-term follow-up from a phase 3 randomized trial. Tumori. 2019 Jun;105(3):205-209. Postmastectomy radiotherapy led to more local (chest wall) symptoms up to 2 years post-randomisation compared with no radiotherapy, but the difference between groups was small: SUPREMO TRIAL ISRCTN registry, number ISRCTN61145589. Velikova G et al. Quality of life after postmastectomy radiotherapy in patients with intermediate-risk breast cancer (SUPREMO): 2-year follow-up results of a randomised controlled trial. Lancet Oncol. 2018 Nov;19(11):1516-1529. Encouraging clinical outcome of a post-operative single fraction of APBI by multicatheter interstitial high dose-rate brachytherapy. Kinj R. et al. Single fraction of accelerated partial breast irradiation in the elderly: early clinical outcome. Radiat Oncol. 2018 Sep 12;13(1): 174.

*Lung cancer*: Radiotherapy induces responses of lung cancer to CTLA-4 blockade. Formenti SC et al. Nat Med. 2018 Dec;24(12):1845-1851. Durvalumab therapy resulted in significantly longer overall survival than placebo. No new safety signals were identified. PACIFIC trial. Antonia SJ et al. Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC. N Engl J Med. 2018 Dec 13;379 (24):2342-2350

*Prostate cancer*: Evidence suggests that prostate radiotherapy improves overall survival for men with metastatic prostate cancer who have a low metastatic burden, but not for unselected patients. Prostate radiotherapy should be a standard treatment option for men with newly diagnosed disease with a low metastatic burden. Parker CC *et al*. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. Lancet. 2018 Dec 1;392(10162):2353-2366.

*Glioblastoma*: lomustine-temozolomide chemotherapy might improve survival compared with temozolomide standard therapy in patients with newly diagnosed glioblastoma with methylated MGMT promoter. Herrlinger U *et al.* Lomustine-temozolomide combination therapy versus standard temozolomide therapy in patients with newly diagnosed glioblastoma with methylated MGMT promoter (CeTeG/NOA-09): a randomised, open-label, phase 3 trial. Lancet. 2019 Feb 16;393(10172):678-688.

*Head and neck cancer:* For patients with HPV-positive oropharyngeal carcinoma, radiotherapy plus cetuximab showed inferior overall survival and progression-free survival compared with radiotherapy plus cisplatin. Radiotherapy plus cisplatin is the standard of care for eligible patients with HPV-positive oropharyngeal carcinoma. Gillison *et al*. Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomised, multicentre, non-inferiority trial. Lancet. 2019 Jan 5;393(10166):40-50.

Compared with the standard cisplatin regimen, cetuximab showed no benefit in terms of reduced toxicity, but instead showed significant detriment in terms of tumour control. Cisplatin and radiotherapy should be used as the standard of care for HPV-positive low-risk patients who are able to tolerate cisplatin. Mehanna H et al. Radiotherapy plus cisplatin or cetuximab in low-risk human papillomavirus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomised controlled phase 3 trial. Lancet. 2019 Jan 5;393 (10166):51-60

Cochlear-sparing IMRT reduced the radiation dose below the accepted tolerance of the cochlea, but this did not lead to a reduction in the proportion of patients with clinically relevant hearing loss. Nutting CM et al. Results of a multicentre randomised controlled trial of cochlear-sparing intensity-modulated radiotherapy versus conventional radiotherapy in patients with parotid cancer (COSTAR; CRUK/08/004). Eur J Cancer. 2018 Nov;103:249-258.

The list of new significant studies will be updated at the moment of the presentation.

## THE ROLE OF THE RADIATION ONCOLOGIST IN MULTIDISCIPLINARY TEAMS, AND THE IMPACT OF HOSPITAL GUIDELINES IN PATIENTS' OUTCOME

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Aims: To investigate the role of the radiation oncologists inside muldisciplinary oncologic teams, and to assess the impact on patients' outcomes of a complete care pathway provided by institutions.

Methods: We undertook a literature search of PubMed using search terms such as "multidisciplinary team", "meetings" or "oncology decision making". In order to identify relevant literature on the issue, we searched for systematic reviews, meta-analysis and comparative studies, assessing the impact of the multidisciplinary team (MDT) meetings and/or of an institutionalized health care pathway on patient's diagnosis, treatment and outcomes.

Results: To find studies assessing MDT effectiveness has proven difficult, as the majority of studies on the issue are retrospective monocentric analysis.

However, we focused on those two meta-analyses and other thirty methodologically valid studies we found that were confronting patient's diagnosis, treatment and outcomes, before and after the implementation of MDTs and/or institutionalized care pathway, and our results showed that the impact of both was significant in all cited items. Between 4% and 35% of patients discussed had changes to diagnostic reports and the percentage of patients who underwent changes in treatment plans range from 19% to 34.5%. Patients discussed in MDT meetings, were more likely to: receive neoadju-

vant or adjuvant treatment; be referred to other disciplines; be managed with greater guidelines adherence and to get a more curative management.

Conclusions: We found some prospective studies, assessing different cancer population, reporting a significant association between MDT discussion and survival, especially in colorectal cancer and lung cancer patients. There is a need to improve team work. A real involvement of physicians from specialities other that surgery or medical oncology leads to better outcomes for cancer patients. We also recognized that radiation oncologists are under-represented in the literature concerning MTDs, and this requires a reflection on our responsibilities as a cancer care specialists.

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Raghid N. Charara et al. Practice and Impact of Multidisciplinary Tumor Boards on Patient Management: A Prospective Study. J Glob Oncol 3, 2016 by American Society of Clinical Oncology

Yara L. Basta et al. The Value of Multidisciplinary Team Meetings for Patients with Gastrointestinal Malignancies: A Systematic Review. Ann Surg Oncol (2017) 24:2669–2678

Jeffrey C. Liu et al. The Impact of the Multidisciplinary Tumor Board on Head and Neck Cancer Outcomes. Laryngoscope, 00:1–5, 2019 The Laryngoscope 2019 The American Laryngological, Rhinological and Otological Society, Inc.

Thomas V. Bilfinger et al. Survival Outcomes Among Lung Cancer Patients Treated Using a Multidisciplinary Team Approach. Clinical Lung Cancer, 2018 Elsevier Inc.


## RADIOLOGIC FEATURES OF TRUE PROGRESSION VS PSEUDOPROGRESSION IN GLIOMA AND BRAIN METASTASES


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Pseudoprogression is a treatment-related reaction, characterized by an increase in enhancing lesion size and/or edema, followed by subsequent improvement or stabilization. Pseudoprogression usually occurs in the 2- to 6-month period after chemio-radiotherapy, and it seems to be induced by a local tissue reaction, with increased edema and vessel permeability. Several studies showed that pseudoprogression results in a better outcome; for this reason, imaging plays a key role in the recognition of this entity.

Conventional MR imaging is limited in the differentiation of early progression of disease and pseudoprogression because both can show increased enhancement after contrast medium infusion and perilesional edema. To overcome this problem, several advanced MR imaging techniques have been evaluated.

Diffusion-weighted imaging (DWI) is a functional sequence that depends on the microscopic mobility of the water. Apparent diffusion coefficient (ADC) values were noted to be lower in the recurrent tumor tissue; however, heterogeneity of tumor content limits the diagnostic performance of this data. A study of Chu and coll. found that histogram analysis based on the ADC of the entire enhancing lesion may be a useful tool in the differentiation of true progression from pseudoprogression in glioblastomas.

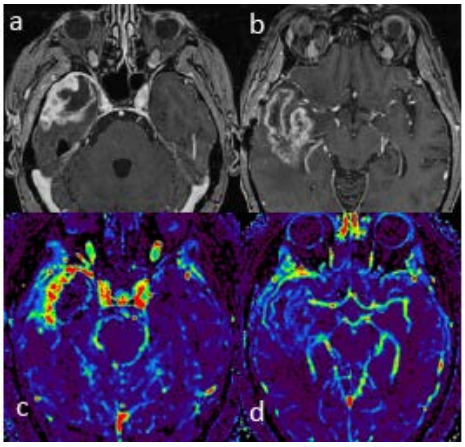


**Figure. GBM. Firts control MR after surgery and chemio-radiation therapy. SE T1 after contrast medium (a-b) shows an area of enhancement in the right temporal lobe and in the insula. MR perfusion shows an high blood volume area in the temporal lobe as recurrence (c- arrow) and low blood volume area in the insula as pseudoprogression (d – arrow).**

Perfusion MR imaging evaluates vascularity and vessels' permeability in the lesion. Dynamic Susceptibility Contrast-Enhanced (DSC) is the most used method for brain perfusion MRI; several studies found that the main DSC parameter, the relative cerebral blood volume (rCBV), is higher in true progression than in pseudoprogression. An alternative technique is Dynamic Contrast-Enhanced (DCE), which measures vascular permeability; some of the pharmacokinetics parameters, such as the volume transfer constant (Ktrans) and the extravascular-extracellular volume (Ve), were significantly higher in true progression of glioblastoma than in pseudoprogression. MR spectroscopy is an advanced MR imaging that offers a biochemical pattern analysis of the tumors. Differential diagnosis is challenging because both type of lesions (progression disease and pseudoprogression) can present decrease of N-acetyl-aspartate (NAA), elevation of

Choline (Cho) and high lactate/lipid values; however, it is found that Cho/NAA ratio has high diagnostic accuracy in the distinction of the two entities.

In conclusion, advanced MR imaging plays a key role in the assessment of treatment response.

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## RE-IRRADIATION OF GLIOBLASTOMA: INDICATIONS, NEW TECHNIQUES, DOSES, VOLUMES AND POTENTIAL TOXICITY

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Despite recent innovation in treatment techniques and subsequently improvement in outcomes, most patients with glioblastoma (GBL) have relapses, especially in loco-regional areas.[1] Such pattern of recurrence is the same between pre-TMZ and post-TMZ eras.[2-4] Recurrent GBM is associated with a median overall survival less than a year and the majority of patients have profound tumor-related symptoms[5,6] and there is no optimal salvage treatment for this group of patients.[6] Interventions such as re-resection, systemic therapy and/or re-irradiation may be of benefit in selected patients, but unfortunately all are administered with a palliative intent and treatment decisions must be individualized. For patients with limited volume recurrence, in a favorable location (*i.e.*, away from brainstem), re-irradiation may be a suitable option. However, the fear of treatment-related toxicity makes this option under-stressed. Although several reports have suggested a reasonable efficacy and safety profile of re-irradiation, most of these have a small sample size with inconsistent findings. A recent expert consensus report surveying 13 experienced radiation oncologists showed that there is significant variability in patient selection for re-irradiation and in preferred radiation regimens.[7] A systematic review shows an OS-6, OS-12, PFS-6 and PFS-12, from time of re-irradiation of 73% , 36%, 43% and 17% respectively [8]. The overall toxicity rate was considered to be low (range 4–10%) although Grade 3+ toxicity was not reported uniformly. The optimal dose-fractionation regimen remains unclear and a wide range of dose prescriptions were used. No difference based on the median EQD2 was found in systematic review and, interestingly, a short fractionation (radiosurgery or hypofractionated raduation with ≤5 fractions) regimen seems to be associated with an improved PFS-6.[8] In our practice, we perform a highly conformal technique with a hypofractionated regimen (such as 30 Gy in 5 fractions), taking into account the volume and location of the recurrent tumor. Our Phase I trial (GLIORAD), which is currently investigating the safety of dose escalated re-irradiation (50 Gy in 5 fractions), has reached the planned accrual and should help clarify the the best way to manage these patients.

In conclusion, local re-irradiation has been established as a feasible option for recurrent GBL in all ages with safety, tolerability, and effectiveness both in survival and quality of life regardless of fractionation schedule. Prospective trials are required to assess neuro-cognitive and quality-of-life endpoints taking into account the molecular profile of the recurrent tumor (O[6]-methylguanine-DNA methyltransferase (MGMT) methylation, EGFR amplification, BRAF V600E mutation) in order to guide the integrated managementfor these patients.

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## BRAIN METASTASES RE-IRRADIATION: INDICATIONS, NEW TECHNIQUES AND POTENTIAL TOXICITIES

V. Pinzi

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Aims: Although historically associated with a median survival of only a few months, long-term survival after the diagnosis of brain metastases is now changed and it is significantly improved.[1-2] However, along with long-term survival, both local and distant brain relapse can occur after longer and variable time intervals, being in need of additional radiotherapy. Neverthless, re-irradiation of brain metastases after radiosurgery to the same target volume is still a controversial approach.[3] The aim of this study is to summarize the results of clinical studies on brain metastes re-irradiation in terms of survival, local control and toxicity.

Methods: A literature review was carried out based on PubMed search. The keywords used were "reirradiation", "re-irradiation", “repeat radiotherapy” “salvage radiotherapy” and “salvage radiosurgery” combined with “brain metastases”, "secondary brain tumor" and “cerebral metastases”. The eligibility criteria were: 5 analysed patients at least; English language; local control, survival and/or toxicity as primary end-points of the study; minimum follow-up of 3 months. A descriptive statistical analysis was performed.

Results: Ten retrospective and 1 prospective studies were identified and analysed. All references were checked for further search. Where reported, the median follow-up ranged from 8,8 to 14 months. The one-year survival rates ranged from 38% to 91%, (median 65%). The one-year local control rates ranged from 68% to 88% (median 79%). The overall radionecrosis rate was 20%, ranging from 10% to 38%. No significant neurological toxicity was reported. However, data related to neurocognitive function or quality of life were not identified.

Conclusions: While the data are scarce, re-irradiation of brain metastes seems to be a viable and safe option for patients who are not ideal candidates for salvage surgery. However, the retrospective design of the studies and the different doses and fractionation used cannot allow us to draw any definitive conclusions. Future studies are required to clarify the role of re-irradiation of brain metastases and its impact on disease and patient-related outcomes.

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## LOCOREGIONALLY ADVANCED DIFFERENTIATED THYROID CANCER: INDICATIONS OF RADIOACTIVE IODINE AND EXTERNAL BEAM RADIOTHERAPY

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Aims: To review the main literature in order to determine the indications for the use of radioiodine and external beam radiotherapy (EBRT) in locally advanced differentiated thyroid carcinoma (LADTC) of follicular origin.

Methods: Given the relative rarity of the disease and its indolent behaviour with the occurrence of relapse even decades after treatment, no randomized clinical trials have been conducted and concluded. Information about the usefulness of radioiodine and EBRT in LADTC can be obtained only by retrospective observational studies, based on single-institution experiences, and usually covering several decades.

Results: the patient population is usually heterogeneous, patients are staged according to different TNM editions and with various diagnostic tools and treated with technologies of varying degrees of complexity. With these limitations the main literature is reviewed in order to give recommendations on the use of radioiodine and EBRT.

Conclusions: The most important therapeutic tool in LADTC remains surgery, which in few cases requires organ sacrifice to be radical. The use of radioiodine with adjuvant intent has a consolidated role in LADTC and international guidelines substantially agree about its use. Many published retrospective observational studies indicate that EBRT can improve locoregional control but, in the absence of a strong evidence, the use of adjuvant EBRT needs a careful evaluation of the risk of recurrence and of acute and late toxicities. In addition, the studies indicate that the following prognostic factors should be considered: pT4 stage, R1 and R2 surgery, extracapsular invasion of LN, disease refractory to radioiodine and patient age.

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## METASTATIC DISEASE IN DTC: INDICATIONS TO 131I TREATMENT AND COMPLEMENTARY THERAPIES

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Differentiated thyroid cancer (DTC) is an indolent tumor in the majority of cases. Even so, up to 10% of patients will develop metastatic disease (MD).[1] Treatment with radioactive iodine (RAI) represents the standard of care in metastatic DTC and usually a dose equivalent to 7400 MBq is administrated. However, retrospective and dosimetric studies have shown that only about one third of these patient can be cured with RAI. These are generally younger (<45 yrs), with well- differentiated disease and small tumoral dimensions (<1 cm).[2] The remaining cases appear to be non-avid RAI disease and this therapy can only have a cytoreductive effect. Dosimetric studies conducted with 124I[3] or with maximum permissible activity to protect bone marrow[4] haven't showed consistent results compared to standard-activity approach. Moreover, it's important to evaluate risk-benefit assessment of repeating RAI treatment with a cumulative dose >600 MBq. MD represents a complex clinical scenario, where treatment is usually patient-tailored and discussed in multidisciplinary team.[5] RAI therapy is usually non curative and integration between different methods (surgery, EBRT, interventional techniques) is used to achieve better local control. Focusing on bone metastases, affecting about 13% of patients,[6] they are usually RAI-refractory and linked to a short overall survival (OS).[7] The MOSCATI study denoted skeletal-related events (SRE) are more frequent in non-avid RAI disease.[8] Besides, Andrade *et al.*[9] showed how the use of Zolendronic Acid could reduce chances of having SRE and impact OS as well. From a retrospective study conducted by Wu *et al.*[10] combining 131I with other therapies may improve OS. In addition to RAI therapy, lymphonodal, lung and brain metastases can be treated with surgery or with stereotactic radiotherapy if lesions are macroscopically evident or in cases of poorly differentiated disease. For liver metastases, an unfrequent occurrence, interventional tecniques5 are an option too. Tyrosine kinase inhibitors are used in cases of metastatic, quickly progressive (doubling time <1yr) and RAI-refractory disease. PET-FDG imaging can provide additive data to CT imaging and shows to be an excellent tool in lesions detection and in the follow-up. In conclusion, RAI remains an irreplaceable therapy in metastatic DTC, but a patient-tailored therapy should be considered, especially in older patients (>45 yrs), poorly differentiated cancer and in case of BRAF or TERT mutations.

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## RADIOACTIVE IODINE REFRACTORY DISEASE AND TREATMENT WITH TKI

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The incidence of differentiated thyroid cancer (DTC) has increased in the past decades and, irrespective of whether overdiagnosis plays a role, there are now more patients who need risk stratification of their disease. Most cases are associated with excellent prognosis with survival rate of 95.8% at 5-year. Distant metastases (DM) are rare on presentation but are found in 6-20% of patients in follow-up and this increases the risk of cancer-specific mortality. On diagnosis of DM, radioactive iodine (RAI) is usual first-line therapy followed by TSH suppression. Progressive dedifferentiation of DTC is accompanied by loss of the sodium iodide symporter that is required for iodine uptake and poorly differentiated foci often exhibit parallel development of 18 F-Fludeoxyglucose (FDG)-PET positivity. When the DTC becomes or is intrinsically refractory to RAI, the prognosis is poor. Patients with DM that retains RAI avidity have a 10-year survival of 60%, and survival falls to 10% when RAI avidity or responsiveness are lost. RAI refractory disease occurs in less than 5% of patients with DTC. The main criteria for consider a disease RAI refractory (with appropriate TSH level) are the lack of uptake in metastatic tissue, also in DM that previously were RAI avid, and the progression of disease despite significant RAI uptake. At times, the definition of "refractory" is in progress and other conditions may suggest the presence of refractory disease: when RAI can be concentrated in some metastases but not others; in presence of high FDG uptake on PET scan; and in the cases of aggressive DTC histology. Those patients who have an unresectable primary DTC tumor should also be included in this classification.

Limited treatment options are available for patients with progressive and refractory DTC. Conventional chemotherapy has limited efficacy and significant toxicities. A greater understanding of the biology of DTC has led to the development of "targeted" therapies, especially anti-angiogenic drugs and some target kinases in the MAP kinase pathway. The optimal time to start these therapies is still a matter of debate, especially for asymptomatic patients. However systemic treatments should be started in patients with progression of measurable lesions, as defined radiologically by RECIST criteria, and must take into consideration tumor burden, site of the lesions, symptoms, and the risk of local complications. With these agents, partial remission were observed and even more importantly median progression-free survival was prolonged in phase III trials when compared with placebo.

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## MODERATE HYPOFRACTIONATION: CURRENT CLINICAL PRACTICE?

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Hypofractionated radiotherapy (HRT) for prostate cancer seems to have a strong radiobiological rationale: the low value of prostate cancer alpha/beta (estimated approximately 1.5-2), slightly lower than adjacent normal tissues, should allow an improvement in therapeutic ratio. Moreover, the use of a smaller number of fractions is increasing, being convenient both for patients and facilities. For these reasons HRT is considered a hot topic in radiation oncology. Several studies have compared conventional (CRT) and moderate HRT in the treatment of prostate cancer patients, and some are still ongoing. Published data concerning the curative treatment of prostate cancer suggest a non-inferiority of HRT, with some studies reporting a better outcome in terms of local or biochemical control, and no significant increase of toxicity, although a longer follow-up is needed to assess both long-term outcome and late toxicity.

Post-operative HRT has also been suggested to be feasible and safe, although some experiences reported a higher rate of late genito-urinary toxicity.

HRT is now widely performed in daily clinical practice, both in curative and post-operative setting.

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## EXTREME HYPOFRACTIONATION: WHAT FURTHER QUALMS?

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Aims: The aim of this presentation is to overcome the reluctance versus the implementation in the clinical practice of extreme hypofractionation in primary prostate cancer radiotherapy, based on available radiobiological, technical and clinical data.

Methods and Result: The obvious interest in extreme hypofractionation is based on the favorable radiobiological characteristics of prostate cancer and supported by advantageous logistic, cost-benefit aspects deriving from short overall treatment time. The clinical validity of short-term treatment schedule is proven by a body of non-randomized studies, using both isocentric (LINAC-based) or nonisocentric (CyberKnife-based) stereotactic body irradiation techniques (SBRT). In a paper by De Bari *et al.*[1] twenty clinical studies, each enrolling more than 40 patients for a total of 1874 treated patients, were revised in terms of technological setting, toxicity, outcome and quality of life assessment. The result of this review showed that as far as the rate of severe acute toxicity is concerned, in all the available studies the treatment was globally well tolerated. While awaiting long-term data on efficacy and toxicity, the analyzed studies suggest that the outcome profile of this approach, alongside the patient convenience and reduced costs, is promising. Forty-eight ongoing clinical trials are also presented as a preview of the expectation from the near future. On this basis the Italian Association of Radiation Oncology endorsed the use of extreme hypofractionation inserting it as an option in the Prostate Cancer Association Guidelines.[2] Another review by Amar *et al*.[3] supports the efficacy and safety of SBRT for PCa. Dosimetric correlations with patient-reported urinary and bowel quality of life were analyzed on a prospective trial by Wang *et al*.[4] Quality of life issues were also reported in a paper by Johnson *et al*.[5] showing that patients who received SBRT or moderate hypofractionation have similar patient-reported change in bowel and sexual symptoms, although there was worse change in urinary symptoms for patients receiving moderate hypofractionation. At present thirteen studies on extreme hypofractionation are active at ClinicalTrials.gov,[6] encouraging update on two extreme hypofractionation ongoing randomized trial (Scandinavian HYPO-RT-PC and Canadian PATRIOT) ,[7,8] and systematic meta-analysis[9] were recently published.

Conclusion: Although randomized clinical trials comparing SBRT with conventionally fractionated radiotherapy are currently underway, the current body of evidence allows the conclusion that extreme hypofractionation is safe, effective and cost advantageous, and should be considered in clinical practice.

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## ANDROGEN DEPRIVATION THERAPY: ONLY IN UNFAVORABLE INTERMEDIATE RISK?

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Patients with intermediate-risk (IR) prostate cancer (PC) are an heterogeneous group with highly variable prognosis. The classification system of National Comprehensive Cancer Network (NCCN)[1] stratifies intermediate-risk patients into favorable and unfavorable according to clinical tumor stage (cT2b or cT2c), grade group (2 or 3), PSA level and percentage of positive biopsy. The combination of radiotherapy (RT) and androgen deprivation therapy (ADT) significantly

reduced biochemical failure rates and improved overall- and cancer-specific survival compared to RT alone.[2] However, several investigators[3,4] have shown that using RT without ADT in men with favorable intermediate-risk PC results in low rates of prostate cancer specific mortality (PCSM) after 10 years (<2%); on the other hand, the addition of ADT to RT for unfavorable risk group has been broadly accepted. EORTC 22991 trial showed that the addition of 6 months of ADT improved biochemical disease free survival compared to RT alone in IR patients.[5] The RTOG 9910 randomised trial compared the efficacy of 4 months to 9 months of ADT and demonstrated that there is no reason to extend ADT beyond 4 months in conjuction of ADT in men with IR disease.[6] Although several randomized trials have shown that short term ADT improves overall survival when added to RT, at least in the context of conventional dose RT. This is not established for patients receiving dose escalated RT.[7] The RTOG 0815 ((NCT00936390) is an ongoing trial in which men receive high-dose RT with or without 6 months of ADT. This study will provide some evidence on whether 6 months of ADT reduces PCSM in men with unfavorable IR PC undergoing high-dose RT and whether high-dose RT alone is sufficient to minimize PCSM in men with favorable IR PC. In conclusion, waiting ongoing trials within the IR subgroups, withholding ADT in men with favorable IR PC and adding 4 or 6 months of ADT to RT in men with unfavorable IR PC are reasonable options based on the available evidence.

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## MOLECULAR AND RADIOMICS SIGNATURE AS PREDICTIVE FACTORS OF TUMOR CONTROL PROBABILITY (TCP)


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Head and neck cancers (HNSCC) represents a unique model to apply the analysis of a large amount of features in order to obtain predictive biomarker of tumor control probability. The "older" analysis of simple tumor size at imaging has moved recently into a deeper analysis of imaging and its finest characteristics in the attempt to identify predictive biomarker of outcome (radiomics). The routine use of computed tomography, magnetic resonance and often positron emission tomography associated to its complex anatomy and heterogeneity of HNSCC, allows different approach in radiomics analysis. Sometimes and surprisingly, the features extracted are exported in different cancer such evidenced by Aert[1] biomarkers extracted from a lung cancer dataset and associated to oncological outcome, were translated and validated in independent datasets of head and neck cancer patients. Many features often emerged from the analysis, and it's very difficult to understand real role and application of these plethora of data. An important contribute about this comes from Parmar's studies[2] the author tried to group in cluster the imaging biomarkers from the vast amount of extracted features and the results evidenced a significant association with patient survival and tumor stage. Recently, the works of Leijenaar[3] provide a proof of concept that a radiomics analysis is able to derive molecular information from standard medical images in HPV positive HNSCC patients: a "bridge" between different aspect. Another recent field of interest was the analysis of molecular characteristics, in order to classified tumor not only and "simply" by histology, but also with the goal of a major precision in our treatment. Gene expression profiles by microarrays or next-generation sequencing platforms have been widely used in developing biomarkers in HNSCC. These gene expression subtypes were correlated with biological features of tumors as well as the clinical outcome of patients. Linge[4] *et al.* reported that high expression levels of hypoxia-induced gene signature and cancer stem cell markers were correlated with poor prognosis after post-operative chemoradiotherapy in HNSCC patients; another[5] showed that the molecular profile of recurrent and metastatic tumors is quite distinct from primary tumors. However, most of these gene signatures were reported as prognostic factors for HNSCC. Little biomarkers have been developed for predicting the clinical benefit of treatment. The molecular and radiomics data today at our disposal are probably the way of future to improve the prediction on outcome. However the great variability and the lack of validation of various model used and the big amount of features potentially extracted, represent actually the real limit of this approach. Standardization of procedure and a rigorous quality

approach probably allows us to identified more limited but also reproducible features.

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## MOLECULAR AND RADIOMIC SIGNATURES AS NTCP PREDICTIVE FACTORS

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From 1970s, several conceptual revolutions were made in the field of normal tissue complication probability (NTCP). Firstly, Rubin and Cassarett introduced the concepts of TD5/5 (i.e. the probability of 5% complication within 5-years from treatment) and TD50/5 (the probability of 50% complication within 5-years).[1] At the beginning of 1990, the Lyman-Kutcher Burman model was the most commonly used tool to assess NTCP. In the same year, the International Commission on Radiological Protection has proposed the concept of organ at risk dose constraint (60 ICRU).[2] After 20 years, the publication of the Quantitative Analysis of Normal Tissue Effects – QUANTEC – has changed the daily clinical practice of Radiation Oncologists.[3]

Recently, the Innovation in medical imaging has led to a dramatic increase of resolution and imaging modalities, reproducible protocols, and image analysis such as Radiomic. It consists in extracting hundreds of quantitative features by an automated or semi-automated software. Radiomic relies on the hypothesis that mineable data can be extracted from medical images and provide additional information on gene protein and tumor phenotype and then used for patient care. The real question could be: are we ready to adopt Radiogenomic in daily clinical practice? Probably no. There is an acute need for rigorous evaluation criteria and reporting guidelines which will allow establishing Radiogenomics as a firm scientific discipline in Radiation Oncology. On the other hand, there is the need to improve the NTCP accuracy for the benefit of head and neck cancer patients. In fact, NTCP has several limitations. NTCP models are usually based on dose–volume histograms, which are not ideal representations of 3-dimensional doses and assume that all the regions of an OAR have an equal functional importance, thus discarding organ specific spatial Information. Moreover, they do not take into account fraction dose variations, nor anatomical variations of the OAR and its dosimetric consequences during treatment. Models taking into account more data such as 3-dimensional dose distribution in OARs, dependencies between the dose delivered at other OARs may enhance toxicity prediction. Dose-volume histograms of the whole organ at risk (that treat the organ as a homogeneous entity) are not a suitable basis for biology-based NTCP models. Depending on the normal tissue complication which is taken as the most critical and needs to be avoided as much as possible, different structures or sub-volumes of the respective critical organ/s at risk have to be delineated.[4]

In the next future, the adoption of molecular and Radiomic signatures could improve the NTCP as accurate predictive factors in a new era of personalized medicine for head and neck cancer.

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## NANOPARTICLES AND RADIOSENSITIZATION: BIOLOGICAL BASIS

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The broad spectrum of properties of nanomaterials may provides a wide range of biomedical applications. In radiation oncology, the main goal is to raise the therapeutic efficacy of ionizing radiations without additional damage to the surrounding structures, thus increasing the differential effect between healthy and tumor tissues. Nanoparticles (NPs), in particular high atomic-number (z) NPs, have been studied in the preclinical setting, showing a radio-sensitizing activity that exceed mere expected physical interaction and may underlie complex biological mechanisms of synergy such as increased ROS generation, cell cycle alteration, vascular damage and, as more recently highlighted, modulation of the immune response. Advances in nanotechnology manufacturing allow to increase the versatility of NPs by transferring new properties in order to enhance tumor selectivity, such as molecular targeting through

chemical coating, or to favor association with other radiosensitizing agents such as hyperthermia, for exemple by employing magnetic NPs. Despite encouraging pioneering trials and initial approval of NPs in association with radiotherapy in specific patient subsets, crucial criteria such as desirable physicochemical properties, route of administration, dosing and irradiation schedule still need to be defined in order to maximize the benefits of NPs in clinical practice.

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## PRELIMINARY RESULTS AND FUTURE DIRECTIONS IN THE USE OF NANOPARTICLES IN COMBINATION WITH RADIOTHERAPY AND SYSTEMIC THERAPIES


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Radiation Oncology (RO) is constantly evolving thanks to progress in radiobiological knowledge, but also advances in treatment options and dose delivery techniques. However, the latter do not necessarily result in a significant change in cure rates for radiotherapy (RT), since multiple variables like tumor resistance, normal tissue toxicity and accurate radiation dose delivery may affect the efficacy of RT. Nanotechnology has also emerged as a promising strategy and offers a number of unique features suited for applications in RO. Nanoparticles can be programmed to preferentially release therapeutic agents to tumor cells, owing to enhanced permeability and drug retention effect, hence a gain in safety and effectiveness from combination therapy. The preferential accumulation of nanoparticles in the tumor cells may lead to: (a) improved contrast enhancement for image-guided RT (IGRT); (b) tumor-specific delivery of chemotherapeutic agents or target therapies in combination with ionizing radiation; (c) increased local radiation dose using particles with high atomic numbers. Different nano-platforms have been investigated for radiotherapeutic applications. Among them, gold nanoparticles were very promising due to their high X-ray absorption coefficient and the ease of their synthetic manipulation. The role of the emerging gold nanoparticles aided radiotherapy modalities was explored in this overview of the available clinical trials, with the aim to assess their establishment as more effective RT treatment options than the actual standard of care for cancer patients.

## MOLECULAR BIOLOGY AND MULTIDISCIPLINARY TREATMENT OF PEDIATRIC BRAIN TUMORS


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Background: The 2016 edition of the World Health Organization Classification of Tumors of the Central Nervous System utilizes integrated diagnosis incorporating both morphologic and molecular features. Despite tremendous successes in understanding their biology in the last decade, brain tumours remain the highest cause of mortality and morbidity rates in childhood and adolescence.

Methods: In the field of pediatric neuro-oncology this has meant a great deal of diagnostic changes especially for medulloblastoma, other embryonal tumors and high-grade glioma patients but the impact on therapeutic decision is a modulation between still important clinical features of patients at different ages and these new acquirements.

Results: Some entities, now more precisely molecularly such as diffuse midline gliomas with histone H3.3 mutations and embryonal tumours with multi-layered rosettes (ETMR), plus molecularly defined subsets of hemispheric high-grade gliomas, medulloblastomas and atypical teratoid/rhabdoid tumours, are still associated with a universally fatal outcome to date. Other entities achieve a better cure rate but with severe late effects of disease and treatments and also require improvements of current treatments. We can only be successful in paediatric neuro-oncology when taking a multi-disciplinary approach – ranging from preclinical teams through to all involved specialized clinical disciplines. These need to address the definition of “preclin-

ical evidence", understanding of the special microenvironment in the brain and its clinical implications, definition of sampling and molecular diagnostics standards (including advanced biomarkers such as liquid biopsies), standards of advanced neuroimaging, neurological/neuropsychological trial endpoints, local delivery trials, radio-sensitizing trials, advanced supportive care, trials in the context of neurodevelopment/neurocognitive late effects and autopsy programs to benefit the next generation of patients, etc.

Conclusions: An improved understanding of the molecular genetics, epigenetics, and cellular biology underpinning childhood brain tumours will potentially enable more effective and less toxic treatment strategies to be developed and implemented. This could spare children from the severely detrimental consequences associated with conventional treatment protocols and improve the outlook for patients with currently incurable disease

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## THE BEST TECHNOLOGY FOR PHOTON BASED RADIOTHERAPY


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Radiotherapy plays a fundamental role in the cure of pediatric brain cancer. It is frequently employed exclusively or as part of a multimodality treatment approach in combination with surgery and/or chemotherapy. Radiotherapy plays a fundamental role in the management of pediatric cancer, with the primary aim of achieving a high therapeutic ratio (the highest probability of cure with the lowest risk of toxicity).

Considering the risk of severe late effects (mainly, neurocognitive deficits, hearing loss and hormonal deficiency for impairment of hypothalamic-pituitary axis) , a major goal of pediatric cancer radiotherapy is to maintain or improve cancer cure rates, while decreasing treatment sequelae. In addition the risk of second malignancy years after treatment may develop. Notably, the late effects of cranial irradiation are affected by a number of critical factors, including total and fractional dose, dose to organs at risk, use of other treatment modalities (chemotherapy and surgery), use of other drugs (steroids and antiepilectic drugs) and patient age during brain irradiation.

A variety of very conformal radiation therapy techniques with photons have been developed to try to limit the high radiation dose region to the tumor target. Fixed beams IMRT, Volumetric Modulated Arc Therapy (VMAT) and Tomotherapy are the most promising techniques. The superiority of IMRT over conventional photon radiotherapy in terms of conformality and dose homogeneity was reported from dosimetric studies addressing different tumour sites. With these treatment modalities, new organs at risk (hypothalamus, pituitary, hippocampus, scalp..) beyond the"classical" ones may be spared.

In addition, the advantages in terms of conformality of modern techniques make reirradiation a reliable option for recurrent pediatric brain tumors. By contrast, the possibility of sparing critical structures may be achieved with these techniques at the cost of increasing the low doses-bath with a potential risk of secondary carcinogenesis.

Deep understanding of individual risk factors, normal tissues anatomy, functional brain regions and dose constraints has to be gained in order to take maximal benefit from technical solutions. Prospective trials that monitor the late effects from "modern" photons treatment (as well as protons treatments) would be needed to confirm the expected reduction in long-term side effects. In addition, the collection of large data in multiinstitutional registries can help in improving evidences in terms of outcome of different technologies.

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## PHOTONIC RADIOTHERAPY. ADVANTAGES AND DISADVANTAGES IN PAEDIATRIC ONCOLOGY

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Radiation therapy is an important component of the multimodal approach to cancer treatment. Continual, significant improvement has occurred in both photon and proton radiation therapy, with more precise dose conformity reduce radiation of adjacent normal tissues and associated risks. Late toxicities are most important in children and include diminished cognition, growth delay, bone deformation, endocrine dysfunction, and second malignancies. This superior dosimetry can translate into clinical benefit with respect to the endpoints of toxicity, tumour control, quality of life, and patient survival. intensity-modulated RT(IMRT) has entered mainstream clinical practice and use, including among paediatric neuro-oncology patients. IMRT has been shown to improve target conformity as well as critical structure sparing when compared to standard 3D-CRT approaches.[1,2] These dosimetric advantages to IMRT are supported by clinical data, which demonstrate comparable rates of disease control with IMRT approaches but decreased RT-related toxicity, particularly: ototoxicity, endocrine dysfunction and cognitive damage. Expanding on IMRT, arc-based therapies have increasingly been utilized. An advantage of VAMAT (Volumetric-modulated arc therapy), in addition to the excellent compliance of the dose and the use of non-coplanar planes, is the speed of treatment delivery. This difference is particularly advantageous for paediatric patients, whose tolerance for treatments may be more limited than adult patients, and many of whom may require sedation while undergoing treatment. But this improvement can come at a cost of greater radiation exposure to non-targeted tissues when compared to less sophisticated techniques. An important assessment is the low-dose bath that these techniques may involve[5] and the daily use of IGRTs. With doses of approximately 3 cGy per CBCT has the potential to substantially increase risk of late effects.[6,7] Advanced radiotherapy techniques have enabled volumes to be reduced with high doses, improving the reproducibility of the treatment. It will be necessary to correct these technological advantages with prospective studies designed to reduce field size and the total dose. Currently many studies, on biological data, are studying a more accurately patient stratification and verifying which of these may receive a lower dose. Careful follow-up, quality controls will be necessary to assess whether advanced techniques can reduce late side effects and only then will it be possible to assess whether the RT with protons is higher.

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## THE APPROPRIATE CHOICE BETWEEN PHOTON AND PROTON THERAPY: COMPARATIVE EXPERIENCES

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Brain tumours are the most frequent solid tumours in children. Late effects of paediatric cerebral radiation therapy, cognitive dysfunction and endocrinopathy are the most frequent side effects of brain radiation therapy. Depending on tumour location; auditive and visual impairment are also frequent. These late effects manifest in a multitude of presentations including impairment of neurocognitive development, hormonal dysfunction secondary to hypothalamic-pituitary axis radiation with resultant growth or gonadal dysfunction, as

well increased risk of secondary malignancies. In an attempt to reduce unnecessary radiation dose to organs at risk for late effects, there has been a strong movement to utilize increasingly conformal modes of radiation therapy. Compared to photon therapy, PRT has a region of high dose deposition, with minimal dose delivery distal to the region of the Bragg Peak. This is in stark contrast to photons, which enter with high energies and deposit their dose not only throughout the tumor but also distal to the target As such, PRT allows significant reduction of the overall integral dose a child receives, potentially reducing risk of late side effects of such a dose "bath". With the advent of improved treatment modalities, our goal for treating pediatric malignancies should be not only to increase survival rates, but also quality of life for these survivors. PRT is an important modality that can help achieve such a profound goal. The utilization of PRT has been considered since as early as the 2000's for the most common childhood CNS malignancies. It has maintained continued interest because it not only shows comparable clinical outcomes to photon therapy but also the dosimetric advantage of reducing dose to unintentionally irradiated tissues.The literature analysis is in favour of the use of proton therapy for paediatric brain tumour in a curative intent, either for focal irradiation, whole ventricular irradiation, or craniospinal irradiation. In addition of the survival literature data is in favour of neurocognitive, sensorial and endocrine benefits with protons compared to photons for all paediatric patients treated for brain tumours in a curative intend.

The analyses showed that this achievement was mainly obtained through the reduction of late toxicity. Actually, reductions in intelligence quotient loss and growth hormone deficiency contributed to the greatest part of the cost savings and were the most important parameters for cost-effectiveness. Many ongoing prospective clinical trials will allow evaluating the efficacy and toxicity of protontherapy. With increasing medical imaging tumour evaluation, one can also suggest that protontherapy could be also used for dose-escalation on resistant tumours (radioresistant clusters identified by molecular imaging) without increased healthy tissue irradiation. The centers of protontherapy with children-dedicated equipment are needed to offer equal access to this therapy. These centres should include general anaesthesia capacity, trained team and could be cost-efficient.

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## RADIOMIC FOR PCR AND OUTCOMES PREDICTION IN RECTAL CANCER


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Rectal cancer treatment is a multistep approach requiring a multi-specialists' cooperation. In particular, Locally Advanced Rectal Cancer is usually treated with preoperative chemoradiation followed by surgery with or without postoperative chemotherapy according to risk factors related to initial staging and pathological tumor response. Oncological outcomes and response to preoperative treatment have a wide range of presentations and several factors need usually to be combined to predict tumor response and outcomes. Among these factors, information coming from imaging play a fundamental role as predictors, also allowing adaptation of therapies throughout the treatment path of the patient. In this frame, Magnetic Resonance Imaging (MRI) has proven to be effective for rectal cancer staging and prognostic evaluation with the use of qualitative and functional information (*e.g.* DWI). Radiomics is a new-born science that aims to extract large amount of quantitative features from medical images. These features have the potential to disclose disease characteristics impossible to be appreciated by the human eye, useful for predicting prognosis and therapeutic response of tumors. The process of radiomic consists in 4 phases: image acquisition, image segmentation, features extraction and quantification, analysis and modelling. Recent experiences of radiomics in rectal cancer tested the feasibility of setting up predictive models of several clinical outcomes (*e.g.* pathological complete response - pCR, Overall Survival - OS, Metastases Free Survival - MFS). Main goal of this talk is to present the meaning and the process of radiomics, giving an overview about the existing radiomics models for outcome prediction in patients affected by rectal cancer and discussing their role in supporting the choice of treatments that could be tailored to tumor phenotype, as coded by the radiomics analysis, and that can be used as an additional tool to identify patients eligible for an organ-preserving treatment. Different models will be presented, focusing both on long terms outcomes and pCR prediction, on staging MRI and radiomics values change during treatment (delta radiomics) with hybrid Magnetic Resonance guided Radiotherapy (MRgRT) machines.

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Radiomics for rectal cancer response prediction with hybrid 0.35 T Magnetic Resonance guided Radiotherapy (MRgRT) : a hypothesis generating study for an innovative personalized medicine approach" Radiol Med. 2019 Feb;124(2):145-153. doi: 10.1007/s11547-018-0951-y.

## THORACIC RADIOTHERAPY IN SCLC: STATE OF THE ART AND INTEGRATED TREATMENTS IN THE EXTENDED DISEASE

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Background: The standard of treatment for patients with stage IV SCLC consists of four to six cycles of palliative chemotherapy (platinum/etoposide). There is still no clear consensus concerning the role of consolidative thoracic radiotherapy (TRT) in this setting.

Methods: We performed a review of the current literature regarding TRT in the treatment of stage IV SCLC, with particular emphasis on the analysis of survival, response rate and disease control results and on the influence of multiple risk factors.

Results: Although phase III CREST trial primary endpoint of OS improvement at 1 year was not met, subgroups analysis revealed an OS benefit in selected patients such as those with residual disease after chemotherapy, limited extrathoracic disease burden and good response after chemotherapy. Other prospective and retrospective studies also showed benefit in local control and survival. Several factors might be considered to recommend TRT: fitness of the patient, extrathoracic tumour burden, initial bulky thoracic disease and response to chemotherapy.

Conclusions: Albeit to date there is no consensus for the indications of TRT in stage IV SCLC, it should be considered for fit patients who responded to chemotherapy and bear limited residual extrathoracic tumor burden.

## PROPHYLACTIC CRANIAL IRRADIATION IN SCLC IN 2019: "MILESTONE" OR OUTDATED THERAPEUTIC OPTION?

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The original rationale for prophylactic cranial irradiation (PCI), as advocated by Hansen[1] in 1973, is that CNS relapse in small cell lung cancer is analogous to isolated CNS relapse in acute lymphoblastic leukaemia. The brain, in fact, was assumed to be a pharmacologic sanctuary where subclinical metastases were protected from cytotoxic drugs by the blood–brain barrier, and it was suggested that cranial irradiation might prevent the development of clinically evident brain metastases. Since then PCI had become the standard of care for many patients treated for small cell lung cancer. The first meta-analysis supporting its use was published in 1999[3] particularly in patients with limited stage disease achieving a complete response. Currently, guidelines recommend low dose PCI, typically 25 Gray in 10 daily fractions in order to minimize late sequelae in long-term survivors. The subsets of high risk patients such as the elderly[3] and patients who have been exposed to cisplatin[4] could develop significant brain radiation injury despite the conservative radiation prescriptions. Whether or not reduction of exposure of structures such as the hippocampus, applying modern technologies in meaningful benefit to patients, is the subject of ongoing trials. To date the PCI seems to be favorable in terms of local control and overall survival in limited stage small cell lung cancer patients aged < 65 years and with low T stage. Conversely, the therapy no significantly ameliorates the overall survival in patients aged ≥65 years with cT3–4 disease and/or females gender.[5] The benefit of PCI in patients with extensive stage disease is controversial even after a complete response to chemotherapy.[6,7] There are evidences that the risk of intracranial relapse has likely been overestimated in the past and the efficacy of contemporary salvage treatments for intracranial relapse may be underestimated especially if provided before patients become symptomatic. The most recent guidelines recommend that only patients who have responded to systemic treatment should be considered for PCI that should be administered only after the completion of all of the planned induction chemotherapy. PCI should be offered to patients in whom asymptomatic small volume brain metastases have recently been excluded by volumetric MR imaging. The role of sparing hippocampus techniques to attempt to reduce neurological toxicities without a negative impact on local control is under investigation.

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## OPEN QUESTIONS IN THE TREATMENT OF SMALL CELL LUNG CANCER: NEW HORIZONS

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Over the past twenty years, many progresses have been made in the treatment of Small Cell Lung Cancer (SCLC). The addition of radiotherapy to systemic treatment and the use of Prophylactic Cranial Irradiation (PCI) are some examples of these improvements in the localized and extended disease. Despite these, SCLC continues to be one of the tumors with the worst prognosis on the global cancer scenario. Research by Radiation Oncologists and Medical Oncologists to improve clinical outcomes remains a challenge. This talk focuses on research that links improvements of clinical outcomes and new strategies in the treatment of SCLC. This presentation highlights some of randomized controlled trials and "real-life" studies in patients affected by SCLC. Firstly, I will outline the research that has be done answering to questions still open (high doses, extra-thorax irradiation, PCI with hippocampal sparing) and then I will focus on the studies which provide evidence. The talk will also present interesting perspective trials we have to wait for the definitive results. There will be time for the audience to give their views at the end.

## IS THERE A ROLE FOR A MOLECULAR BIOLOGY CLASSIFICATION OF RISK GROUPS TO DETERMINE ADJUVANT TREATMENTS IN ENDOMETRIAL CANCER?

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Endometrial cancer (EC) has generally a good prognosis because it is typically diagnosed at low stage and low grade is the most common subtype. Although this, EC in about 20% of patients, has an unexplained aggressive behavior that cannot be justified by its clinico-pathologic findings. In clinical practice, radiation treatment of EC is decided according to a classification into prognostic risk groups derived from the well-known and historic PORTEC study[1] which takes in consideration the tumor type and grade, the stage and the presence of lymphovascular space invasion. In 2013, TCGA[2] analyzed the molecular genetic basis of EC development and defined four molecular subclasses, based on mutation burden and copy number alterations. As a consequence, Talhouk *et al.*[3] have published and validated a new prognostic classification of EC based on the molecular categories identified in The Cancer Genome Atlas (TCGA): POLE (polymerase-epsilon mutation), associated with an excellent prognosis, MSI (microsatellite instable EC) and low copy number EC, in particular B-catenin mutated EC[4], associated with an intermediate prognosis, high copy number, especially P53 mutated EC, associated with un unfavorable prognosis. The authors developed the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE).[5] According to this new idea, the PORTEC study group elaborated a randomized clinical trial (the PORTEC-4a)[6] investigating a molecular profile-based adjuvant treatment in women with high-intermediate risk endometrial cancer (EC), comparing individualized adjuvant treatment based on a molecular-integrated risk profile to standard adjuvant treatment, as defined by the international guidelines. Our lecture will focus on the previous studies and will discuss the classification system elaborated in our Institution, based on both clinico-pathologic and molecular findings, not only for the HIR EC patients, but also for low-intermediate and high risk EC patients. This will lead to a better understanding of EC and hopefully it will improve individualization of treatment for each patient.

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## ADJUVANT RADIOTHERAPY AND CHEMOTHERAPY IN ENDOMETRIAL CANCER: WHEN, HOW AND WHY

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Endometrial cancer is the most common gynecological cancer in developed countries. Most patients are diagnosed at an early stage with a low risk of relapse. However, there is a group of patients with a high risk of relapse and poor prognosis. The optimal adjuvant treatment for endometrial cancer remains poorly defined despite the prevalence of the disease and a large number of completed prospective studies. This ambiguity can be attributed to inadequate power in many of these studies due to heterogeneity in patient selection criteria, low recurrence rates in early stage endometrial cancer, and competing risk of death from other causes in women with endometrial cancer. The most important prognostic factors identified in endometrial cancer are: FIGO stage, histological subtype, grade, depth of myometrial invasion, lymphovascular space invasion (LVSI), and age. In the near future, the molecular advances could be used for outcome prediction and may aid in optimal distinction of the risk groups. Many Institutions try to provide evidence-based guidelines for adjuvant therapy in the treatment of endometrial cancer. Despite the recent publication of randomized trials, the adjuvant treatment of endometrial cancer is still to be defined and there are many open questions about the best approach and the right timing.

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## MR-LINAC: INITIAL EXPERIENCE AT SACRO CUORE DON CALABRIA HOSPITAL

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Aim: A combination of high precision radiation techniques and daily set-up verification with the use of on-board cone-beam CT (CBCT) increased significantly the quality and accuracy in radiotherapy. Recently, we are entering in a new technological era where on-board Magnetic Resonance Imaging guided-radiotherapy with hybrid MR-Linac accelerator systems will allow a direct tumor and surrounding organ at risk (OAR) real-time visualization. Elekta Unity™ is a hybrid Linac with an on-board 1.5 Tesla (T) MR. This system received FDA approval in 2018 and it is now available for clinical use. The 1.5 T on-board MR provide high quality morphological and functional imaging, both useful in radiation oncology clinical practice. More specifically, morphological imaging are used for adaptive strategies due to its high resolution with no additional ionizing radiation administration. Moreover, functional sequences could be relevant for potential predictive evaluation in the radiomics era.

Method: In July 2019, the Advanced Radiation Oncology (ARO) Department at IRCCS Sacro Cuore Don Calabria Hospital completed the first 1.5 T MR-Linac installation in South Europe. A clinical protocol with the aim to define 1.5 T MR-Linac oncological eligible patients was produced by the collaboration between with Rete Oncologica Veneta (ROV) and Regione Veneto.

Results: Four different oncological scenario have been defined: 1) low-intermediate risk prostate cancer eligible to a radical treatment, with a maximum volume of 80 cc and an International Prostate Symptom Score (IPSS) <15; 2) inoperable or borderline pancreatic cancer; 3) oligometastatic patients with ≤4 disease presentation (including primary tumor) and a maximal diameter of 40 mm; 4) re-irradiation of soft tissue, brain, head and neck, abdominal or pelvic disease in patients with good performance status (0-1) and a previous radiation treatment for at least 6 months. A total number of 230 patients will be recruited. The primary outcome is to collect real data of patients treated with 1.5 T MR-Linac. Secondary outcomes are to define the feasibility of the treatment procedures, a workflow process and evaluate cost/benefit in order to establish a reimbursement by Regione Veneto and the National Health System.

Conclusions: Hybrid 1.5 T MR-Linac system is an innovative technological approach, which might change modern radiotherapy clinical practice. In October 2019, the first oncological patient will receive a radiation treatment with 1.5 T MR-Linac and we are expecting to complete the accrual in 12 months.

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## THE ONCOLOGICAL RADIOTHERAPIST REGARDS TO THE NEW EUROPEAN REGULATIONS

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The Directive is the new Business Support System. Important technological and scientific developments have determined a considerable increase of patient exposure. The Directive highlights the necessity of justifying exposure and information offered to the patients. The quality of programms developed and dealt with by the insurance companies is necessary, including the study of the risks of radiotherapy. A high level of competence is fundamental and a clear definiton of responsability of tasks taken out by all the professionals,doctors, fisicists and technicians for an adeguate protection of the patients who have to undergo a procedure of medical therapy. The dosage in oncological therapy represents one of the most important points, of around which rotates medical exposure for curative performance, neoplastic control, or/and palliatives. The State members ensure that the specialist in Medical Physics is responsible of the dosage, including the fisical measures for the rating of the doses administered to the patient and other people who are subject to medical exposure. The final responsability of treatment and care remains that of the Radiotherapist. The Directive 59/13 defines and promotes more the role of the medical physic inside the assistance structure of radiotherapy. On the 25 May 2019 terminated the period of tollerance for the execution of GDPR on privacy which entered into force in 2018. Il Guarantor has adopted a uniform interpretation for healthcare. Doctors can treat dates of their patients for treatment purposes without having to ask their consent, but must give complete information on what these dates will be used for. Necessity of consent for handling of data relative to an electronic health dossier or for consultation of referts on line. Disclosures have to be concise, transparent, comprehensible and easily attainable, written simply and clear and must contain information regarding, for example, those concerning the period of conservation of the dates. The Authorities clarify that it is obligatory for all health operators to keep a register where all the activities of handling of data are listed of each patient. This document represents an essential element for the management of treatments and for an effective detection of those at greater risk , and for demonstrating the respect of the principle of accountability. It underlines that every project based on artificial intelligence should respect human dignity and the basic princple of lawfulness, fairness, specification of purpose, proportionality of the treatment, protection of dates right from the design, responsability, transparency, safety of dates and management of risks.

## TRIPLE NEGATIVE BREAST CANCER: DOES CELLULAR HETEROGENEITY GUIDE OUR MEDICAL DECISIONS?

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Chemotherapy is the primary established systemic treatment for patients with triple-negative breast cancer (TNBC) in both the early and advanced-stages of the disease. The lack of targeted therapies and the poor prognosis of patients with TNBC have fostered a major effort to discover actionable molecular targets to treat patients with these tumours. Massively parallel sequencing and other 'omics' technologies have revealed an unexpected level of heterogeneity of TNBCs and have led to the identification of potentially actionable molecular features in some TNBCs, such as germline *DTEC314* mutations or 'BRCAness', the presence of the androgen receptor, and several rare genomic alterations. A subgroup of TNBCs shows a high degree of tumour-infiltrating lymphocytes that also correlates with a lower risk of disease relapse and a higher likelihood of benefit from chemotherapy. Proof-of-principle studies with immune-checkpoint inhibitors in advanced-stage TNBC have yielded promising results, indicating the potential benefit of immunotherapy for patients with TNBC. The efficacy of programmed cell death protein 1 (PD-1) blockade in metastatic triple-negative breast cancer (TNBC) is low, highlighting a need for strategies that render the tumor microenvironment more sensitive to PD-1 blockade. Preclinical research has suggested immunomodulatory properties for chemotherapy and irradiation. Starting from this context, both pre-clinical and clinical data involving the combination of systemic therapy and radiotherapy for the treatment of TNBC will be addressed.

## THERAPEUTIC APPROACHES IN BRCA MUTATION CARRIERS BREAST CANCER PATIENTS: WHEN GENETICS HELPS THE CLINIC

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Triple negative breast cancer (TN BC) patients are characterized by earlier recurrences, decreased survival and high rate of distant metastases,[1] mainly to the brain and lungs, while liver, bone and lymph nodes are less frequently involved. The TNBC is an heterogeneous group, including also tumors with basal phenotype and BRCA mutation. BRCA-related BC frequently pres-

ent DNA repair defects, TP53 mutations and defective G2/M checkpoint activation in response to DNA damage, genomic instability and disorganized apoptotic mechanisms.[2] As a result, although TNBCs are considered resistant to standard chemotherapy, those associated to BRCA dysfunction present higher sensitivity to oncologic therapies, which might lead to better response.[3] The BRCA1/2- dysfunction resulting in defective DNA repair pathways is known as "BRCAness. The DNA damage induced by radiation or chemotherapeutic agents is magnified by a mutation in BRCA genes, which are either 'gatekeeper' (controlling cell cycling, proliferation and apoptosis) and 'caretaker' (correcting errors and repairing DNA). This synergism is known as synthetic lethality. Radiation-induced DNA damage essentially consists of base damage, single-strand breaks, and double-strand breaks (DSB). Patients with oligometastases BC can benefit for ablative radiation treatment with the aim of achieving cure or prolonged survival, although the heterogeneity of the population and treatment schemes, the absence of randomized trials, has not yet pinpointed the best candidates.[4] Chemotherapeutic agents can act at different levels, based on destabilizing the DNA through intercalation (anthracyclines), affecting DNA repair cascade by targeting genomic instability (taxanes), the G2–M phase of the cell cycle (Eribulin), PARP inhibitors give rise to accumulation of DSB. First- line agents comprise combinations with platins (carboplatin/cisplatin) and taxanes or anthracyclines plus cyclophosphamide. The phase II study tnAcity showed that the combination of nab-paclitaxel and carboplatin significantly prolongs progression free survival (PFS) compared to nab-paclitaxel + gemcitabine and gemcitabine+carboplatin.[5] At progression, the use of PARPis, fluorouracil/capecitabine, eribulin, gemcitabine, cisplatin/carboplatin, vinorelbine are alternatives. The effects of anthracyclines are based on destabilizing the DNA through intercalation while taxanes affect DNA repair cascade by targeting genomic instability. Eribulin the G2–M phase of the cell cycle and disrupts the mitotic spindle architecture, eliciting accumulation of double-stranded DNA breaks (PARP inhibitors). Eribulin as first line or further-line setting significantly improved overall survival, especially in TNBCs.[6] Regarding the use of platinum salts, while in TNBCs patients not selected according to BRCA status, carboplatin was not more effective than docetaxel, in patients with BRCA mutation, the objective response rate (ORR) doubled with carboplatin compared to docetaxel.[7] Similar results were also obtained in the phase II study TBCR009, where the ORR was 54.5% in patients with BRC mutation compared to 25.6% in unselected population.[8] In this settings, the knowledge of BRCA status led to better outcome. Regarding PARP-inhibitors, the results of 2 phase III trials, Olympiad and EMBRACA,[9,10] enrolling HER2 negative metastatic BC with germline mutation of BRCA gene, pretreated with up to 2 lines of chemotherapy, showed a higher ORR and median PFS in patients receiving ParP inhibitors than control arm consisting of standard chemotherapy (capecitabine, eribulin, gemcitabine, vinorelbine). Understanding the alteration in tumor biology, especially the deficiency in DNA repair pathways, show a potential in future cancer therapy.

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## NOVEL APPROACHES IN HER2 POSITIVE BREAST CANCER DISEASE


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Overexpression of the human epidermal growth factor receptor type 2 (HER2) occurs in approximately 15 to 20% of invasive breast cancers and was historically associated with poor clinical outcomes. In recent years, numerous published studies have changed the type of treatment in Her 2 positive disease: 1) Neosphere[1] demonstrated that pertuzumab and trastuzumab plus docetaxel significantly increased the patho-

logical complete response (pCR) rate vs other arms; 2) APT study[2] evaluated the possibility of omitting anthracyclines for patients with stage I HER2-positive breast cancer (BC); 3) Katherine study[3] demonstrated an advantage of Trastuzumab emtansine in reducing the risk of recurrence in some HER2- positive breast cancers following neoadjuvant chemotherapy and with residual disease; 4) ExteNET[4] showed that 1 year of neratinib, an irreversible pan-HER tyrosine kinase inhibitor, significantly improves 2-year invasive disease-free survival after trastuzumab-based adjuvant therapy in women with HER2- positive BC. HER2-positive BC has high radioresistance that is correlated to the transactivation of the NF- κ B-mediated HER2 promoter inducing HER2 overexpression, β-catenin expression during epitelial mesenchimal transition (EMT) and the Fak-mediated pathway.[5] The role of elective nodal irradiation (ENI) in ypN0 patients following neoadjuvant chemotherapy and in pN1-3 Her 2 positive breast cancer patients is not clear. Few and retrospective data are available in literature.[6-7] No clinically accepted biomarkers are as yet available to predict the response to anti-HER2 therapy. Therefore, novel approaches to estimate clinical outcomes of HER2-targeted therapy are still needed. Plasma miRNA or Circulating Tumor DNA [8-9] gave promising evidence for further examination of response to anti-HER2 agents. A radiogenomic signature from the tumor and its environment, characterizing the response-associated HER2-E subtype, was identified in a recent study, applied to estimate response to anti-HER2 therapy and then correlated with pathologic immune response on corresponding biopsy images.[10] With additional validation, these features could eventually result in a non invasive method to help characterize tumor biological characteristics in HER2+ tumors and evaluate benefits of targeted therapy.

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## CONTOURING AND SET-UP IN THE TREATMENT OF LIVER METASTASIS

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The liver is a common site of metastases and in some cases it may be the only site of disease. Over the past decade, there has been an increasing use of radiotherapy (RT) for the treatment of liver metastases, and most often, in selected patients with oligometastases and limited liver involvement, ablative doses are deliv-

ered to focal liver metastases, instead of whole-liver RT, aiming to improve time to progression and overall survival.[1] Ablative RT, using stereotactic body RT (SBRT), involves immobilization and high precision treatment planning, typically resulting in highly conformal dose distributions encompassing the planning target volume (PTV) with steep dose gradients toward the surrounding normal tissue. Multimodal imaging, accurate outlining of the gross tumor volume (GTV) and the clinical targeting volume (CTV), advanced planning, IGRT, and motion management are then mandatory to improve the treatment accuracy. Extensive data has been published describing advantages and drawbacks of computed tomography (CT) or magnetic resonance imaging (MRI) for GTV delineation for liver metastases. Moreover, it remains questionable if microscopic tumor spread beyond the macroscopic tumor border or tumor capsule can reliably be evaluated with the current imaging methods. Few studies have analyzed microextension characteristics in liver metastasis. In histopathologic specimens, liver metastases from colorectal cancer frequently show microscopic tumor spread beyond the tumor margin (microsatellites) and a safety margin should be applied to consider them. T1w or T2w MRI are recommend to ensure that the target volume contains "macroscopic" tumor, and also potentially tumor cell-baring inflammatory reaction or microsatellites.[2] In addition, data from 129 patients with liver metastases from colorectal cancer showed that the extent of tumor invasion (62.8% patients, between 1.0 − 7.0 mm) correlated with high levels of CEA (p = 0.002), primary tumor site in colon (p=0.008), and multiple lesions (p=0.045). These predictors factors may potentially be used as a scoring system for determining GTV-to-CTV expansion.[3] Finally, it is agreed that in SBRT for liver metastases, a safety margin should be added to the tumor visible in CT and/or MRI to compensate for residual respiratory tumor motion and setup inaccuracies.

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## DOSE-CONSTRAINTS AND TOXICITY


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Aims: Conventional radiotherapy in the treatment of liver lesions has historically played a marginal role due to the low tolerance of the whole liver to high radiation, while Stereotactic body radiotherapy (SBRT) has become an emerging treatment option for liver lesions in patients unsuitable for surgery We aimed to analyze the role of SBRT in the treatment of HCC and colorectal liver metastases.

Methods: Local control (LC), overall survival (OS) and progression free survival (PFS) were analyzed in patients with un-resectable liver metastases enrolled in Phase I and II Trials on liver SBRT. Toxicity was focused on - although not limited to - the clinical and radiological appearance of the radiation-induced liver disease (RILD).

Results: Phase I/II clinical trials show local control rates between 60% and 100%, respectively, in patients with HCC and liver metastases. Interpretation of the reported survival rates is confounded by the significant heterogeneity in the included patients. Clinical features and dosimetric parameters should be tailored on candidates to SBRT in order to reduce the occurrence of adverse reactions. Most series have reported low rates of treatment toxicity, with rates of CTCAE grade 3 or 4 toxicity (range from 1 to 10%). About RILD most studies have reported rates of < 1% of RILD after SBRT in treatment of liver metastases.

Conclusions: Several studies have demonstrated that SBRT for liver lesions is associated with optimal control rates and low toxicity profile (uncommon G3 gastrointestinal toxicity), confirming that it may represent a safe and effective alternative local therapy for liver lesions.

## DELIVERY TECHNIQUES FOR THE RADIOTHERAPY TREATMENT OF LIVER METASTASIS


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For liver tumors, precise stereotactic body radiotherapy (SBRT) delivery with advanced motion management techniques can have an impact on treatment success as a large multi-center analysis has recently reported.[1] Developments in SBRT technology have allowed the application of high radiation doses with minimal safety margins.

The two main delivery methods with advanced motion management are 1) a free-breathing treatment with tumor tracking and 2) a linac-based gating in deep inspiration breath-hold (DIBH) with additional ultrasound monitoring. Less sophisticated techniques without advanced motion management are also reported in literature (e.g. internal-target-volume concept, mid-ventilation principle or gating approach in a planning study based on 4D dose calculations with or without motion-compression). 1) Tumor tracking continuously adjusts the beam aperture according to the last available time-averaged position of the target. One possible approach is a CyberKnife robotic SBRT (RS) with fiducial-based real-time target tracking.[2] Radiopaque fiducial markers can be implanted near the tumor and used as surrogates for its position. Another option is to estimate the internal target motion from an external surrogate signal. However, the correlation between external and internal motion can be unstable. A hybrid solution combines external and sparse x-ray–based internal monitoring systems and has recently been demonstrated for online clinical use with conventional linacs.[3]

Experiences with liver SBRT have been reported also with the Calypso system (Varian Medical Systems, Palo Alto, CA).[4-6] Another option is tumor trailing on a magnetic resonance linear accelerator (MRI-linac), which allows for direct monitoring of intrafractional motion without being invasive, needing surrogates, or exposing the patient to additional radiation. A recent report investigating whether the tumor trailing on a MR-Linac can improve target coverage in liver stereotactic body radiation therapy (SBRT) showed promising results.[7] 2) Gantry-based SBRT in DIBH with additional ultrasound-based surveillance has also been reported as an effective SBRT method for liver metastases.[8,9] A recent paper reported the results of a new method for assessing the in-vivo dose delivery accuracy of both gantry-based and robotic SBRT plans.[10] The overall treatment accuracy was below 5 mm, without statistically significant differences between the two techniques.

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## RADIOTHERAPY TREATMENT IN STAGE III NSCLC ACCORDING TO EBM


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Non-small cell lung cancer (NSCLC) represents approximately 80% of all lung cancers and 35-40% of NSCLC is in phase IIIA-IIIB at diagnosis. Stage III NSCLC includes very different clinical entities that require very different therapeutic approaches. About one-third of patients with locally advanced stage III tumors are not subjected to surgery and for these patients the results in terms of long-term outcome are poor.[1-4]

Until 1990, radiotherapy alone was the standard treatment for patients with inoperable NSCLC, but the 5-year survival rate was low (less than 10%).[5] Over the past two decades, numerous studies have shown that both chemotherapy and radiotherapy can prolong survival and are recommended as a treatment for locally advanced disease.[6]

Combination of radiotherapy plus platinum-based chemotherapy for locally advanced NSCLC shows survival benefits compared to radiotherapy alone and it is considered the current standard of care with median survival time for combination therapy ranging from 12 to 14 months compared to only radiotherapy that has a median survival time ranging from 9 to 12 months. The combination of radio- and chemotherapy has been recommended by the guidelines for the treatment of locally advanced diseases to reduce the risk of distant metastases and to maintain loco-regional control.[7] Chemotherapy drugs can also increase the radio sensitivity of tissues and increase the effectiveness of radiation treatment.

Combined chemotherapy and radiation therapy can be given simultaneously or sequentially. Although concomitant therapy is associated with increased toxicity, particularly at the esophageal level, several studies and meta-analyzes indicate that concurrent therapy is superior to sequential therapy in the treatment of this disease.[8] However, the use of chemo-radiotherapy requires the total absence of negative clinical prognostic factors, including poor performance and weight loss.[9]

However, only 15% of patients who received chemo-radiotherapy were alive at 5 years; therefore it is necessary to consider the significant increase in progression-free survival with Durvalumab, an anti–programmed death ligand 1 antibody, in patients with unresectable NSCLC who who did not have disease progression after two or more cycles of platinum-based chemoradiotherapy, according to the results of the PACIFIC trial.[10]

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## CARDIOTOXICITY AND OUTCOMES IN RECENT CHEMO-RADIOTHERAPY STUDIES FOR PATIENTS WITH LOCALLY ADVANCES NON SMALL CELL LUNG CANCER

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Aims: A literature review of radio-chemotherapy associated cardiac toxicity studies in patients with locally advanced non small cell lung cancer treated with curative intent.

Results: Recently, there has been significant interest on cardiac dosimetry in the outcomes of radical treatment for NSCLC patients, especially after results of RTOG 0671 protocol and the reported "excess of cardiac related deaths". Radiation-induced heart disease can manifest as a number of cardiac disorders such as myocardial ischemia, cardiomyopathies, conduction abnormalities, or pericarditis. Most of cardiac events occurred within 2-3 years after treatment. In the past 3-4 years many retrospective studies have been published on this topic. More than 100 dosimetric parameters are assessed as predictors of cardiotoxicity e.g mean heart dose, V5, V30, V50. No clear association between any cardiac dose parameter and survival was identified in many studies; actually the relation between heart dose and cardiac mortality is more consistent. Of course pre-existing cardiac disease is strongly correlated with cardiotoxicity and should be taken in consideration. Intersting data are known also on effect of immunosuppression and survival; heart dose is found to be related with immunosuppression (in particular with neutrophil to lymphocyte ratio). Moreover, heart dose is predictive for pulmonary toxicities, and the interplay between heart and lung must be better defined. There is a need to find dosimetric constraints not only for the whole heart but also for all the anatomic sub-structures (pericardium, atria, ventricles, coronary arteries). The challenge is to find which dosimetric parameter is correlated with which cardiotoxicity (ischemic, conduction etc). Also contouring of the heart is controversial and should be standardized. The radiotherapy tec. nique is differently correlated with cardiac dose, and immunosuppression also. Nowadays Intensity Modulated Radiation Therapy should always be considered the standard.

Conclusions: Cardiotoxicity is a challenging and important topic and prospective analysis of dosimetric and clinical data should be performed.

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## THE ROLE OF PET IMAGING IN THE MANAGEMENT OF OLIGO-METASTATIC RECURRENT PROSTATE CANCER

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Target treatments for locally recurrent or oligo-metastatic recurrent prostate cancer (PCa) are gaining importance.[1,2] Salvage therapies,[3] namely early salvage radiation therapy (SRT)[4] and metastases-directed therapies,[5] demonstrated to improve on patients' outcome

and delaying the administration of palliative androgen-deprivation therapy (ADT). However, these treatments are far to be considered curative since a non-negligible number of patients develop PSA failure after salvage treatments, either SRT[3] or salvage pelvic lymph-node dissection (S-PLND).[6] Salvage therapy is only curative if recurrent disease is completely encompassed by the treated volume.[7,8] The effectiveness of any target therapy should depend on accurate imaging to rule out areas of disease that would remain untreated. In this scenario, considering the lack of sensitivity of conventional radiological imaging for recurrent PCa, together with the presence of an accurate biomarker of early disease recurrence (PSA serum level), the presence of a diagnostic tool able to precisely localize PCa recurrence would be crucial. Thus, there is an unmet clinical need to improve target delineation in patients with potentially treatable PCa with early recurrence.

The introduction of novel molecular imaging technologies significantly influenced the therapy management of recurrent PCa, leading to "imaging-guided" approaches.[2] Positron emission tomography (PET) imaging targeting the prostate specific membrane antigen (PSMA)[9] (68Ga-PSMA-11) gained importance recently. At present, the use of 68Ga-PSMA-11 PET/CT has been introduced by the European Association of Urology (EAU) guidelines which currently suggest to perform this imaging modality in all men with PSA failure after radical therapy.[1] $^{68}$Ga-PSMA-11 PET/CT demonstrated its higher accuracy compared to other PET imaging procedures, namely choline and fluciclovine, also at low PSA levels.[9,10]

Nevertheless, the real impact of $^{68}$Ga-PSMA-11-PET/CT on patient outcome has not been tested, so far. Despite there are strong evidences regarding the impact of PET imaging on patient management, there is a lack of data concerning the efficacy of PSMA-guided therapy to control the disease in the recurrent setting. Whether or not PET-positive metastasis-directed therapy improves progression-free or overall survival remains unclear. Furthermore, inappropriate management due to false positive findings cannot be excluded and even if $^{68}$Ga-PSMA-11-PET/CT detects disease recurrence earlier and more accurately compared to other imaging modalities, the clinical implications remain uncertain.

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## NODAL OLIGORECURRENT PROSTATE CANCER AFTER PRIMARY LOCAL TREATMENT: WHEN IS SALVAGE LYMPH NODE DISSECTION INDICATED?

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Image-informed metastasis-directed therapy is a novel and appealing treatment paradigm for patients with oligometastatic prostate cancer (PCa) [1-3]. The aim of this lecture is to provide the latest evidence on the role of salvage lymph node dissection (sLND) in patients with nodal oligorecurrence of PCa after primary local treatment. A recent systematic review including 27 studies of men with oligorecurrent PCa diagnosed with modern PET/CT imaging and followed for a mean 29.4 months has shown that complete biochemical response after sLND was achieved in 13% to 79.5% of cases [4]. Five-year biochemical progression-free survival rates ranged from 6% to 31%, while 5-year overall survival rate was approximately 84%. Major complications were observed in approximately 10% of cases, and mainly consisted of lymphoceles requiring drainage. Main limitations were: i) retrospective design of single-centre series; ii) inter-study heterogeneity in

terms of study population, definition of progression, adjuvant treatment delivered and clinical endpoints; and iii) lack of matched controls and long-term outcomes. In a recent multi-centre retrospective study published after the previous meta-analysis and including 654 patients submitted to sLND for oligorecurrent PCa, a novel risk stratification tool to predict early (i.e. within 1 year) clinical recurrence after sLND was developed [5]. In this study, roughly 25% of men developed early clinical recurrence after surgery. Independent predictors of early clinical recurrence were grade group 5 (hazard ratio [HR] 2.04; p<0.0001), time from radical prostatectomy to PSA rising (HR 0.99; p=0.025), hormonal therapy administration at PSA rising after radical prostatectomy (HR 1.47; p=0.0005), retroperitoneal uptake at PET/CT scan (HR 1.24; p=0.038), three or more positive spots at PET/CT scan (HR 1.26; p=0.019), and PSA level at sLND (HR 1.05; p<0.0001). Based on these factors, patients who would benefit the most from sLND from other patients who should be spared from surgery can be quite accurately identified. In conclusion, a growing body of accumulated data suggests that sLND is a safe metastasis-directed therapy option in nodal oligorecurrence after primary local treatment. However, to date, high level of evidence is still missing to draw any clinically meaningful conclusions about the oncological impact of sLND on long-term endpoints. Thus, sLND should be still regarded as an experimental treatment alternative for oligorecurrent PCa.

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## IL PUNTO DI VISTA DEL RADIOTERAPISTA ONCOLOGO: PRO TERAPIA PELVICA


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About 80% of nodal recurrences of prostate cancer (PC) are diagnosed in the pelvis.[1] This pattern of relapse is correlated with a better 10-year cancer-specific survival compared with extrapelvic nodal recurrences.[2] PET/CT is generally employed for the detection of nodal oligometastatic disease. To date the available evidence on Metastasis Directed Therapy (MDT) comes from studies in which the diagnosis of oligometastatic disease was made mainly with Choline PET. A dedicated systematic review of Choline PET in nodal recurrence of PC reported a pooled detection rate of 36%.[3] In addition a PET/CT limitation in the "low volume" disease is represented by a limited accuracy in defining both its exact burden (missing of the micro metastatic disease) and its perfect distribution.[4,5] Although stereotactic body radiotherapy (SBRT) can boast a higher number of dedicated studies and more robust data to support its use in oligorecurrent disease, some experiences suggest the whole pelvis approach (WPRT) with a boost (sequential or SIB) to PET-positive nodes. In a well-known review, Ost et al. underline the good toxicity profile of radiation treatment in oligorecurrent disease (both SBRT and WPRT).[6] The authors also observe how, despite the heterogeneity of adjuvant treatments, some WPRT experiences show a better outcome (1-3year PFS) compared with exclusive SBRT series. More recently, Tran et al. report in a retrospective study a 5-year biochemical disease-free (bDFS) and a distant progression-free survival (DPFS) rates of 43% and 58%, respectively, in patients with pelvic oligorecurrent nodal PC who underwent WPRT with SIB.[7] These data are similar to those reported by Fodor *et al.*[8] and they suggest, when compared with similar data from SBRT series, a possible advantage of the WPRT approach. An open issue concerns the selection criteria for patients with pelvic oligorecurrent nodal PC for WPRT instead of SBRT. Créhange et al. suggest the use of WPRT in patients with multiple nodal recurrences, high PSA values, PSA Doubling Time <6 months or risk of lymph node involvement at diagnosis> 15%.[9] In order to better understand the role of WPRT in this patient setting, several studies are ongoing and their results are eagerly awaited. The OLIGOPELVIS GETUG P07 study is a phase II trial that explores the role of pelvic irradiation using IMRT and SIB on PET-positive nodal sites in oligorecurrent patients with up to 5 pelvic nodes. An arm of the German PLATIN trial is focused on the role of pelvic IMRT-SIB in a comparable setting of patients. Even more fascinating is a recently opened randomized phase II trial: PEACE V STORM. It provides the randomization of pelvic oligorecurrent patients between MDT with or without WPRT. By Implementing modern imaging techniques and liquid biopsies, the study aims to find the best treatment strategy in terms of

extrapelvic metastasis-free survival as primary endpoint for this subset of patients.


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## THE POINT OF VIEW OF THE RADIATION ONCOLOGIST: PRO METASTASIS-DIRECTED THERAPY


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Following primary PCa treatments a significant number of men will recur in the loco-regional nodes.[1] Radiotherapy has proved its role as a metastasis-directed therapy (MTD).Two strategies have been developed in this clinical setting.[2] They include stereotactic body radiation therapy (SBRT) and the elective nodal region RT (ENRT), which target the entire chain in which the affected lymph node is located or the entire pelvic chains with integrated boost of the affected lymph nodes.[2] A recent meta-analysis indicates the rate of local tumor control of 98% in men receiving SBRT alone for nodal oligorecurrent Pca.[3] The 3-year progression-free survival (PFS) in the SBRT series was in the range of 26-33%.[3] The frequency of loco-regional failure after SBRT is rather high (68%) with patterns of recurrence occurring in outfield loco-regional nodes.[4] However, a relatively small number of men (25-38%) still remain amenable to a new course of ablative SBRT.[5] An alternative approach is ENRT.[6,7] In two studies using ENRT in nodal oligorecurrent PCa,[6,7] the 3-year PFS was around 60% comparing favorably to the data of SBRT (3-year PFS of around 26-30%).[3] These data was further confirmed by a recent large multi-institutional, analysis conducted on 506 hormone-sensitive men (SBRT: 309, ENRT: 197) with nodal oligorecurrent Pca (<5 nodes).[8] ENRT was associated with fewer nodal recurrences compared with SBRT. Men with one recurrent node had longer metastasis-free survival after ENRT. Late toxicity was higher after ENRT compared with SBRT (16% *vs.* 5%, $p<0.01$).[8] The treatment volumes for ENRT are uncertain. Spratt suggested that extending the pelvic field superiorly to L4/L5 covered 93% of men with nodal oligorecurrence.[9] In line with this evidence, the use of salvage extended field radiotherapy (s-EFRT) was associated with an improved 3-year failure rates (88.3%) compared with salvage involved field radiotherapy (s-IFRT) (55.3%). No differences were in acute or late GI and GU toxicities was observed.[10] Similarly, the optimal dose is not defined but some recommendations may be derived from studies investigating radiation treatment of cN1 Pca at the initial diagnosis. In this clinical setting literature recommends a does ≥60 Gy EQD2 to the involved nodal GTV and at least of 45–54 Gy EQD2 to the elective nodal region. In the SBRT, a local tumor control of 99% is achievable for biological equivalent dose >100 Gy ($\alpha/\beta_{10Gy}$) with a very favorable side-effect profile.[3] In conclusion, RT has shown to play a role in improving clinical outcomes of men with nodal oligorecurrent Pca. A significant degree of uncertainties remains and high level evidence must be generated in order to provide more definitive recommendations for this group of patients especially in the era where new imaging modalities can detect nodal involvement at an earlier stage.


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## TECHNOLOGICAL BREAKTHROUGHS IN INTERVENTIONAL RADIOTHERAPY: BRACHYTHERAPY

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In the past 20 years we have seen a significant improvement in the field of interventional radiotherapy (brachytherapy) that touched in particular the "planning", the "delivery" and surgical techniques with a multidisciplinary approach.[1] These innovations, together with the widespread use of 3D imaging techniques, such as the use of CT but also Magnetic Resonance Imaging (MRI), PET/CT and ultrasound, have led to the emergence of Image Guided Interventional Radiotherapy (or Image Guided BrachyTherapy, IGBT)[2] resulting in important clinical benefits. A significant contribution to this evolution has come from the industry through the development of machines with miniaturized sources (Remote After Loading HDR and PDR devices) and high-tech applicators that are increasingly smaller, easier to handle and MRI/CT compatible.[1] The spread of single source devices has allowed the implementation of treatment plans with the possibility of optimizing the coverage of the target by limiting the dose to organs at risk (Intensity Modulated Interventional Radiotherapy or Intensity Modulated BrachyTherapy, IMBT).[3] This, while leading to an increase in treatment accuracy, has also led to the development of complex image-based implant stability control systems[1] and quality assurance protocols.[4] The use of IMBT alongside the IGBT has led to major clinical and economical benefits in terms of increased local control and decreased toxicity.[5,6] The need to perform complex IGBT modalities has stimulated research in the radiobiological field for the identification of increasingly hypofractional therapeutic protocols.[1,8] The main advances in the field of "planning" have been determined by the introduction of systems of "image fusion", personalization of dose distribution, biological planning, automatic reconstruction of catheters and improvement in calculation of dose distribution considering also inhomogeneity.[7,8] Particular attention must be paid to the reconstruction of the applicators, especially when using Magnetic Resonance Imaging. These improvements in brachytherapy led to a progressive spread of this technique in the recent years. In the time being, many authors report about a new era of brachytherapy. The preliminary results of the use of biological planning in brachytherapy are encouraging, although extensive validation is still required.[9] Multicenter pooling of pre-treatment and treatment imaging and their correlation with clinical outcome data could contribute to build predictive treatment response models by creating supportive tools to improve catheter placement and treatment planning.[10]

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## TECHNOLOGICAL INNOVATIONS IN INTRAOPERATIVE RADIOTHERAPY: IORT

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Intraoperative radiotherapy (IORT) is a special technique allowing the delivery of a single high radiation dose during the surgical procedure.

The direct visual control of the target volume allows high precision in the delivery of the dose, avoiding the irradiation of the surrounding healthy tissues. It can be combined with external beam radiation therapy (EBRT) or used as a single radiation treatment.[1] The first case was reported in 1905[1,2] in a patient with endometrial cancer, and other applications were described in the 60ies, by using single high doses of gamma-rays of Cobalt units and electrons of Betatrons. The use of IORT increased significantly in the 90ies, when dedicated mobile electron linear accelerators and a miniaturized low-energy X-rays machine were put on the market. Since then the number of patients has remarkably increased and a wider spectrum of tumor sites has been considered suitable for IORT. While gastro-intestinal tumors, and in particular colorectal cancers, were initially the most numerous cases, nowadays early breast cancer represents the main indication)[2].

IORT may be delivered with high-energy electron beams generated by conventional or "dedicated" linear accelerators (Mobetron, Novac, Liac), as well as with low energy photons (Intrabeam) or with an electronic brachytherapy system (Xoft Axxent).[3]

The technological progress involved:

Radiation delivery, including the upgrade of the IORT equipment, the development of suitable applicators and shielding devices

- Radiation dosimetry and quality assurance and more recently:
- Risk assessment methods of the whole procedure
- Treatment planning system (TPS) and in-room imaging (RADIANCE , IORT ECHO TPS)[3-5]

All these technological innovations are useful for the optimization of the procedure, but above all TPS turns out to be particularly important. Planning technology has not evolved in IORT over the years, resulting outdated in comparison to current state of the art in external radiation therapy. Only recently a planning software for IORT has been launched on the market to help in the treatment decision making process and to document radio-surgical technique, target definition, and dosimetric beam distribution.[6]

Technological improvement has made IORT more feasible in a large number of Centers and may facilitate the clinical advancement and thus contribute to promote multicenter prospective trials.

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# *Selected Oral Communications*

**B001**

## PROTON THERAPY RE-IRRADIATION OF RECURRENT HIGH-GRADE GLIOMAS: ANALYSIS OF RADIATION-INDUCED EDEMA

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Aims: During and after re-irradiation of relapsed high-grade gliomas (rHGG) variation of edema (ED) is a common event and may translate into neurological symptoms, clinical deterioration and steroid use modification. In magnetic resonance imaging (MRI), ED is usually evaluated with T2 or fluid-attenuated inversion recovery (FLAIR) sequences. Aim of the study was to report a quantitative analysis of radiation-induced ED during and after proton therapy (PT) re-irradiation of rHGG.

Methods: Between January 2015 and April 2019 thirty-one patients (pts) with rHGG were re-irradiated with PT at our institution. 22 pts underwent MRI early before, during, at the end as well as 1 month after the treatment and were included in the analysis. All pts received 36 GyRBE in 18 fractions. ED was evaluated and contoured on 88 MRI scans using T2 and FLAIR sequences (5 mm thickness). ED volume (in cc) was quantified as any T2 and FLAIR changes excluding the Gross Tumor Volume. We analyzed the temporal change of ED.

Results: Eighteen pts were treated for recurrent glioblastoma and 4 for anaplastic gliomas. Median (Med) CTV was 78,48 cc (range, 12-259 cc). Med ED volume at the baseline, mid-therapy, at the end, and 1 month after treatment was 63 cc (range, 7-265), 83 (range, 9-242), 85 (range 10-194), 69 (range 9-200), respectively. During treatment ED increased in 16 pts (72%) and decreased in 6 (27%). Such increase of ED volume was associated with mild symptoms only in 8 pts (50%) and was controlled with modification of steroids dose. One month after treatment ED decreased in 10 pts (45%), increased in 7 (32%) and was stable in 5 (23%). Six out of 7 pts (86%) with increased ED needed modification of steroids dose. During follow up 2 pts (9%) developed radionecrosis (RN - diagnosed at imaging) with mild symptoms controlled with steroids. In pts who presented RN, ED volume increased of 130% during treatment. In pts who registered increased ED without RN, the mean ED volume increase during the treatment was of 82%. Pts who presented RN had a mean CTV volume of 67.39 cc.

Conclusion: PT re-irradiation of rHGG is frequently associated with increase of ED volume during treatment. Such variation often does not need modification of steroid use. ED volume seems to decrease after the end of the treatment. ED volume during treatment significantly increase in pts who experience RN after re-irradiation and could predict the development of RN. CTV volume does not seems to predict the development of RN.

B002

## DIFFERENTIATED THYROID CARCINOMA OF THE PEDIATRIC AGE: GENETIC AND CLINICAL SCENARIO

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Introduction: Follicular-derived differentiated thyroid carcinoma is the most common endocrine and epithelial malignancy in children. The different clinical and pathological features between pediatric and adult thyroid carcinomas could be related to a different genetic profile. However, few studies are currently available and most of them involved a limited number of patients and mostly focused on radiation-exposed population. A greater knowledge of the genetics might improve the diagnostic frame and lead to an individualized therapy.

Materials and methods: We considered 59 pediatric patients who underwent surgery for diagnosis of differentiated thyroid carcinoma between 2000 and 2017. After surgery, Radioactive Iodine ablation/therapy was administered to 48/51 (94%) patients. The presence of mutations in BRAF, NRAS, PTEN, PIK3CA genes, and in TERT promoter, were analyzed through sequencing. RET/PTC rearrangement has been investigated with Fluorescent in situ hybridization and real□time polymerase chain reaction. Clinical-molecular features of pediatric patients were compared with those of 178 adult patients.

Results: In pediatric age, male gender and subjects < 15 years have a more extensive disease and more frequent lymph-nodes and distant metastases. The presence of distant metastases resulted significantly associated with younger age (p=0.01), higher tumor size (p<0.01), as well as with cervical lymph node metastases (p = 0.02). At the multivariate analysis, only the T4 status was identified as independent predictor of distant metastases (OR 43.75, CI: 4.04 to 474.27). Compared to adults, in pediatric patients there is a higher frequency of lymph-nodes and distant metastasis (p<0,01); moreover, pediatric patients are more prone to have a second treatment (p<0,01). The frequency of BRAFV600E mutation is lower in pediatric DTCs (p<0,01). NRASQ61R, NRASQ61K and TERTC250T are rare in children and adolescents; no mutations were found in PTEN and in PIK3CA.

Conclusions: Pediatric differentiated-thyroid cancer has a greater aggressiveness at diagnosis and a greater risk of recurrence than adult's one. Differently from adult, point mutations have not a genetic key role.

B003

## SINGLE FRACTION URETHRA-SPARING PROSTATE CANCER SBRT: PHASE I RESULTS OF THE ONE SHOT TRIAL

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Aims: To present the phase I results of single fraction urethra-sparing stereotactic body radiotherapy (SBRT) for localized prostate cancer (PCa) from single arm, multicenter phase I/II ONE SHOT trial.

Methods: Inclusion criteria were: cT1c-2cN0M0; Gleason ≤3+4; PSA ≤15 ng/ml; prostate volume ≤70 cc; no significant tumor in the transitional zone. Prescribed dose was 19 Gy in single fraction to the prostate ± seminal vesicles (PTV= CTV + 5 mm isotropic expansion, except 3 mm posteriorly). The prostatic urethra, with a surrounding margin of 2 mm, received a dose of 17 Gy. All patients were treated using a VMAT technique and intrafractional motion control using intraprostatic electromagnetic transponders. Genitourinary (GU) and gastrointestinal (GI) toxicity, IPSS, IIEF-25 and QoL scores were assessed at baseline, at 5 days (5D), 6th (6W) and 12th weeks (12W) since SBRT. Primary endpoint of the phase I was safety as assessed by occurrence of Grade ≥3 acute side effects during the first 3 months in a ""3 + 3"" cohort-based.

Results: From 08/2017 to 12/2018, 6 patients with low- and intermediate-risk PCa were recruited. Median age and PSA at SBRT were 75 years old and 8.1 ng/ml. All pts underwent SBRT without interruption and doses constraints were respected for all plans. The toxicity stopping rule was never triggered, with no Grade ≥3 acute side effects observed during the first 3 months. Pts experienced mostly grade 1 or 2 GU toxicities (frequency/urgency) resolving from W6 (50% of grade 2 GU) with no grade 2 GI side effects and no rectal toxicity at W12 (33% of grade 1 GI). IPSS increased from baseline to D5 and W6 (mean, from 3.5 to 13.2 and 16.2, respectively) decreasing progressively at W12 (mean, 7.2). The EPIC urinary domain mean score was 92 pretreatment, 73 at D5, 79 at W6 and 87 at W12, while the EPIC bowel domain mean score remained overall stable over weeks (95, 91, 85, 90 at the four endpoints). No impact of SBRT was observed on IIEF-25

scores and the EPIC sexual domain between baseline and W12 (mean, from 10 to 9 and from 46 to 44, respectively). The PSA values showed a bounce at D5 (mean, from 7.9 to 18.3 ng/ml) decreasing successively up to a value of 3.3 ng/ml at W12.

Conclusions: Single fractions of 19 Gy SBRT on whole prostate with urethra sparing to 17 Gy was feasible and well tolerated. This trial represents the first multicenter phase I/II trial assessing the efficacy and safety of a single-dose SBRT monotherapy as a radical treatment for localized disease.

## B004

## NEURAL NETWORKS BASED RADIOMICS AND HPV IDENTIFICATION IN OROPHARYNGEAL CANCER PATIENTS

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Aims: HPV status is a well known prognostic factor for classifying oropharyngeal cancer (OC) patients. The definition of HPV status still uses P16 positiveness in order to detect the cancer tissue involvement by virus. The accuracy of P16 has been proven to be lower respect to genetic markers like HPV DNA and RNA analyzed from biopsy. Radiomics is being used as a tool to classify patients images and to identify classes according different type of outcomes. In this field neural networks represent an application of artificial intelligence being largely adopted in many computer science and radiological tasks. Aim of this work is to build a classifier to detect HPV+ patients without using biopsy and invasive or expensive techniques. This classifier has been built by training a convolutional nerural network (CNN).

Methods: OC patients, with available T2fs MR axial images and HPV RNA and P16 status defined on bioptic samples have been recruited. Nodal and primary GTVs have been delineated on MR images and ROIs containing the voxel data representation have been analyzed by an in-house developed software. A CNN has been trained splitting the outcome of patients between RNA+ and RNA-. The training process has been achieved by dividing the patients dataset in a training and a testing set with 75% and 25% of total number in each subset. During training phase the model performance has been tuned by calculating the accuracy on the testing set. Having at disposal a small number of patients, the process has been repeated 20 times, in order to prevent overfitting and detecting a range of performance on a set of trained models. For each cycle the 4 best performing model have been evaluated. Finally the accuracy and k-statistics of each model have been calculated and compared to HPV RNA test values.

Results: 510 images in 24 patients have been analyzed. Training sets had 16 patients and testing sets had 8 in each repetition of the modeling processes. The summary of all training processes is summarized in Table 1. The mean accuracy of CNN is .788, and average k-statistics is .564 being very close to the performance of P16 when compared with HPV RNA gold standard.

Conclusions: Despite the use of a small number of patients the CNN has revealed an interesting level of accuracy in detecting the HPV RNA patients when compared with performance of P16. Analysis on larger population could lead to apply this neural network in place of invasive biopsy with accuracy similar to P16 itself.

**Table 1. Overall 80 best models performances.**

| | Accuracy | Kappa statistic | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|
| Mean | 0.788 | 0.564 | 0.839 | 0.733 | 0.780 | 0.801 |
| Min | 0.542 | 0.000 | 0.538 | 0.375 | 0.538 | 0.333 |
| Max | 0.958 | 0.913 | 1.000 | 1.000 | 1.000 | 1.000 |

## B005

## INCORPORATING VOLUME DOSE METRICS IN MACHINE LEARNING-BASED NORMAL TISSUE COMPLICATION PROBABILITY (NTCP) MODEL OF RADIATION-INDUCED LATE DYSPHAGIA (RILD) RESULTING FROM HEAD AND NECK CANCER CHEMO-IMRT

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Aims: To develop a predictive NTCP model for severe RILD upon a prospective monocentric study by introducing SWOARs in the DVH analysis and using machine learning approach.

Methods: Naso and oropharynx cancers (Stage II-IVA) candidates for radiochemotherapy requiring bilateral neck irradiation were enrolled. A dysphagia assessment including Videofluoroscopy was performed to assess the Penetration Aspiration score (P/A-VF) at baseline and at 6 and 12 months (m) after treatment. All RT plans were optimized to reduce dose to the SWOARs. Models of severe RILD were developed using dose to 9 SWOARs (superior, medium and inferior constrictor muscle, SPCM; MPCM; IPCM; base of tongue, BOT; supra and glottic larynx, SL and GL;

parotid glands, PGs; cricopharyngeal muscle, CPM; cervical esophagus, EC) and P/A-VF data at 6 and 12 m after treatment. A total of 72 features for each patient were extracted (8 features for each SWOAR: Dmin,Dmax,Dpeak,Dmean,V35,V45,V55,V65) and analyzed with linear Support Vector Machine (SVM) and Bagged Tree Classification (BTC). Performances were evaluated computing the Area (AUC) under the Receiver Operating Characteristic (ROC) curve, estimated in leave-one-out cross validation. Features were ranked for importance using out-of-bag predictor importance estimates by permutation.

Results: The relevance of SWOARs DVH features in predicting severe RILD emerged both at 6 and 12 m: AUC 0,82 with SVM and AUC 0,83 with BTC (6m); AUC 0,86 with SVM and 0,93 with BTC (12m). The SWOARs and the correspondent features with the highest importance to avoid severe RILD at 6 m resulted BOT (V65 and Dmean), SPCM (Dmean), MPCM (V45,V55;V65;Dpeak;Dmean;Dmax and Dmin), and PGs (Dmean and Dpeak) whereas those with the highest importance at 12 m were MPCM (V55; Dmax and Dmean), IPCM (V55, V65 Dmin and Dmax) together with GL (V55 and Dmin), CPM (Dmin) and EC (Dmin) (Figure 1).

Conclusions: We have trained and cross validated a NTCP model of severe RILD with a high discriminative ability both at 6 and 12 m after RTCT. We expect to improve the generalization capability of this model enlarging the number of training data with the ongoing prospective Italian Multicentric Study (NCT 03448341) in order to be suitable for clinical and planning decision-support.

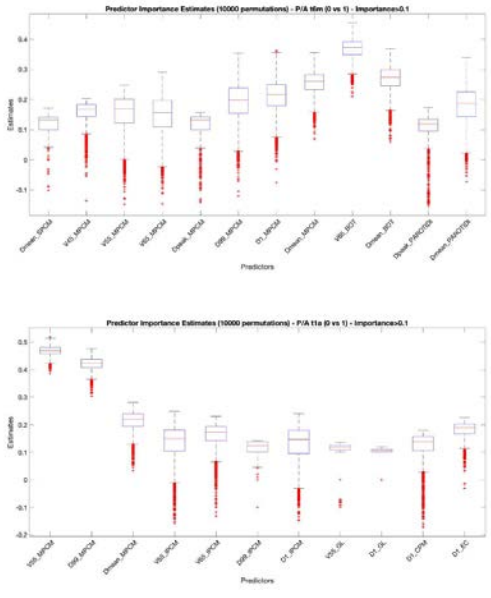


**Figure 1. Bootstrapped feature importance values for the variables included in the NTCP model. The whiskers indicate the 95 percentile confidence intervals.**

**B006**

## COULD FRACTIONATED IRRADIATION BE A POSSIBLE PARTNER FOR IMMUNOTHERAPY STRATEGIES IN CANCER TREATMENT? AN IN-VITRO STUDY OF IMMUNOGENIC CELL DEATH INDUCTION

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Aims: Immunogenic cell death (ICD) is one of the crucial steps of radiation-induced anticancer immune response. Most publications argue in favor of hypofractionated radiotherapy (RT), but several clinical settings rely on normofractionated regimens and systematic analyses on fractionation sensitivity and radiobiological parameters are scarce in this field. We aimed to assess ICD induction systematically after different radiation schedules using a biomathematical model.

Methods: A standard glioblastoma (GBM) cell line, U87MG, and two patient-derived, stem cell enriched GBM cell lines, LKVII and LKXVII, were analyzed for in-vitro detection of damage-associated molecular patterns (DAMPs) driving ICD: calreticulin (CRT) cell surface membrane exposure, high mobility group box1 (HMGB1) extracellular release. CRT was assessed 24h after single dose (2-24Gy) and daily fractionated RT (5x2Gy, 5x3Gy, 5x4Gy). Percentage of CRT positive cells after single dose RT was fitted with a non-linear least square fit to a Hill function. We used the obtained equation to calculate equivalent single fraction RT doses for membranous CRT after fractionation. HMGB1 confirmed ICD induction, normalized to number of viable cells 48h after single dose RT for U87MG and LKVII.

Results: There was a vast difference in basal CRT positivity in unirradiated controls (6.9±0.24% for U87MG, 9.5±0.09% for LKVII, 15.3±0.18% for LKXVII, respectively). All cell lines showed significant ICD induction after ≥8Gy single dose irradiation and 5x3Gy and 4Gy. The data were well fitted by a Hill function (R2>0.98). For both patient-derived cell lines, 10Gy normofractionation significantly increased CRT membrane exposure. Corresponding single doses for fractionated RT were higher for LKVII and LKXVII compared to U87MG. Significant HMGB1 release was observed for 8Gy irradiation in LKVII and 16Gy in both LKVII and U87MG (8.9±0.9 pg/106 cells vs 21.1±1.5 pg/106 cells, 4.0±0.7 pg/106 cells vs 47.4±9.35 pg/106 cells, respectively).

Conclusion: Single doses of 8Gy or higher elicit ICD as well as fractionated RT in GBM cells, a highly radioresistant tumor entity. Daily fractionation seems to cause cellular damage accumulation hence driving

DAMPs release. A clinically low lethal dose 5x2Gy induces ICD in patient-derived, stem cell enriched cultures. Thus at least as the initial step of effective anti-tumor immune response our findings may be the starting point to combine normofractionated RT and immunotherapy strategies.

**B007**

## QUALITY CONTROL IN PEDIATRIC RADIOTHERAPY: THE SIOPE-EORTC "QUARTET" PROJECT

G. Scarzello and L. Gandola, on behalf of SIOPe-EORTC QUARTET Group

*I.O.V.-I.R.C.C.S, I.N.T.*

High-quality RT, mostly in children, plays an essential role in achieving better outcomes reducing both local recurrence and long-term toxicity. In May 2016 a group of European experts in pediatric RT kicked-off the project QUARTET (Quality and Excellence in Radiotherapy and Imaging for Children and Adolescents with Cancer across Europe in Clinical Trials) in Brussels. QUARTET is assessing the quality and effectiveness of RT through an entirely online platform: SIOPe and EORTC are joining forces in this initiative, the first for pediatric cancer in Europe, with the aim of improving RT through a centralized prospective review of treatment plans for every patient entered in one of SIOPE's trials. QUARTET started analyzing patients treated for neuroblastoma, soon it will cover children and adolescents with rhabdomyosarcoma, renal and brain tumors (national initiatives are already ongoing in Italy, Germany, France, UK, Scandinavia) and successively it will include Hodgkin lymphoma, reaching an estimated number of 500 patients per year. Supported by Fondatioun Kriibskrank Kanner, this project is inscribed in the wider scope of the SIOPe Strategic Plan "A European Cancer Plan for Children and Adolescents", endorsed by the pediatric cancer community. The double ambition of QUARTET is to increase the cure rate of pediatric cancers and to ensure minimal side effects, which could potentially affect survivors' quality of life. QUARTET will ensure a centralized review by dedicated experts of prospective fields and radiation treatment plans for every child and adolescent before RT, in order to make necessary amendments if needed. More specifically, the project will:

- develop standards for RTQA for pediatric tumors;
- report the inter-observer variability when following the trial-specific delineation guidelines;
- apply existing TCP and NTCP models to estimate variation in outcome from contouring variation;
- determine whether the outcome of the RTQA benchmark case can predict the quality of RT;
- assess the quality of the RT, reporting the conformity and homogeneity index, and also the integral dose delivered, looking to determine whether geographical location or treatment center size have any impact on this;
- assess the cost-effectiveness of RTQA for the respective cancer types and determining the role for RTQA for future trials;
- research into novel treatment schemes or techniques, including proton and brachytherapy;
- validate the concept of prospective quality review in RT.

**B008**

## CORRELATION BETWEEN BODY MASS INDEX AND LATE TOXICITY IN ENDOMETRIAL CANCER PATIENTS SUBJECTED TO ADJUVANT RADIOTHERAPY WITH IMRT-IGRT TECHNIQUE

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Aims: Evaluation of Body Mass Index (BMI) and correlation with toxicity in patients undergoing radiation treatment for endometrial cancer using IMRT-IGRT technique.

Methods: 19 patients were analyzed after adjuvant treatment with a dose of 50.4 Gy on pelvis and 45 Gy on lomboaortic lymphonodes from 2015 to 2018 for IB-IIIC endometrial cancer. Patients were divided, according to their BMI, into 3 categories: normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9) and obese (BMI greater than or equal to 30). We evaluated late toxicity according to CTCAE 5.0 scale in patients with a median follow-up of 24 months.

Results: Only one normal-weighted patient had G1 GU toxicity and one G1 pelvic pain; among overweight group one patient developed G2 GU toxicity; in the obese group one patient had G1 GU toxicity and two patients G1 GI toxicity. G1 pelvic pain was observed in two patients among this group.

Conclusions: bmi greater than or equal to 30 is associated with risk of late toxicity G1 gastrointestinal and G1 genito-urinary but in no case no g2 toxicity has been found. Based on the toxicity recorded and considering the low number of patients followed they need further studies with larger population will clarify this report.

B009

## THE ROLE OF RADIOTHERAPY TREATMENTS IN OLIGOMETASTATIC BREAST CANCER SETTING: PRELIMINARY ANALYSIS OF ADVANTAGE ON PFS-2

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Background: In the last years, thanks to diagnostic advantages and new target therapies, oligometastatic disease is an even more common presentation of cancer patients (pts). At the same time, oligoprogression is a reality too, that is raising the issue of maintaining systemic therapies that can be considered still efficacy. Stereotactic body radiotherapy (SBRT) or Stereotactic Radiosurgery (SRS) are emerging as part of oligometastatic disease in many tumours as prostate cancers. In this preliminary study, we analysed the role of hypofractionated and SBRT/SRS radiotherapy in breast cancer setting.

Material and Methods: All the patients with oligoprogressive breast cancer (OPBC) during systemic therapy that underwent hypofractionated VMAT, SBRT or SRT were included into the study. Data on age, tumor characteristics at diagnosis, systemic therapy, radiotherapy performed were retrospectively collected. Progression free survival-2 (PFS-2) was defined as the time (months) from end of radiotherapy to new progression without changing systemic therapies. A Kaplan-Meyer analysis was performed for PFS-2.

Results: Eighteen pts were enrolled for this study. Median age was 58 (35-86). Sixteen % of pts was IIIC stage at diagnosis. Systemic therapies ongoing at the moment of oligoprogression were: 50% anti-Her2 drugs; 16,6% anti-CDK4/6 agents; 22% cytotoxic agents; 11,4% endocrine therapy. Radiotherapy was administered with VMAT or SBRT/SRS FFF technique on brain (72.2% of pts) with a schedule of 50 Gy/5Gy, 30 Gy/3Gy or 25 Gy/8,5Gy; lung (16,6% of pts) with a schedule of 50 Gy/10Gy; bone (11.2% of pts) with a schedule of 30 Gy/6Gy. Mean PFS-2 was 10.63 months (1-25), with a positive trend of the Luminal subtype respect Her2+ at chi-square test (CI=95%, p<.001).

Conclusion: Introducing focal hypofractionated /SBRT/SRS treatments in OPBC treatments, can improve PFS-2, prolonging sistemic therapies, especially in good prognosis subtypes. Further studies are needed on large series to confirm these preliminary results, also with new target therapies ongoing.

B010

## STEREOTACTIC BODY RADIATION THERAPY IN UNRESECTABLE OLIGOMETASTATIC PATIENTS WITH LIVER LESIONS

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Aims: Evaluate outcomes of Stereotactic Body Radiation Therapy (SBRT) in patients with liver metastases with oligometastatic disease.

Methods: Unresectable oligometastatic patients with documented liver lesions were evaluated at our institution for SBRT. Sites of primary tumor, size and prescribed dose for each lesion was recorded. The prescribed dose was modulated according to location of the lesion and tolerance of the surrounding organs at risk: lesions were treated with 3-8 fractions to a median total dose of 40.5 Gy (ranged from 30 to 62.5 Gy). Local control (LC), Progression Free Survival (PFS) and Overall Survival (OS) were evaluated using Kaplan Meier analysis.

Results: Between 2010 and 2019, 54 metastatic patients were treated at our institution with 58 total liver lesions. Patients had a median age of 76 years (35-90 years). Primary tumor was: colon-rectum cancer (46.3%), lung cancer (20.4%), breast cancer (9.3%) and others (24%). Median tumor volume was 20.5 mm (range 7-56 mm). At a median follow-up of 7.87 months (range 0.83-112.93 months), Local Control rates at 1 and 2 years was 75.2% and 59.3% respectively. Most common pattern of failure was in other sites of liver. PFS at 1 and 2 years was 53% and 29.9% respectively with a median of 12.7 months. OS at 1 and 2 years was 75.2% and 59.3% respectively with a median of 28 months.

Conclusions: SBRT is an effective therapeutic option for treatment of liver metastases in unresectable oligometastatic liver disease, with a high local control rate.

B011

## VMAT TECHNIQUE RADIOTHERAPY IN LOCALLY ADVANCED LUNG CANCER PATIENTS: RATE AND DEGREE OF LATE PULMONARY TOXICITIES IN PATIENTS TREATED WITH CONCOMITANT CHEMOTHERAPY

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Aims: To assess the rate and degree of observed late pulmonary toxicity among locally advanced lung cancer patients treated with VMAT technique and concurrent chemotherapy.

Methods: Locally advanced lung cancer patients underwent concomitant radio-chemotherapy using

VMAT technique. After concomitant chemo-radiation treatment, all patients underwent periodic clinical and radiological follow-up: if occurred, radiation pneumonitis was graded according to the National Cancer Institute Common Toxicity Criteria (vers.4.03).

Results: From January 2016 to December 2017, 38 patients [median age 64 years (range 44-83)] underwent concomitant radio-chemotherapy with VMAT technique: 27 male (71%), 11 female (29%); histologically 24 adenocarcinoma (63 %), 8 squamous cell (21%), 6 small-cell lung cancers (16%). Mean radiotherapy dose delivered was 53,94 Gy using VMAT technique. With a median follow-up of 19.28 months, late pulmonary toxicity (CTCAE scale G=2) was reported in 2 patients (5%), radiological pulmonary toxicity without symptoms (CTCAE scale G=1) occurred in 12 patients (32%), 24 patients (63%) completed the treatment without pulmonary toxicity.

Conclusions: In locally advanced lung cancer patients, concomitant radio-chemotherapy using VMAT technique is a well tolerated treatment with acceptable lung toxicity. In order to spare organs at risk and obtain a better target coverage, VMAT technique can be used with encouraging clinical results.

**B012**

## INTRAOPERATIVE RADIOTHERAPY (IORT) IN BREAST CANCER: ANALYSIS OF 9.897 CASES FROM ISIORT DATABASE

C. Pisani[1], F.A. Calvo[2], F. Sedlmayer[3], C. Schumacher [4], F. Cazzaniga[5], M. Alessandro[6], A. De Paoli[7], E. Russi[8], M. Kruszyna[9], R. Corvò[10], F. Wenz[11], R. Mazzarotto[12], F. Fusconi[13], A. Ciabattoni[14], R. Weytjens[15], G. Ivaldi[16], A. Baldissera[17], C. Leonardi[1], V. Morillo[18], M.F. Osti[19], N. Bese[20], G. Catalano[21], A. Stefanelli[22], C. Iotti[23], L. Tomio[24], V. Fusco[25], I. Azinovic[26], M. Aguilar[27], F. Richetti[28], N. Kirsanova[29], W. Polkowski[30], A. Di Grazia[31], A. Gava[32], L. Abdach[33], C. Vidali[34], J.B. Dubois[35], V. Valentini[36], L. Badinez[37], A. Altinok[38], U. Ricardi[39], A. Milella[40], O. Alan[41], P. Lara[42], U. Ganswindt[43], M. Topeshashvili[44], J. Yin[45], M. Krengli[1]

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Aims: A comprehensive collection and analysis of clinical and technical data from 45 centres part of the International Society of Intraoperative Radiation Therapy (ISIORT) was performed, in order to identify the range of IORT indications and techniques for the different tumour sites. The present study reports the results concerning the breast cancer.

Materials and Methods: As of 2007, ISIORT participants collected in a common database demographic, clinical and technical data related to IORT procedures. Both prospective and retrospective data entry was allowed. The current study analyses 9.897 breast tumours.

Results: According to all ISIORT registry collected data, 9.897 of all IORT procedures were performed on patients with breast cancer. The median age of breast patients was 62 years. There were 22 (0.2%) cases of male breast cancer treated with IORT. In 7.391 cases, IORT was performed with radical intent for primary, newly diagnosed disease, while in 90 cases (0.9%) it was an attempt to rescue localized recurrent breast cancer. IORT was performed as a boost before or after EBRT in 3.644 cases (36.8%) with doses of 4–12 Gy. In 3.398 cases (34.3%), IORT was used as single radiation treatment modality with doses of 7-21 Gy, mostly between 18-21Gy (76.2%). Patients enrolled in study protocols were 2.725; in detail, 1834 (67.3%) were treated with a single dose (18-21 Gy in 88.8% of cases) and 846 (31%) were treated with a boost dose. IORT was delivered after and before tumour removal in 71.9% and 19.6% of cases, respectively. In 8.714 cases (88%), IORT was performed using electrons of 4-12 MeV energy. The patients treated with a 50-kV x-ray source were 763 (7.7%).

Conclusions: At present, the ISIORT database represents the largest available clinical and technical IORT data collection. Breast cancer is the most frequent IORT treatment performed in the 45 centres taking part in the study. This analysis shows that in most cases IORT on breast patients was used as a single shoot of 18-21 Gy, the most employed treatment modality was electron beam and the procedure was most frequently performed after the tumour removal. Only a minority of patients was included in clinical trials. These analyses could enhance the multi-institutional performance and serve as a basis for clinical trials design, in order to better define the role of IORT in tailored multimodal therapeutic approaches.


# *AIRO GIOVANI*
# *Oral Communications*

**C001**

## PRELIMINARY EVALUATION OF LONG-TERM TOXICITY IN YOUNG PATIENTS WITH CHORDOMA TREATED WITH HADRONTHERAPY AT CNAO

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Aims: Chordomas are rare slow-growing tumors characterized by a locally aggressive growth pattern, representing 50-60% of bone tumors. The 50–60% of cases are localized in the sacrum-coccix followed by skull-base (25–30%), cervical (10%) and thoracolumbar tract (5 %). The site of origin is commonly located nearby organs performing important functions. The main treatment for chordoma is still represented by radical surgery. In most cases the resection with wide margins is complicated by severe dysfunctions. In young patients, in full social and working activity, the aggressive surgery is complicated by strong disabilities with remarkable impact on their quality of life (QoL) and socio-economics contribution. In the last decades particle therapy seems to be a safe alternative to radical surgery in sacral chordoma, and the best radiotherapy technique in post-operative treatment of skull-base and spine chordoma in terms of local control and lower late effects. Aim of the study is to evaluate toxicity and quality of life in young patients (pts) undergoing hadrontherapy for chordoma.

Methods: Between June 2012 and December 2018, 36 young pts with median age of 36 years (9-40) with histologically proven chordoma, were treated with charged particle therapy using active scanning beam delivery system at CNAO. We treated 22 skull-base chordomas, 9 spine chordomas (level from C1 to L5) and 5 sacral chordomas (level S1-S3 and below). 17 pts were treated with proton therapy (PT) median dose 74Gy RBE (range 36-74) while 19 pts with carbon ion therapy (CIRT) with median dose 70.4Gy RBE (range 64-73.6). We evaluated toxicity according to CTCAE v.4 and investigated QoL using EORTC QLQ-C30 questionnaires.

Results: Median follow-up time was 26 months. Late G3 toxicity was observed in 2 patients with skull-base chordoma (carotid stenosis and seizures). Temporal lobe necrosis G2 was observed in 4 patients, G1 in 2 patients. Six patients with spine/sacral chordoma developed neurosensitive peripheral neuropathy: 3 patients experienced G1 toxicity, 3 patients G2 toxicity. No one showed bladder or bowel dysfunctions. No patient had walking impairment.

Conclusions: These data seem to confirm encouraging results of hadrontherapy for chordoma especially in young patients, taking into account the lower late severe side effects compared to the disabilities expected from aggressive surgery. All patients were able to keep working and having a normal social life after treatment.

## C002

### LONG-TERM QUALITY OF LIFE AND TOXICITIES IN YOUNG PATIENTS (<=35 YEARS OLD) TREATED WITH STEREOTACTIC RADIOTHERAPY (SRT) FOR FUNCTIONAL AND BENIGN BRAIN DISEASES

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Aims: Advanced radiotherapy techniques, such as Stereotactic Radiotherapy (SRT), represent effective treatment modalities both for those benign brain tumours whose complete surgical resection is impossible or associated to high risk of sequelae and for functional brain diseases in which alternative therapeutic choices have failed. The aim of this study is to assess the long-term quality of life (QOL) and the late toxicities in young patients treated with SRT for functional and benign cerebral diseases.

Methods: From July 2007 to February 2019, 46 young patients (<=35 years old) with functional and benign cerebral diseases including arteriovenous malformation (22), meningioma (9), vestibular schwannoma (8), craniopharyngioma (3), pituitary adenoma (2), hemangioblastoma [1] and trigeminal neuralgia [1] were treated with SRT. They were 54% female and 46% male, and median age at diagnosis was 28 years (range 8-34 years). The median follow-up time from treatment was 73 months (range 4-140 months). Subjects have been surveyed using the Spitzer QOL-Index (SQLI) to investigate the quality of life, and the Radiation Therapy Oncology Group (RTOG) scale was used to assess late radiation therapy-related toxicities.

Results: At baseline, 38/46 patients (83%) were symptomatic: 24 headaches, 6 hearing disorders and dizziness, 5 motor disorders, 2 visual disorders with endocrinological symptoms, and 1 facial pain. Headache was resolved in 70%, improved in 10%, unchanged in 20%; hearing disorders and dizziness remained unchanged in 82% and reduced in 18%; both patients with pituitary adenoma assisted to a successful reduction of ACTH secretion; a reduction in facial pain was observed too. As suggested by these data and confirmed by the SQLI<=8, compared to pre-SRT more than half of the symptomatic subjects (21/38) reported an improvement in the global health status after treatment. Regarding SRT toxicities, no patients reported visual deficit worsening, new motor or cranial nerves deficits and new hemorrhages, with a RTOG<=1.

Conclusions: SRT provides a good local response while being reasonably safe as it facilitates the delivery of high-dose radiation to increasingly limited target volumes with a low risk of functional radiation-related damage to surrounding healthy tissues. For this reason, it is a feasible and effective therapeutic option also for young patients with functional and benign brain diseases and it ameliorates their QOL without severe toxicities.

## C003

### ITALIAN RESULTS OF AN INTERNATIONAL SURVEY ON ELECTRONIC PATIENT-REPORTED OUTCOMES (EPRO) BY THE EORTC YOUNG RADIATION ONCOLOGY GROUP.

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Aims: Patient reported outcomes (PROs), defined as direct expressions of patients' health status without the interpretation of a clinician, have been shown to be

clinically significant to assess adverse events (AEs) related to radiation therapy (RT). As part of the development of an application to evaluate electronic PROs (ePROs), the young Radiation Oncology Group (yROG) of the European Organisation for Research and Treatment of Cancer (EORTC) conducted an international survey to evaluate the use and perceived benefits of PROs, and to rank desirable features for the ePRO tool.

Methods: The survey was addressed to professionals (physicians, radiation therapists, nurses) regularly involved in treating patients with RT. The questionnaire included 40 items and rated ePRO tool features on a 5-point bipolar Likert scale, ranging from 1 (very unimportant) to 5 (very important).

Results: From July 2018 to December 2018, 354 valid replies from 26 countries worldwide were collected, 47 (13.3%) of which from Italy (IT), the second most participative country after Germany (24.3%). Most Italian participants were radiation oncologists (95.7%), mainly working in university hospitals (87.2%). The PROs utilization rate among Italian respondents was 59.6%, the highest value reported [international (int) rate 42.4%; p=0.03]. PROs were considered important for RT treatment [int average (avg) 4.1 points (pts); IT avg 4.3 pts; p=0.11], leading to a higher accuracy of AE assessment (int avg 3.6 pts; IT avg 3.9 pts; p=0.022). Only a small proportion of respondents used ePROs in their clinical practice (int avg 27.2%; IT avg 36.2%; p=0.013), although nearly all of them (IT 97.9%; int 96.9%) would regularly use ePRO if available. The highest ranked feature for an ePRO tool in Italy was ease-of-use by patients (int/IT avg 4.7 pts). Benefits of ePROs ranked more appropriate in the setting of curative patients (int avg 4.5 pts; IT avg 4.6 pts). The highest ranked cancers to benefit from ePRO were head and neck (total avg 4.5 pts; IT avg 4.6 pts) and gastrointestinal (int avg 4.2 pts; IT avg 4.4 pts).

Conclusions: Among Italian respondents, PROs utilization was higher than internationally, still identifying room for improvement regarding the usage of ePRO tools. This survey indicates a high demand for ePROs in the field of radiation oncology. An app to assess PROs for RT-related AEs was successfully created and its design will be adapted to better satisfy the users' expectations.

**C004**

## DEEP INSPIRATION BREATH HOLD RADIOTHERAPY: INNOVATIVE ORGAN PRESERVATION TECHNIQUE. OUR EXPERIENCE

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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: Thirteen patients with left breast carcinoma and candidate to radiotherapy were enrolled consecutively from 01/12/2018 to 15/02/2019. 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.

**Table 1.**

| | FB | | DIBH | | Δ |
|---|---|---|---|---|---|
| Heart | | | | | |
| Dmean (Gy) | 2,69 | (0,76-5,9) | 1,44 | (0,54-3,74) | p<0,001 |
| V5% | 0,109 | (0,00-0,46) | 0,04 | (0,00-0,18) | p<0,001 |
| V20% | 0,0254 | (0,00-0,09) | 0,003 | (0,00-0,03) | p<0,001 |
| V25% | 0,02 | (0,00-0,08) | 0,001 | (0,00-0,02) | p<0,001 |
| LAD | | | | | |
| Dmean (Gy) | 10,13 | (2,17-32,27) | 4,96 | (1,19-17,37) | p<0,001 |
| Dmax (Gy) | 29,96 | (6,69-49,69) | 15,69 | (2,29-51,87) | p<0,001 |
| V20% | 0,13 | (0,00-0,74) | 0,04 | (0,00-0,41) | p=0,005 |
| Ipsilateral Lung | | | | | |
| V5% | 0,2 | (0,09-0,29) | 0,206 | (0,12-0,28) | p=0,935 |
| V10% | 0,14 | (0,06-0,23) | 0,13 | (0,08-0,23) | p=0,841 |
| V20% | 0,96 | (0,03-0,18) | 0,08 | (0,02-0,17) | p=0,128 |

Results: All 13 patients were treated with DIBH with good compliance and no interruption. The mean

heart dose was 2.69 Gy in FB vs 1.44 Gy in DIBH with an average reduction of 46%. The mean LAD dose was 10.13 Gy in FB vs 4.96 Gy in DIBH with an average reduction of 52%. 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 (Tab 15). The exposure of the ipsilateral lung dose were analyzed. The analysis by subgroup showed that 4 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 time (from 20 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.

## C005

### TOXICITIES AND OUTCOMES IN YOUNG GYNAECOLOGICAL CANCER PATIENTS TREATED WITH IMRT

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Aim: To evaluate toxicity and outcomes in young patients (pts) with gynaecological cancers treated with Image-Guided Intensity Modulated Radiotherapy (IG-IMRT) in our institution.

Material and method: From 09/2007-02/2018 21 pts ≤ 40 year old with gynaecological cancers (16 uterine cervix, 2 ovarian, 1 vulvar and 2 endometrial) were treated with adjuvant (n= 13) or radical (n=8) IG-IMRT. Median age was 35.7 (21-40) years. Neoadjuvant chemotherapy (CHT) was prescribed in 7 pts (all pts received paclitaxel-carboplatin), concurrent CHT in 9 pts (7 pts weekly cisplatin, one patient daily capecitabine and one patient cisplatin- 5FU). Fifteen pts were treated with helical IMRT and 6 pts with volumetric arc IMRT. Pelvic +/- lumbar- aortic (LA) LN planning target volume (PTV) and tumour PTV median dose prescription was 50.4 (50-55) Gy in a median of 28 (25-28) fr. Exclusive mediastinic and / or LA chains were treated in 3 pts to 50.4 Gy. Seven pts received a simultaneous integrated boost (SIB) on PET positive LN with dose ranging from 60.4 to 63.2 Gy and one patient 60 Gy to parameters. Six pts were treated with brachytherapy boost (12 Gy/2fr-30 Gy/6 fr), and 3 with external beam boost (15 Gy/3 fr-24 Gy/12 fr).

Results: Median follow-up is 37.5 (1.8-138.5) months. Acute and late gastro-enteric (GE), rectal (GI), urinary (GU), hematologic and epithelial toxicities are included in Table 1. Two pts died after 2-4 months after RT due to systemic disease progression and late toxicity was not evaluated. Only one acute hematologic G3 toxicity was registered (which required one-week treatment interruption) and two G3 epithelial toxicities. Only one patient developed a grading≥3 late toxicity. She was treated with SIB to a PET positive LN near the right ureter and later developed a right hydro-nephrosis requiring surgery to re-implant the right ureter into the bladder. Histological examination demonstrated the complete response of the tumour. With 3 years of follow-up, local control was 86% and distant progression was registered in 28% of pts. Seventy-six % of pts were alive at the last follow-up, all with disease control.

Conclusions: IG-IMRT in the treatment of young pts with gynecological cancer is safe with a very low rate of acute and late ≥G3 toxicities, and with good outcomes even in advanced disease and pts not suitable for brachitherapy boost.

**Table 1.**

| Toxicity | G0 | G1 | G2 | G3 | G4 |
|---|---|---|---|---|---|
| Acute GE | 20% | 52% | 28% | 0 | 0 |
| Late GE | 79% | 21% | 0 | 0 | 0 |
| Acute GI | 34% | 39% | 27% | 0 | 0 |
| Late GI | 90% | 5% | 5% | 0 | 0 |
| Acute GU | 48% | 43% | 9% | 0 | 0 |
| Late GU | 90% | 0 | 5% | 0 | 5% |
| Acute Hematologic | 71% | 10% | 14% | 5% | 0 |
| Late Hematologic | 58% | 42% | 0 | 0 | 0 |
| Acute epithelial | 38% | 33% | 19% | 10% | 0 |
| Late vaginal stenosis | 58% | 16% | 26% | 0 | 0 |

## C006

### DYSGEUSIA AND NAUSEA DURING AND AFTER RADIOTHERAPY IN HEAD AND NECK CANCER PATIENTS

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Aims: Dysgeusia and nausea are common adverse events occurring when treating Head and Neck cancer (HNC) patients with radiotherapy (RT). As consequence, patients' Quality of Life and treatment-compliance can result severely affected. The aim of the present study was to prospectively evaluate dysgeusia, during treatment and follow-up, using the chemotherapy-induced taste alteration scale (CiTAS), a metrics based on 18-items exploring three dimensions (quantitative and qualitative changes in taste perception, and diet-related issues) identified through a four-factor analysis: decline

in basic taste, discomfort, phantogeusia–parageusia, and general taste alterations. Herein we report a further update, at 1 year, of Our analysis.

Methods: Between 2016 and 2018, 31 HNC patients were treated with Volumetric Modulated Arc Therapy (VMAT) within a definitive or adjuvant setting (RT or CMT, 6 or 7 week overall treatment time). As well, we scored, according to Common Toxicity Criteria Adverse Events, nausea and other treatment-related toxicities. We prophylactically employed a ginger-based supplement named Naumix/Naugin (Gamfarma, Milan, Italy), to potentially mitigate both nausea and taste impairment.

Results: Using the CiTAS scale, we highlighted a progressive increase in all dysgeusia dimensions, peaking at the VII week of treatment and a subsequent partial late recovery. In particular, we observed a recovery for discomfort, phantogeusia–parageusia, and general taste alterations at 6 and 12 months (see details in Figure 1). Grade 2 nausea, observed to be as low as 12.9% potentially due to the use of ginger, peaked at the III week of treatment. Of interest, for patients experiencing G1–G2 nausea a significant correlation was found with the score of the dysgeusia dimension of discomfort (II-VI week of treatment, $p<0.05$).

Conclusions: Our prospective clinical data point out the multidimensional pattern of dysgeusia and its trend during RT or CMT in HNC patients. The prophylactic use of ginger may have limited the number of patients experiencing clinically significant nausea and, supposedly, reduced taste impairment. Further analyses (2-years follow-up) are planned in the close future.

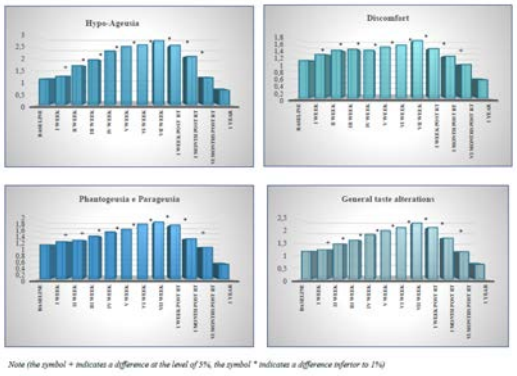


Figure 1. CiTAS Scale Trend.

## C007

## STAGE I TESTICULAR SEMINOMA: OUR EXPERIENCE OF RADIOTHERAPY FOR <40 YEAR-OLD-PATIENTS

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Introduction and aims: Radiotherapy (RT) and chemotherapy represent adjuvant options for testicular cancer which is the most common solid cancer in males between 20 and 40 years of age. After radical inguinal orchiectomy, surveillance is the preferred approach for pT1-pT3 tumors but there is a risk of locoregional lymph node micrometastases of 20% if no adjuvant therapy is administered, especially for tumor size of 4 cm or more and invasion of the rete testis. During the past years RT treatment fields were larger and radiation doses were higher than those currently used causing inacceptable side effects. Our study aims to evaluate efficacy and toxicity of limited-volume and low-dose lymph node RT for <40-year-old patients with stage I testicular pure seminoma.

Methods: Between 2005 and 2014, thirty young patients (<40 years) with stage I seminoma were treated at Radiotherapy Department in Taranto. Median age was 30 years (range between 18 and 37 years). All patients underwent orchiectomy and received histological diagnosis of pure seminoma, no patient received chemotherapy. RT was delivered using opposed anteroposterior and posteroanterior fields and RT fields extended from the superior border of T11 vertebral body to the inferior border of the L5 vertebral body +/- renal hylum. Until 2007 RT was delivered with a total dose of 25.2 Gy (1.8 Gy per fraction) and from 2008 with a total dose of 20 Gy (2 Gy per fraction). Acute and late gastrointestinal and genitourinary toxicities were evaluated. Relapse rate, Disease Free Survival (DFS) and Overall Survival (OS) were calculated.

Results: Median follow-up was 8.5 years. Forty-three percent (43.3%) of patients were treated with paraaortic RT while the remaining part was treated with paraaortic RT plus renal hilum RT. Acute toxicity was mainly digestive, 36.6% of patients presented acute mild/moderate nausea and one patient diarrhea. No acute genitourinary toxicity was observed. No late toxicities were observed. No local relapse and no distant metastases were observed. One patient experienced controlateral testicular cancer and he was successfully treated with surgery and chemotherapy. DFS and OS were 100% since all patients were alive in complete remission at last controls.

Conclusions: Our ten-year experience on young patients showed that limited-field and low-dose RT represents a valid option for stage I testicular seminoma with acceptable toxicity and excellent results in terms of disease control and survival rates.

C008

## PEDIATRIC BRAINSTEM CANCER: A RETROSPECTIVE STUDY ON OVERALL SURVIVAL

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Aims: Brainstem tumors are the second most common form of cancer in children under the age of 15 (after leukemia) and the second cause of cancer death. The brainstem cancer treatment is still an open challenge, due to possible and severe acute side effects, such as respiratory failure. Specifically, radiotherapy (RT), generally associated with chemotherapy, is fundamental for the standard of care, trying to improve quality of life and increase overall survival (OS). In our center from March 2009 to May 2019 were treated eleven pediatric patients, aged between 5 and 15, with diagnosis of anaplastic astrocytoma, glioblastoma and diffuse glioma, with brainstem localization. In this retrospective study we report data relating to OS and relapse-free survival (RFS).

Methods: The diagnosis of this class of tumors was achieve by imaging/biopsy. All patients had performed brain CT and MRI with and without contrast pre-treatment. All patients underwent concomitant chemiotherapy (nimotuzumab and vinorelbine or temozolomide) and RT with VMAT on VersaHD by Elekta, previously immobilized with custom systems.

Results: The performance status was by 0 to 2 and all patients were symptomatic at diagnosis. RT was continuously delivered at conventional fractionation of 1.8 Gy for fraction (fx), at dose of 54 Gy in 30 fx in 6 patients, at dose of 59.4 Gy in 33 fx in 4 patients. One patient at dose of 43.2 Gy (24 fx) stopped RT for pulmonary toxicity G4; he resumed at the resolution of the interstitial pneumonia, reaching the dose of 63 Gy. No other G1-G4 toxicity was reported. After the treatment all the patients had an improvement of the initial symptoms and all were eligible to perform sequential chemotherapy. The median OS, calculated from the time of diagnosis, was 11 months (range from 1-47 months). Eight patients had local relapse. The median RFS was 10 months (range 2-31 months). At progression disease (PD) only 5 patients performed re-irradiation, 3 patients at doses of 19.8 Gy in 11 fx, 1 patients at the dose 36 Gy in 20 fx and 1 at doses of 18 Gy in 10 fx. Of the 11 patients enrolled in the study, 6 patients are still alive without evident signs of toxicity, included in a regular program of follow-up.

Conclusions: Based on our experience, despite the risk of severe acute side effects, the radiotherapy prove to be a valid option to challenge brainstem tumors with a discrete tolerability profile.

C009

## EVALUATION OF RADIATION PULMONARY TOXICITY PROBABILITY IN LEFT-SIDED BREAST RADIOTHERAPY: A COMPARISON BETWEEN VMAT AND FIELD-IN-FIELD (FIF) TECHNIQUES

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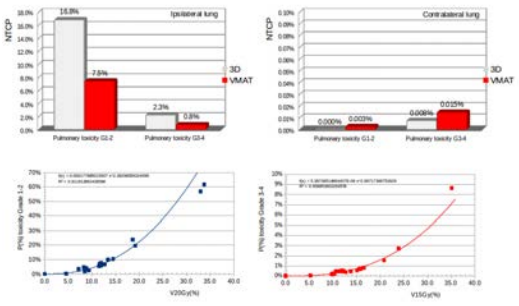
Aims and scopes: Purpose of this work is to compare the risk of radiation-induced pulmonary toxicity in the treatment of the left breast irradiated using VMAT or FIF technique.

Materials and Methods: 10 patients undergoing left breast radiotherapy were evaluated: the estimate of pulmonary toxicity, with the relative serial model, had a range from 0.0% to 61%. Two treatment plans were optimized for every patient, one with FIF technique (2Gy/fr x 25fr, boost 2Gy/fr x 5fr) and one with VMAT (1.8Gy/fr x 28 fr, SIB 2.1Gy/fr x 28 fr).The fractionation schemes were chosen to keep, as possible, the same BED values both on the target and the organs at risk. EQD2 was calculated from the dose absorbed by the lungs (both ipsilateral and contralateral) and then the Relative Seriality model for radiation pneumonitis was used as method to evaluate the probability of pulmonary toxicity for both lungs (Grade1-2: α/β=3Gy, s=0.15, D50=16.3Gy, g=1.08; Grade 3-4: α/β=3Gy, s=0.01, D50=30.1Gy, g=0.97).[1]




| pulmonary toxicity grade G1-2 | Probability |
|---|---|
| V20Gy < 11% | 5% |
| V20Gy < 14% | 10% |
| V20Gy < 18% | 20% |

| pulmonary toxicity grade G3-4 | Probability |
|---|---|
| V15Gy < 17% | 1% |
| V15Gy < 30% | 5% |
| V15Gy < 38% | 10% |

**Figure 1.**

Results: The probability of developing pulmonary toxicity increases in contralateral lung when using VMAT (Figure 1), although these probability values are very low. Instead in ipsilateral lung the pulmonary toxicity probabilities, either of Grade 1-2 or of Grade 3-4, are lower with VMAT respect to FIF technique. Some correlations between pulmonary toxicity and Dose Volume (DV) parameters have been found: they depend

of the toxicity Grade but are independent of the technique used (Figure). By choosing the acceptable probability value, it is possible to find DV constraints in terms of V20Gy for toxicity of Grade 1-2 and V15Gy for toxicity of Grade 3-4.

Conclusions: Among the side effects of the left breast irradiation the pulmonary toxicity, both of Grade 1-2 and Grade 3-4, has to be carefully evaluated. In our study, VMAT increases the probability of pulmonary toxicity for the contralateral but not for the ipsilateral lung. A cautious evaluation of the irradiation technique is therefore recommended.

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## C010

## HOME RESPIRATORY TRAINING IN PATIENTS UNDERGOING RADIATION THERAPY FOR LUNG CANCER

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Aims: The prevention and minimization of pulmonary toxicity is a very important goal for patient who perform radiation therapy for lung cancer. Respiratory rehabilitation in thoracic oncology is often indicated after surgery, while there is no evidence about its use in radiotherapy. The aim of the study is to evaluate the effectiveness, in terms of exercise capacity, dyspnea and fatigue, quality of life and respiratory function, of a home rehabilitation (H-RH) program in patients undergoing radiation therapy for lung cancer.

Methods: From March 2018 to May 2019 23 patients, 12 "cases" (CA) and 11 "controls" (CO), were considered for a H-RH program in a single Institution. The preliminary evaluation was conducted on 12 patients (8 CA and 4 CO). Severe cardio-circulatory diseases, orthopedic and neurological problems or inability to understand the instructions were considered as exclusion criteria. All patients were treated with high-dose radiotherapy (adjuvant or radical). Patients features are described in the Table 1. The 8 cases underwent an 8-week training program (5 days a week), while the controls did not. All patients were evaluated, before RT, by 6-minute walking test (6MWT), Borg scale, SF-36 health questionnaire and respiratory function test. These tests were repeated at the end of the treatment. Each patient had a self-compilation chart for monitoring dyspnea and fatigue during exercise.

Results: The 6MWT improved by 33.83m (+ 7% of predicted) in the CA and worsened by 22m (-7% of predicted) in the CO, with a difference higher than 55m. Regarding fatigue during exertion, the final average score reduced by 0.6 in CA and increased by 1 in CO. For dyspnea, a slight deterioration was observed in the CA (+ 0.3) and worsening of greater intensity in CO (+1). Quality of life worsened in both groups. On the other hand, the lung function tests did not show any significant changes.

Conclusions: The exercise capacity and the fatigue-dyspnea pairing improved in the cases, while the respiratory function and quality of life seem to remain unchanged during the 8 weeks of radiotherapy and H-RH treatment. To our knowledge this is the first report about the use of a H-RH program in patients treated with high dose lung RT. Even if the number of patients is limited it appears an innovative approach in order to improve respiratory function of these kind of pts.

This study is still ongoing on a selected group of patients treated with radical chemoradiation.

**Table 1.**

| | CASES | | CONTROLS | |
|---|---|---|---|---|
| | PRELIMINARY SERIES | TOTAL | PRELIMINARY SERIES | TOTAL |
| SBRT | 1 | 1 | 1 | 1 |
| Radical Chemoradiotherapy | 5 | 9 | 1 | 8 |
| Adjuvant Radiotherapy | | | 1 | 1 |
| Pleural Mesothelioma | 1 | 1 | | |
| Palliative radiotherapy | 1 | 1 | 1 | 1 |

## C011

## PRELIMINARY ANALYSIS OF ANXIETY EVALUATION IN RADIOTHERAPIC PATIENTS

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Aim: To evaluate anxiety of patients undergoing radiation therapy.

Methods: We included all the patients undergoing radiation therapy at our Department in four days, each a week for a month. All the patients that gave their consent were asked to fulfill a validated questionnaire (STAI-Y, State trait anxiety inventory scale) and the Anxiety thermometer (from 0 to 10 score). We took into account also sex, age, week of radiation treatment and disease. For the STAI-Y we considered as cut-off 40 to detect clinically significant anxiety, whereas the thermometer was analysed as a continuous variable. We calculated the differences in anxiety scales for the clinical variables (sex, age, disease, week of treatment) with Chi-square test (for STAI-Y) and with Anova test (for Anxiety thermometer).

Results: We included 198 patients (108 males and 90 females), with a median age of 65 years (mean 64,8 years, range 34-84 years). STAI-Y median score was 39 (mean 39,4, range 19-71), 100 patients (50,5%) showed a STAI-Y <40 and 98 patients showed a score ≥40 (49,5%), whereas the median score of Anxiety thermometer was 4 (mean 3,8, range 0-8). There were no differences among sex (p:0,483), whereas patients at the first week of treatment showed the highest anxiety (for both test, p<0,001). Taking into consideration the different disease, the patients showing highest anxiety were head and neck cancer patients (75% patients showing STAI-Y>40), followed by brain cancer patients (66%), lung cancer (50%), gastrointestinal cancer (41%), breast cancer (35%) and prostate cancer (15%), p<0,001.

Conclusions: Anxiety evaluation in patients undergoing radiation therapy is higher than expected. These measurements could be useful in order to start medical humanities programs with the aim of decreasing anxiety scores.

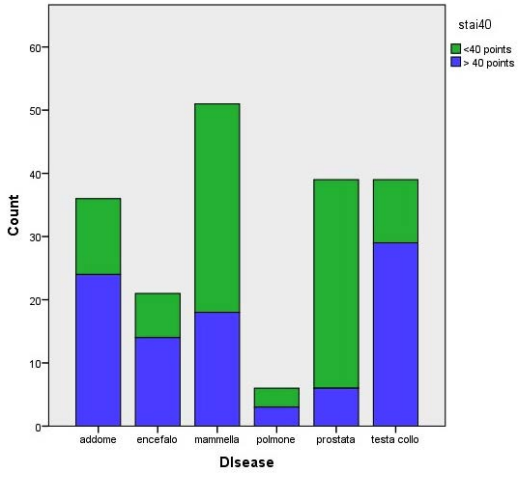


**Figure 1.**

**C012**

## INOPERABLE PELVIC SIDEWALL RECURRENCE OF GYNECOLOGICAL CANCER TREATED WITH PARTICLE THERAPY: CNAO PRELIMINARY EXPERIENCE

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Aims: Pelvic recurrences of gynecological cancer are generally resistant to RT/chemotherapy and most of these women need to take into consideration the possibility that normal tissues (such as bowel) might receive a high cumulative dose. For their biological and physical characteristics particle therapy (PT), with protons and carbon ions (CI), could be an interesting alternative treatment with curative intent. The aim of the current study was to evaluate the feasibility, acute toxicity and early clinical outcome of PT in patients (pts) with pelvic sidewall recurrence (PSWr) of gynecological tumors.

Methods: Between May 2014 to May 2019, 11 patients (median age 56) with PSWr within or at the edge of the previously irradiated field were treated using PT. They had recurrence of: cervical(5), endometrial(4), uterine(1) and ovarian(1) cancer. Previous RT dose prescription dose ranged from 45 to 59.4 Gy and 6 patients underwent to brachytherapy (range: 7-28 Gy). Two patients, with marginal lymph node recurrence, were irradiated with protons with up to a total dose of 25 GyRBE and 51 GyRBE respectively. The remaining women underwent to CIRT with a median total dose of 50.4 GyRBE (range: 36-57) administered in a median number of 12 fractions. Seven patients with PSWr received surgical spacer placement by open surgery to keep intestinal tracts apart from the tumor, as the distance between tumor and nearest intestinal tracts was not sufficient. No pts received concurrent chemotherapy. Preliminary local control (LC) and toxicity profile according to CTCAE V4.03 scale were evaluated.

Results: All patients completed the planned treatment and no acute toxicities G>2 were observed. For the evaluable patients, 1 case of intermediate G≥3 toxicity was reported in women received sequential Bevacizumab (BV). For pts with a follow-up ≥ 3 months, median LC was 9 months (range: 6-14), median metastasis-free-survival was 7 months (range: 3-21) and median overall survival was 9 months (range: 6-20). 1 pt experienced local progression and 4 pts died for systemic progression. Patient recruitment and data are still ongoing.

Conclusions: For pts with PSWr a PT approach seems to be feasible and our results showed a promising short-term outcome and limited radiation-related side effects. It is still unclear how PT and BV interact. Preliminary results are encouraging but a longer follow-up and large patient accrual are required.

**C013**

## HELICAL TOMOTHERAPY RE-IRRADIATION FOR PATIENTS AFFECTED BY LOCAL RADIORECURRENT PROSTATE CANCER

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Aims: Salvage re-irradiation in patients affected by radiorecurrent prostate cancer might be a valid as well as challenging treatment option. The aim of this study was to evaluate feasibility and toxicity of salvage external beam radiotherapy (EBRT) re-treatment in patients affected by radiorecurrent prostate cancer within the prostate gland or the prostate bed.

Methods: 15 patients underwent EBRT re-treatment using helical tomotherapy (HT), with daily Megavolt computed tomography image-guidance. We registered toxicity according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Biochemical relapse was defined as a PSA increase > 20% compared with the pre-EBRT re-treatment value. Survival curves were calculated using the Kaplan-Meier method.

Results: All patients received a total dose of 50 Gy (25 x 2 Gy), and 7 (46.6%) had concomitant androgen deprivation therapy (median duration of 12 months). With a median follow-up of 40.9 months, the 2-year and 4-year biochemical relapse-free survival were 55% and 35%, respectively. Acute and late genito-urinary (GU) toxicity ≥ 2 were recorded in 4 (26.6%) and 5 (33.3%) patients, respectively, and the 4-year late GU toxicity was 30%. Acute gastrointestinal toxicity ≥ 2 was recorded in 2 (13.3%) cases, whereas no patient experienced late toxicity.

Conclusions: Despite the inherent bias of a retrospective analysis, our long-term results showed a low toxicity profile with a relatively low rate of biochemical control for HT re-treatment in patients affected by local radiorecurrent prostate cancer. Prospective trials are needed to investigate the role of EBRT in this setting.

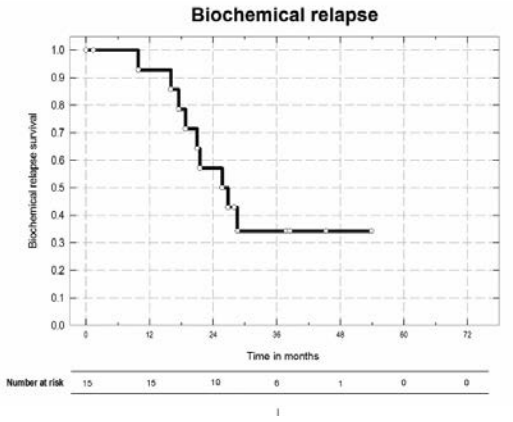


**Figure 1.**


# *Oral Communications*

**CO001**

## 68GA-PSMA PET-TC-GUIDED METASTASES DIRECTED STEREOTACTIC BODY RADIOTHERAPY IN PROSTATIC CANCER PATIENTS: A MONOISTITUTIONAL PRELIMINARY EXPERIENCE

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Aims: To investigate the efficacy and toxicity of 68Ga-PSMA PET-CT-guided stereotactic radiotherapy (SBRT) in the treatment of oligometastatic prostate cancer.

Methods: A total of 34 prostate cancer patients with biochemical relapse (22 castration sensitive and 12 castration resistant) were treated with Volumetric Modulated Arc Therapy and Image-Guided RT (VMAT-IGRT) on ≤5 metastastatic sites detected by 68Ga PSMA PET-CT. Androgen deprivation therapy was continued in castration resistant (CR) patients.

Results: A total of 74 metastases in 34 patients were treated with SBRT. The involved sites were pelvic lymph or paraaortic nodes (n = 53), bone (n = 13), seminal vesicles (n = 1), lung metastases (n = 2) and relapses in prostate or prostatic bed (n = 5). The median PSA prior to RT was 0.65 ng/mL (range 0.14 – 6.49 ng/mL), the median PSA-doubling time was 5.9 months (range 0.61 – 140) and the median PSA post RT was 0.61 ng/mL (range 0.02-30). A median dose of 35 Gy (range 25–70 Gy) was delivered by VMAT-IGRT in 5–10 fractions (the median BED2Gy was 144 Gy). At a median follow-up of 12.6 months (range 3–24 months), 16 patients out of 34 patients irradiated (47%) were in remission and 18 were in progression. In particular, 8 out of 12 castration resistant (CR) patients (67%) and 8 out of 22 castration sensitive (CS) patients (36%) were in progression. The actuarial 1-year LC, PFS and CSS rates were 93, 47 and 100%. Systemic treatment free survival was 8 months (range 2-24 months). No one patient experienced grade ≥3 acute gastrointestinal or urinary toxicity.

Conclusions: By providing optimal LC, low toxicity and a promising PFS, 68Ga PSMA PET-CT-guided metastases directed SBRT may be considered a promising treatment strategy in patients with oligometastatic prostate cancer, allowing to postpone systemic therapies. Further studies could confirm this promising findings.

## CO002

### EVALUATION OF PROGNOSTIC FACTORS IN PROSTATE CANCER PATIENTS WITH POST PROSTATECTOMY BIOCHEMICAL RELAPSE AND RE-STAGED WITH CHOLINE PET/CT: A MULTICENTRIC RETROSPECTIVE SERIES

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Aims: To describe outcomes after choline PET/CT re-staging in a multi-institutional cohort of prostate cancer (pCa) patients with locoregional or distant recurrence after primary surgery.

Methods: Data of 410 PCa patients treated in four Italian Centers were retrospectively reviewed. All patients underwent re-staging with choline PET/CT for post-prostatectomy biochemical recurrence. Patients were defined as oligometastatic (OM) if PSMA PET/CT detected <3 non-visceral lesions (either bone or nodal), according to Italian Association of Radiotherapy and Clinical Oncology (AIRO) definition. Pattern of treatment after re-staging and survival outcomes were analyzed. Association between risk class (low/intermediate vs high), site of metastatic disease (bone vs nodal) and PSA subgroup levels at biochemical relapse (<0.25, 0.25-0.49, 0.5-0.74, 0.75-0.99, 1-1.49, >1.5) with overall survival was explored performing Kaplan meyer analysis.

Results: At diagnosis, median age was 65.5 years (45-88) and median PSA level was 20.9 ng/mL (4-320), majority of patients (78,5%) was affected by high risk disease. Median time to biochemical relapse after primary treatment was 51 months (1-1381) and median PSA level at relapse was 3,5 ng/mL (0,1-134). Choline PET/CT had a crude detection rate of 68.5%, with 96% of positive exams detecting OM disease. 17.8, 44.1 and 6.3% of patients were treated with SBRT, exclusive androgen deprivation therapy (ADT) and chemotherapy+ADT, respectively. Median overall survival was 7.4 years (0-24). Only PSA at biochemical relapse showed significant impact on survival. Surprisingly, patients with PSA at relapse had a longer median survival if compared to others (102, 71, 84, 79, 102, 110 months in patients with <0.25, 0.25-0.49, 0.5-0.74, 0.75-0.99, 1-1.49, >1.5 ng/ml, respectively, p 0,013).

Conclusions: Based on the present experience, high PSA level at relapse, site of metastatic disease and baseline high risk-class should not be considered as negative prognostic factors in order to guide therapeutic approach in this setting. Literature data show that metastasis directed therapy could improve outcome in particular subset of patients, and none of the available treatment approaches (e.g SBRT) should be avoided based on abovementioned factors. Currently, treatment should be tailored on the basis of burden of disease detected at re-staging.

## CO003

### DETECTION RATE, PATTERN OF RELAPSE AND INFLUENCE ON THERAPEUTIC DECISION OF PSMA PET/CT IN PATIENTS AFFECTED BY BIOCHEMICAL RECURRENCE AFTER RADICAL PROSTATECTOMY, A RETROSPECTIVE CASE-SERIES

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Aims: (68Ga) Prostate-specific membrane antigen (PSMA) PET/CT is widely used in patients with biochemical recurrence (BCR) after radical prostatectomy.[1] Furthermore, standard restaging imaging has been proven to be significantly less sensitive than PSMA PET/CT.[2] According to National Comprehensive Cancer Network (NCCN)[3] use of PSMA should be limited to clinical trials or registry, however, due to its high detection rate, application in clinical practice is increasing[4,5] PSMA PET/CT showed to impact clinical decision in the scenario of early BCR.[6]

Methods: Data about PSMA PET/CT after BCR in four different institutes were collected. All patients underwent radical surgery and developed BCR (defined as PSA rise above 0.2 ng/ml[7]), with a PSA <1 ng/ml.

Patients were defined as oligometastatic (OM) if PSMA PET/CT detected <3 non-visceral lesions (either bone or nodal), according to Italian Association of Radiotherapy and Clinical Oncology (AIRO) definition.[8] Treatment after PSMA PET/CT scan were also reported. Gleason score <7or>7, Low/intermediate or High risk baseline classification, PSA at recurrence <or>0.5 ng/ml, PSA DT <or>10 months and time to recurrence (TTR) <or> than median of the analysed cohort (29.5 months), were considered as binomial variables and Chi-squared test was performed in order to evaluate the impact of these factors on PSMA PET/CT detection rate and the probability to detect OM disease. Chi-squared test was used to explore the association between the administration of RT with ablative instead of palliative-only intent and the probability to undergo ADT during the clinical history.

Results: 92 patients from 4 institutes were included. PSMA PET CT detection rate was 56.5% (52/92) and OM disease was detected in 92.3% of patients. After positive scan 13.5% of patients still lies on observation, ADT alone was administered in 30.8% of cases, Stereotactic body RT (SBRT) alone was delivered to 44.2% of patients and 11.5% of patients underwent concomitant SBRT and ADT, as summarized in Table 1. Chi-squared test showed a higher rate of positive PSMA PET/CT for patients with Gleason score >7 (p=0.004) and TTR shorter than 29.5 months (p=0.003). SBRT significantly reduced the risk of systemic ADT (p=0.03).

Discussion: PSMA PET/CT showed a high detection rate. OM disease was detected in most cases, avoiding unnecessary prostate bed RT, and PSMA PET/CT guided SBRT seems to have significant impact on this specific setting.

**Table 1.**

| | |
|---|---|
| Detection rate | Positive 52/92 (56,5%)<br>Negative 40/92 (43,5%) |
| Site | Locoregional 35/52 (67,3%)<br>Distant 17/51 (32,7%) |
| Disease burden | Oligometastatic: 48/52 (92,3%)<br>Plurimetastatic: 4/52 (7,7 %) |
| Therapeutic Choice (For Positive PSMA PET) | **ADT**<br>Yes 22/52: 42,3%<br>**RT with ablative intent**<br>28/52 (53,8%)<br>ADT alone (no ablative RT): 16/52 (30,8%)<br>ADT+RT (Ablative intent): 6/52 (11,5%)<br>RT (Ablative intent) alone: 23/52 (44,2%)<br>None:7/52 (13,5%) |

**CO004**

## RESULTS AT LONG-TERM AFTER RADIOSURGERY OF VESTIBULAR SCHWANNOMAS. A MULTICENTRE RETROSPECTIVE ANALYSIS

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Purpose: This retrospective report regards patients with sporadic vestibular schwannomas (VS) treated with a single dose of SRS with a minimum follow-up > 3 years. The aim of the study was to analyse tumor control and toxicity associated to SRS.

Methods: Patients included received Linac-based (LB) SRS or Cyber-Knife (CK) SRS. Patients not able to discriminate words or not hearing at all, were scored as 'non-serviceable hearing'. Trigeminal and facial nerve functions were assessed before and after treatment.

Results: Between 2002 and 2016, 153 VS were treated in 153 patients. 116 (76%) VS received LB-SRS and 37 (24%) CK-SRS. Male/female ratio was 70/83. Median age was 60y (range, 20-84). Median prescribed dose was 14Gy (range, 12-20). Median tumor diameter was 5 mm (range, 0.2-23). SRS was performed as salvage therapy for recurrent or progressive tumors in 36 (23%) patients already submitted to total or subtotal resection (10-28% and 26-72%, respectively). The other 117 (77%) patients underwent SRS alone. 25 (16%), 61 (40%), 52 (34%) and 15 (10%) VS were classified as Koos tumor grade I, II, III and IV, respectively. 147 (96%) patients had hearing loss as an initial symptom, of which 73 (48%) with "non-serviceable" hearing function. Trigeminal neuralgia and facial pain/paraesthesia were presenting symptoms in 9 (6%) and 27 (17%) patients, respectively. At a median follow-up of 6 years (range, 3–16), 32 patients (21%) had an objective improvement of their initial symptoms, 94 (61%) stable symptoms, and 27 (18%) worsened their pretreatment symptoms. Only in 1 case MRI showed progression of VS. Among patients with "serviceable-hearing" (80-52%), 54 (67%) maintained their functional hearing score, 11 (14%) improved and 19 (19%) worsened. 5 of 126 (4%) patients without pre-SRS facial toxicity, developed incomplete facial nerve palsy, that regressed in a median time of 6 months. 15 of 144 (10%) patients without pre-SRS trigeminal neuralgia developed trigeminal toxicity which was transient or stable/mild during follow-up in 13 (9%) patients. In only 2 cases (1%) trigeminal toxicity was severe and appeared at a median time of 12 months. Crude radiologic tumor control rate was 98%.

Conclusions: SRS in VS allowed an excellent tumor control and hearing preservation rate. Neurological toxicity resulted acceptable and similar to that reported

in literature. Prospective studies are needed to draw definitive conclusions.

## CO005

### INTRODUCING CONTRAST-DELAYED MAGNETIC RESONANCE IMAGING IN RADIOSURGERY TREATMENT OF GLIOBLASTOMA.

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Aims: Stereotactic radiosurgery (SRS) of intracranial lesions is based on the accurate delivery of very high doses of radiation. Milestone of this technique is therefore the acquisition of appropriate imaging for a really optimized treatment planning. Conventional magnetic resonance imaging (MRI) may not be able to differentiate tumor to non-tumor enhancing tissues. In this study we introduced treatment response assessment maps (TRAMs), based on the concept of delayed contrast extravasation MRI, into a radiosurgery treatment planning system (TPS) for target identification purposes.

Methods: Five patients presenting with disease progression of gliobastoma multiforme (GBM), previously treated according to our clinical practice, were enrolled in this study. For all patients an irradiation target volume was defined by contouring the enhancement area on a 3D T1-weighted MRI sequence (1-mm slice thickness, contiguous slices) acquired after contrast agent intravenous injection. TRAMs were obtained subtracting the post-contrast 3D T1-weighted images from the same MRI sequences acquired about 75 minutes after. Tumor burden was then also identified and outlined on TRAMs images, specifically processed to be imported in the TPS. Maintaining the target coverage maximization as primary objective (prescription dose to 95% of the target) for comparison purposes, plan optimization tests were performed in two ways for each patient: considering only the conventionally delineated target or considering only the TRAMs delineated target. The plans obtained for each patient were compared in terms of target volume and dose volume histogram (DVH) data.

Results: For all patients the target volume contoured on the TRAMs images was smaller than the one contoured on conventional MRI, with a fraction of approximately ½ in one case. Non-overlapping areas were also identified. Consequently, the percentage of healthy brain volume receiving 12 Gy was always in favour of the TRAM target case, with a reduction from 1.5 to 5%. Doses to other OARs adjacent to the target were also reduced.

Conclusions: The addition of delayed contrast extravasation MRI information in the identification of the radiosurgery treatment target can affect the planning optimisation process in the re-irradiation scenario of relapsing gliobastoma multiforme. Further investigations on the actual clinical impact of this imaging modality seems appropriate.

## CO006

### NON-COPLANAR MONO-ISOCENTER STEREOTACTIC RADIOTHERAPY (HYPERAR TM) FOR THE SIMULTANEOUS TREATMENT OF MULTIPLE BRAIN METASTASES FROM SOLID TUMORS: UPDATED RESULTS FROM THE FIRST WORLDWIDE EXPERIENCE

L. Nicosia[1], V. Figlia[1], N. Giaj-Levra[1], R. Mazzola[1], F. Ricchetti[1], M. Rigo[1], R. Ruggieri[1], F. Alongi[1]

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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). We reported the updated results of the first world-wide experience using a dedicated mono-isocenter non-coplanar LINAC-based technique (HyperArc™ Varian Medical System) in the treatment of multiple BMs.

Materials and Methods: patients with BMs (maximum diameter 30 mm), life expectancy >3 months and good performance status were treated with HyperArc™ and retrospectively evaluated. Local progression-free survival (LPFS), intracranial progression-free survival (iPFS), overall survival (OS) and intracranial overall survival (iOS) were evaluated. Predictive and prognostic factors were assessed.

Results: 102 patients accounting for 677 BMs with a median follow-up of 12 months were treated. Median treated metastases number was 7 (1-21). Primary tumor histology was NSCLC (42.1%), breast (30.3%), melanoma (13.7%), others (13.9%). Six and 12-month LPFS were 93.2% and 82.5%, respectively. At the univariate analysis NSCLC and breast histology correlated with a better LPFS (p=0.00001). Median time to iPFS was 5 months (range 3-10) irrespective from histology (p=0.97). Fourteen patients received 19 further courses of HyperArc™ (range 2-5) in case of intracranial oligoprogression. The 6- and 12 months iOS were 85.1% and 65.5% respectively, regardless of BM number (≤ 5 versus 6-9 versus ≥10; p=0.48). WBRT was administered to 10 patients after median 5 months (range 5-14), and 4 out of them received WBRT after a second HyperArc™ course. No acute adverse event higher than grade 2 occurred; 1 (0.14%) patient had histologically confirmed radionecrosis occurred 12 months after SRS.

Conclusions: HyperArc™ is a safe and effective technique for multiple BM treatment also in case of multiple courses. The reduced overall treatment time and the possibility to spare safely normal brain give the possibility to deliver multiple SRS/SFRT courses and in

selected cases to delay the administration of WBRT. A future prospective study is needed to evaluate the long-term effectiveness of multiple BM SRS/SFRT.

## CO007

### A RADIOMIC APPROACH TO PREDICT NODAL AND DISTANT RELAPSE IN A COHORT OF PATIENTS TREATED WITH STEREOTACTIC BODY RADIATION THERAPY FOR EARLY STAGE NON SMALL CELL LUNG CANCER

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Aims: Regional and distant relapse remain a significant issue in the treatment of early stage non small cell lung cancer with Stereotactic Body Radiation Therapy (SBRT). In this work we present a radiomic approach using features extracted by routine planning CT, to predict the risk of nodal and distant recurrence.

Methods: A cohort of 102 patients was retrospectively investigated. All patients were affected by early stage (T1-T2) lung cancer and received the same radiation treatment with 48Gy delivered in 4 fractions. For all patients, a set of 45 radiomics textural features was computed for the tumor volumes segmented on the treatment planning CT images. Patients were split into two independent cohorts used for training (70% of cases) and validation (30% of cases). A stepwise backward linear discriminant analysis (LDA) was applied as a classifier to identify patients at risk of lymph-nodal progression. The performance of the model was assessed by means of standard metrics derived from the confusion matrix. Furthermore, all textural features were correlated to survival data to build predictive models: the features/predictors found significant at univariate analysis and to elastic net regularization, were included in a multivariate model to predict disease specific progression free survival (PFS) and disease specific survival (DS OS). Low and high risk groups were identified by maximizing the separation by means of the Youden method.

Results: In the total cohort (77 (75.5%) males and 25 (24.5%) females, median age 76.6 years), 15 patients presented nodal progression at the time of analysis (11 in the training and 4 in the validation sets); 19 patients (18.6%) died because of disease specific causes, 25 (24.5%) died for other reasons, 28 (27.5%) were alive without disease and 30 (29.4%) with either local or distant progression. The mean tumor volume was 5.6±6.4cm$^3$. Table 1 summarizes the performance results of the LDA classifier. Figure 1 illustrates the actuarial curves for PFS and DS OS over the entire training and test cohorts (in both cases the difference was not significant) and the same data stratified in low and high risk groups identified. In all case highly significant differences were identified.

Conclusions: Radiomics features extracted from treatment planning CT images can distinguish patients with low and high risk of tumor progression and disease specific death in early stage lung cancer treated with SBRT.

**Table 1. Performance results of the linear discriminant analysis classifier.**

| | Training | Validation |
|---|---|---|
| Specificity | 0.84±0.14 | 0.83±0.24 |
| Sensitivity | 0.89±0.01 | 0.87±0.01 |
| Accuracy | 0.87±0.07 | 0.85±0.12 |
| AUC | 0.84±0.04 | 0.73±0.05 |

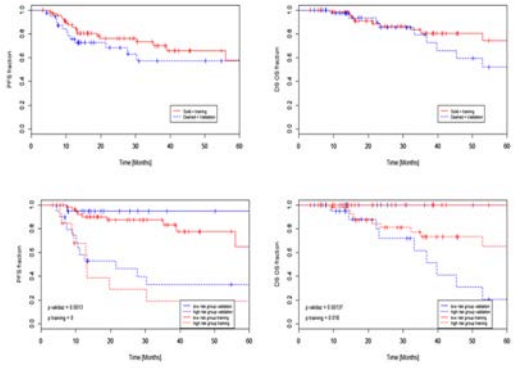

**Figure 1. Actuarial curves for PFS and DS OS over the entire training and test cohorts (in both cases the difference was not significant) and the same data stratified in low and high risk groups identified.**

## CO008

### A PRACTICAL DOCUMENT ON IMRT IN MEDIASTINAL LYMPHOMAS

S. Meregalli[1], A. Di Russo[2], G. Simontacchi[3], A. Alghisi[4], M. Buglione[4], P. Ciammella[5], G. De Marco[6], V. De Sanctis[7], B. Lanfranchi[6], M. Levis[8], S. Vagge[9], U. Ricardi[8], A.R. Filippi[10], Commissione Radioterapia FIL

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Aims: Advances in therapy have resulted in improved cure rates and an increasing number of long-term lymphoma survivors. However, radiotherapy (RT)-related late effects are still a significant issue, particularly for young patients with mediastinal disease (heart, second cancers). In many Centres worldwide, RT technological evolution substantially changed radiation dose planning and delivery. This consensus document aimed to analyze and summarize the current knowledge on IMRT and IGRT for mediastinal lymphoma, providing the basis for standardization among FIL studies.

Methods: A working group was set up within the FIL (Fondazione Italiana Linfomi) in May 2018. After a first meeting, the group adopted a dedicated platform to share articles and material. Two group coordinators redacted a first document draft, that was further discussed and finalized in a subsequent meeting. Topics of interest were: 1) IMRT techniques; 2) specific dose constraints for the following OAR: heart, lungs, thyroid, breasts; 3) IGRT protocols.

Results: According to the planned schedule, the final document has been presented at FIL National meeting in November 2018. Data review clearly showed that IMRT, mainly if combined with IGRT, may allow for shrinkage of irradiated volumes and therefore an essential reduction of high dose to OAR. IMRT emerged as superior to conformal RT for heart sparing and for reducing the dose to the thyroid gland. Low dose spread to the lungs and breast can be limited by using specific dose constraints. Suggested constraints for low/intermediate dose to optimize planning for all organs at risk have been created and approved by the whole group (Table 1). The use and frequency of IGRT resulted widely variable among Centres, as the use of breath control techniques, and the group advised for routine use without specifications. An individual approach considering the different age, gender, and finality of RT has been strongly recommended.

Conclusions: As lymphoma therapy continues to evolve, with an emphasis on treatment reduction, radiation oncologists should use at best the available tools to minimize the dose to organs at risk. This consensus document provides for the first time indications on the use of IMRT/IGRT techniques for mediastinal lymphomas. It will be rapidly adopted by FIL for future trials and might be useful for clinical practice.

**Table 1.**

| Dose constraints OAR | |
|---|---|
| **Breast** | V4<50% |
| **Heart** | Mean Dose <5 Gy |
| **Thyroid gland** | V5<93%<br>V20<82.4%<br>V25<63,5%<br>V30<62% |
| **Lung** | MLD<10 Gy<br>V5<55%<br>V20<30% |

**CO009**

## ONCE-DAILY PARTIAL BREAST IRRADIATION (OD-PBI): PRELIMINARY LONG TERM RESULTS WITH HELICAL TOMOTHERAPY HI-ART

U. De Paula, C. Ghini, A.D. Andrulli, G. Apicella, R. Barbara, C. Caruso, S. Gomellini, E. Ponti, A. Caccavari, L. Costarelli, M. La Pinta, M. Mauri, P. Scavina, A. Petrocchi, R. Rossi, L. Broglia, A. Loreti, L. Fortunato

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Aims: Accelerated partial breast irradiation (APBI) has become a valid treatment in the field of breast conservative therapy for pts with early-stage breast cancer. The current schedule (38,5 Gy in 10 fraction b.i.d. over 5 days) is often associated with good local control at the expense of greater toxicity and worse cosmetic results respect to standard fractionation. We report long-term results in 162 pts treated with once-daily PBI (OD-PBI). We analyzed local recurrence (LR), regional recurrence (RR), axillary failure (AF), toxicity and cosmesis. Secondary end-point were: disease free survival (DFS), distant-disease-free-survival (DDFS), cause-specific-survival (CSS) and overall-survival (OS).

**Table 1.**

Patient's charatheristics

| | N (%) |
|---|---|
| *Median age: 65,3 (range: 50-85 aa)* | |
| **Breast** | |
| Right | 71 (44%) |
| Left | 92 (56%) |
| **Histology**: | |
| Ductal | 136 (83%) |
| Lobular | 17 (10%) |
| Others | 10 (7%) |
| **Grading:** | |
| G1 | 45 (28%) |
| G2 | 67 (41%) |
| G3 | 51 (31%) |
| **T-Stage** | |
| Ia | 21 (13%) |
| Ib | 66 (40%) |
| Ic | 68 (42%) |
| IIa | 8 (5%) |
| **Lymph nodes:** | |
| N0 | 146 (89%) |
| N1 | 16 (11%) |
| **Adjuvant Chemotherapy:** | |
| No | 157 (96%) |
| Yes | 6 (4%) |
| **Stanford classification:** | |
| Luminal A like | 115 (71%) |
| Luminal B like | 36 (22%) |
| Neu-positive | 9 (5%) |
| Basal-like | 3 (2%) |

Methods: From December 2010 to December 2018, 347 pts with invasive breast cancer (mean age:65,2 yrs; range 50-86) underwent OD-PBI (38,5 Gy delivered in 10 daily fractions) delivered by Helical-Tomotherapy. We present results on 162 pts with a minimum follow-up of 55 months (Table 1). Eligibility criteria included unifocal disease up to 3 cm with R0 (at least 2 mm of clear margins) without extensive (<25%) intraductal disease or LVSI. Pts with pN1a involvment without

extracapsular invasion were included. All genetic subtypes (Stanford's classification) were admitted. Patients and physicians assessed cosmesis during FU according to EORTC Cosmetic Rating System.

Results: With a median FU of 72.3 months (range: 53-101) no LR, RR and AF were reported. All pts completed the treatment without any interruption; 17 pts (10%) experienced a grade 1 and 2 pts (1,2%) grade 2 acute skin toxicity. In 4 pts a grade 1 (2,4%) late skin toxicity and in 9 pts (5,5%) subcutaneous fibrosis according to CTCAE v4.0, was observed. The patients assessed percentage of (respectively) "excellent" and "good" cosmetic results were 66% and 32% at baseline; 75% and 22% at 1 year; 77% and 19% at 2 yrs. The same assessment given by the physicians occurred in 70% and 27% (baseline); 87% and 12%, (1 year) and in 82% and 15% (2 yrs). A very low rate of pts and physicians (1% and 4%, respectively) judged as "fair" or "poor" the cosmetic outcome at any time. One pt developed a contralateral breast tumor 12 months after the end of the OD-PBI. There were no cases of distant metastases. OS rate at 3 and 5 yrs were 98.8 % and 96.3%, respectively.

Conclusions: OD-PBI with Helical Tomotherapy HI-ART yielded good cosmetic results without compromising local control efficacy in pts who have undergone conservative surgery.

## CO010

### PROGNOSTIC VALUE OF LYMPH-NODE STATUS AFTER ONCE-DAILY PARTIAL BREAST IRRADIATION (OD-PBI) WITH HELICAL-TOMOTHERAPY HI-ART: PRELIMINARY RESULTS

C. Ghini, A.D. Andrulli, G. Apicella, R. Barbara, C. Caruso, S. Gomellini, E. Ponti, L. Costarelli, A. Caccavari, M. Mauri, P. Scavina, R. Rossi, L. Broglia, L. Fortunato, M. La Pinta, P.D. Trifan, U. De Paula

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Aims: According to the update of the Consensus Statement of the ASTRO of January 2015, the involvement of the axillary lymph nodes pN1a (one to three nodal metastases) is not yet considered eligibility criteria for pts applying to APBI. Recently, several studies have shown, instead, has no prognostic significance on the incidence of loco-regional recurrences. The purpose of this analysis is compare outcomes after once-day partial breast irradiation (OD-PBI) between N- and N+ pts.

Methods: From December 2010 to December 2018, 347 pts with invasive breast cancer (mean age:65,2 yrs; range 50-86) underwent OD-PBI (38,5 Gy/10 daily fractions) delivered by Helical-Tomotherapy. We present results on 162 pts with a minimum follow-up of 55 months including 18 node-positive (N+) cases. Of these 13 pts (72%) were pN1a and 5 (28%) pts were pN1mi. Clinical, pathologic, and treatment-related factors were compared between node-negative (N-) and (N+) cohorts. Local recurrence (LR), regional recurrence (RR), axillary failure (AF), distant metastases (DM), disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS) were analyzed.

Results: N+ pts were slightly younger (mean age: 63,7 yrs vs 64,9 yrs; p=0,37), had larger tumors (DM: 14,1 mm vs 10,6 mm; p= 0,04), and not were more likely to receive chemotherapy. Sixteen (89%) had a pure IDC histological type while 11% were ILC (p= 0,01). Eleven pts (61%) had a Luminal A-like genetic sub-type, 5(28%) were Luminal B-Like and 2(11%) were HER 2+ non Luminal. Only 3 pts (17%) had a degree of differentiation G1, while 83% had a degree of differentiation G2/G3 (p=0,008). Median FU was 73,4 mths for N+ pts and 69 mths for N- pts (p=0,47). No differences were seen in 5-year actuarial rates of LR (0% vs. 0%), AF (0% vs. 0%), RR (0% vs 0%), DM (0% vs 0%),CSS (100% vs 100%), or OS (88% vs. 97.2%, p=0,47) between the two groups. One pt N- developed a contralateral breast tumor 12 months after the end of the OD-PBI. Since no recurrence event was detected, age, tumor size, receptor status, chemotherapy, histological type and N- stage were not associated with LR, RR and AF.

Conclusions: No differences were seen in the rates of LR, RR or AF between N- and N+ pts after OD-PBI. These results support the continued enrollment of N+ pts in Phase III trials evaluating the efficacy of APBI including the National Surgical Adjuvant Breast and Bowel Project-B39/Radiation Therapy Oncology Group 0413.

## CO011

### INSPIRATION LUNG VOLUME AS PREDICTOR OF DOSIMETRIC BENEFIT IN BREAST CANCER PATIENTS TREATED WITH DEEP INSPIRATION BREATH HOLD

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Aims: Deep inspiration breath hold radiotherapy (DIBH RT) has been demonstrated to reduce heart doses in patients with left side breast cancer. However, its routine use requires patients' compliance and increases staff workload and treatment time. The aim of this study was to identify treatment planning characteristics that correlate with heart sparing and therefore guide patients selection.

Methods: We retrospectively reviewed treatment plans of 210 patients with left-sided breast cancer treated with breast adjuvant radiotherapy at our institution. All patients had both free-breathing (FB) and DIBH treatment plans. Mean and maximum heart dose (mHD, MHD), maximum dose to LAD (LAD Dmax), were recorded form both plans and the differences were cal-

culated (Δ, delta values). Pearson correlations of Δ values with patient related parameters (PTVcc, inspiration lung volume, distance from the heart wall to the tangent field during free breathing and DIBH, breast separation) were carried out. Furthermore, receiver-operating characteristic (ROC) analysis was performed to select the threshold of values of patients related parameters that may predict the benefit for heart dosimetry of DIBH over free-breathing.

Results: Four hundred twenty plans were evaluated. DIBH plans decreased mHD, MHD and LAD Dmax by 21%, 66% and 47% respectively (see table 1). Delta MHD correlated positively with lung inspiration volume (p=<0.05). A negative correlation was found between Delta LAD Dmax and breast separation and PTVcc (p=0.07). Inspiratory lung volume > 2163 cc achieved the 50% benefit of delta MHD (p=0.008, AUC= 0.650).

Conclusions: Most patients have significant dosimetric benefit with DIBH. Inspiratory lung volume > 2163 cc may be used for selection of patients who benefit the most of DIBH technique.

**Table 1. Comparison of dose metrics between free-breathing (FB) and breath hold (BH) plans.**

| | FB plans | BH plans | p |
|---|---|---|---|
| Heart mean dose (Gy) | 1,38<br>DS=0,77 | 1,14<br>DS= 0,57 | <0.001 |
| Heart maximum dose (Gy) | 32,5<br>DS= 12.7 | 19,6<br>DS= 12.3 | <0.001 |
| LAD maximum dose (Gy) | 12,54029<br>DS=5,9 | 8,52751<br>DS=3,9 | <0.001 |
| Lung V20 Gy (%) | 7,100156<br>DS= 4,7 | 7,5739512<br>DS=4,0 | <0.001 |

*LAD: left descending artery; V20 Gy= lung volume receiving 20 Gy.*

## CO012

### MANAGEMENT OF PATIENTS WITH CARDIAC PACEMAKERS (PM) OR IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR (ICD) IN RADIOTHERAPY WORKFLOW. DEVELOPMENT OF A PROTOCOL AND SAFETY REPORTS

S. Di Biase[1], F. Fenu[1], S. Costantini[1], F. Cucciarelli[1], M. Di Benedetto[1], L. Fabbietti[1], M. Madia[1], A. Maucieri[1], M. Montisci[1], G. Travaglini[1], M. Valenti [2], L. Vicenzi[1], G. Mantello[1]

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Aims: Radiotherapy (RT) can influence cardiac implantable electronic devices (CIED) functioning. Consensus document from AIAC, AIRO and AIFM has been recently published but data on this issue are still limited. We report our protocol for the management of patients (pts) with PM or ICD undergone RT and our results in terms of CIED malfunctioning.

Methods: 34 consecutive CIED pts admitted to our Institution were evaluated. Pts were stratified into three classes. The first group included pts with PM and spontaneous activity; the second one, pts with PM but without any residual spontaneous activity; the third group included pts with ICD. For the first two groups, the cardiologist of reference evaluated pts before and after every RT fraction, setting PM in asynchronous mode during RT delivery. In the third group, the cardiologist disabled and enabled ICD before and after every RT section, monitoring cardiac activity during the treatment delivery. Pts were classified in high risk and low risk when CIED distance from target was ≤10 cm and > 10 cm, respectively. CIED functioning was evaluated during and at the end of RT course.

Results: 8/34 pts were treated with tomotherapy. Total dose ranged from 8 Gy to 78 Gy. 23/34 pts had PM, 11/34 ICD. In 17 cases CIED distance from the target was ≤10 cm and in 17/34 distance was >10 cm. 8/17 and 2/17 low risk pts belonged to the first and the second group, respectively. Among these pts (both dependent and independent), 7 were treated with 6 MV photons, the remaining 3 pts were treated with > 6 MV. 7/17 low-risk pts were ICD wearers: 5 were treated with 6 MV photons, 2 with > 6 MV photons. 13/17 high-risk pts had PM (dependent or independent), among these, 11 were treated with 6 MV photon and 2 pts with > 6 MV. 4/17 high-risk pts were ICD carriers: 3 pts were treated with 6M photons while 1 pt with > 6 MV. During or at the end of RT course, 24/34 pts showed not CIED malfunctioning, 3/34 had atrial fibrillation and 7/34 cases had ventricular events with no major clinical effects. After a mean follow-up of 19 months (range 2-41), 12 pts were evaluable for late assessment of CIED functioning and no ventricular event was observed.

Conclusions: The introduction of a protocol for the management of pts with CIED allows a standardization of the cardiological evaluation in RT workflow. In our experience, RT seems to be safe for CIED wearers. A larger number of pts will be required to confirm these preliminary results.

## CO013

### PHASE 2 TRIAL EVALUATING STEREOTACTIC BODY RADIOTHERAPY (SBRT) AFTER INDUCTION CHEMOTHERAPY FOR PATIENTS WITH LOCALLY ADVANCED UNRESECTABLE PANCREATIC CANCER (LAPC02; NCT03158779): FEASIBILITY AND SAFETY PRELIMINARY RESULTS OF EUS-GUIDED PLACEMENT OF NEW GOLDEN FIDUCIAL MARKERS

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Background and Aim: Radiation therapy plays an emerging role in the multi-modality treatment of locally advanced pancreatic cancer (LAPC). Stereotactic body radiation therapy (SBRT) is an innovative radiation technique, characterized by high prescription dose delivered in few fractions with a short overall treatment time and increased local control rate. Endoscopic ultrasound (EUS)-guided fiducials placement allows to accurately evaluate the target motion during SBRT delivery. The aim of our study is to report the technical feasibility, safety and migration rate of fiducial marker placement in patients with LAPC enrolled in a phase II study of SBRT after induction chemotherapy (LAPC02) who underwent EUS-guided fiducial marker placement for IGRT

Material and Methods: Patients with histologically proven unresectable LAPC, treated with induction chemotherapy according to FOLFIRINOX or Gemcitabine-Abraxane schedules, with tumor cannot exceed 5 cm in maximum diameter and without limphnodal metastases, were treated with ablative dose of SBRT (54 Gy in 6 daily fractions) in a prospective phase II study (NCT03158779). In selected enrolled patients, gold markers were implanted into the tumor under EUS-guidance, before SBRT simulation. A new dedicated needle was used: a 22G needle preloaded with 4 gold fiducials (0.43 mm width for 5 mm length), EchoTip® Ultra Fiducial Needle (Cook Medical).

The fiducials were released under EUS guidance and it were placed at the opposite extremities of the tumor. Fluoroscopy was used to confirm the position.

Migration, defined as a change in inter-fiducial distance, was evaluated at the time of simulation phase and treatment delivery.

Results: From May 2017 to March 2019, 12 patients (8 F/4 M) aged 66.5 years (53-80 range) were enrolled in LAPC02 trial and candidated to fiducials placement. Induction chemotherapy was Gemcitabine-Abraxane in 9 patients and Folfirinox in 3 patients, with a median time of 4.1 months (range 3-6 months). At restaging the disease was still locally advanced, with no distant progression. The tumors were localized in the head (5), uncinate process (3),body (3) and tail of pancreas (1). Mean size was 31 mm (12-46 mm range). In all but one patient 2-4 markers were placed. In 5 of 12 patients procedure had no technical difficulties. In 7 patients, fiducial placement was made difficult due to: increased hardness of lesion, nearest vessels (infiltrated portal vein or collateral vessels due to portal hypertension), poor control in the first marker release (two fiducials released in the same position). Patients started SBRT with a median gap time of 10.2 days (range 6-19 days) between the fiducials placement and the first fraction. Simulation included a contrast-enhanced CT scan and a 4D-CT scan to registered the patient's breathing pattern. Slice width was 3 mm for both studies. Only one patient, in whom the simulation CT was performed at the same day of the fiducial placement, showed a minimal migration of one fiducial (<3 mm) when SBRT was started. No severe adverse events occurred. One patients presented abdominal pain responsive to paracetamol. The procedures were performed in an outpatient setting.

Conclusions: This preliminary evaluation demonstrated the feasibility and safety of the EUS-guided fiducial placement using the new dedicated preloaded needle. Only minor technical difficulties due to the stiffness of the tumor did not affect the correct placement of the fiducials. Imaging at the time of simulation also revealed the migration rate to be extremely low.

## CO014

## SURGICAL MARGINS STATUS AND POSTOPERATIVE COMPLICATIONS AFTER SBRT AS NEOADJUVANT APPROACH FOR PANCREATIC CANCER

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Aims: R0 resection rate in pancreatic cancer (PC) using axial slicing technique with a minimum 1-mm margin for pathologic evaluation was reported from 26 to 32%. Preoperative Stereotactic Body Radiation Therapy (SBRT) is an emerging neoadjuvant approach in patients (pts) with Borderline Resectable (BR) or Locally Advanced (LA) PC. This study aims to investigate the effects on surgical margins status and post-operative complications of SBRT following induction chemotherapy.

Methods: Pts with BR and LA PC undergoing induction chemotherapy and preoperative SBRT and selected for surgical exploration from November 2016 to November 2018 were included in the analysis. SBRT was delivered over 5 consecutive fractions using a simultaneous integrated boost (SIB) prescribing 10 Gy/fraction to the region of vessel abutment/encasement and 6 Gy/fraction to the remaining Planning Target Volume (PTV) tumor. We reduced the dose to 5 Gy/fraction on the overlap area between the PTV and Organs at Risk (OARs). R0 resection was defined as the absence of microscopic tumor invasion within 1 mm of resection margins, assessed by axial slicing of the surgical specimen. Surgical complications were defined according to the International Study Group of Pancreatic Surgery (ISGPS).

Results: The study population consisted of 44 pts. 38 pts underwent pancreatic resection and 6 were found to have unresectable tumor at surgical exploration, with a resection/exploration ratio of 86.4%. R0 resection was achieved in 19 pts (50% of those undergoing surgical resection). Two patients were classified with a tumor regression grade 0. Postoperative overall morbidity was 54.5% and 30-days mortality was nil. Post-Operative Pancreatic Fistula (POPF) occurred in 4 pts (10.5% of cases) while Post Pancreatectomy Hemorrage (PPH) was detected in 3 pts (8%), with one needing re-intervention.

Conclusions: SBRT following induction chemotherapy is a safe option in the context of a total neoadjuvant approach for BR and LA pancreatic cancer. The rate of negative margins is promising, especially in the setting of complex long-course downstaging and challenging indication to surgery.

## CO015

### CARBON ION RADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER TREATED AT CNAO: PRELIMINARY RESULTS

V. Vitolo[1], A. Barcellini[1], L. Cobianchi[2,3], A. Vanoli[4], M.R. Fiore[1], B. Vischioni[1], A. Iannalfi[1], M. Bonora[1], S. Ronchi[1], E. D'Ippolito[1], R. Petrucci[1], P. Fossati[1], G. Viselner[1], L. Preda[1,3] S. Molinelli[1], S. Durante[1,5], F. Cuccia[1,6] E. Scipilliti[1,7] F. Valvo[1]

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Background: Complete surgical resection is the only curative treatment for pancreatic adenocarcinoma, but is available only up to 15%-20% of all patients at the time of diagnosis. In the remaining patients major vessel involvements either local tumor extension are obstacles for a surgical therapy. Considering the suboptimal efficacy of conventional therapeutic alternatives and the consensus on the inclusion of these patients in clinical trials, locally advanced pancreatic cancer (LAPC) could be an ideal disease to test the efficacy o carbon ions radiotherapy (CIRT).

Aim: To evaluate response and toxicity of CIRT for LAPC.

Methods: We retrospectively analyzed 16 patients with LAPC who have been treated with CIRT at National Center of Oncological Hadrontherapy (CNAO) between September 2014 and February 2019. All patients presented a local progression after at least one line of chemotherapy and 25% of patients were admitted for CIRT already in recurrent situation after surgery. All patients will be positioned in customized cushions and immobilized with a solid thermoplastic mask. A set of 2-mm-thick 4D computed tomography (CT) images will be taken for treatment planning with the immobilization devices. The Anzai system (Anzai Medical, Tokyo, Japan) will be used to acquire the patient breathing signal for retrospective 4D CT reconstruction. Median total dose was 57.6 GyE (range: 43.2-57.6 GyE) delivered in median number of 12 fractions (range: 8-12 fractions). Median dose for fraction was 4.8 GyE (range: 4.6-4.8 GyE). Intensity modulated particle therapy (IMPT) was employed. Toxicity was recorded according to CTCAE 4.0.

Results: All patients completed the scheduled treatment and CIRT was well tolerated. Acute toxicity was mild, no grade 3 side effects were observed. No severe late toxicity (grade 3) was scored. Two patients underwent to surgery after CIRT with a LC of 22 and 55 months respectively after surgery and no significant toxicities, including surgery-related were observed. Overall, we observed local progression in 4 (25%) patients translating into estimated 1- and 2-year local control (LC) rates of 71 and 55%. Metastasis Free Survival (MFS) were reached in 43% of patients (median-MFS of 11 months ; range: 4-55 months).

Conclusions: In our experience, CIRT in LAPC has shown a promising LC and good toxicity profile. However, a larger series of patients and a longer follow-up are needed to better investigate outcomes, especially in terms of late toxicity.

## CO016

### CLINICAL OUTCOME IN PATIENTS WITH SKULL-BASE CHORDOMA TREATED WITH PROTON AND CARBON ION RADIOTHERAPY AT CNAO: AN UPDATE

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Aims: The management of skull base chordoma is challenging, and particle therapy is the treatment of choice in both adjuvant then exclusive setting. Post-operative radiotherapy is a predictor of improved progression-free survival. Our purpose was to evaluate the long-term results in terms of local control (LC), overall survival (OS) and toxicity profile of pts with skull-base chordoma treated with proton therapy -PT- and carbon ion therapy –CIRT and to better identify factors influencing clinical outcome

Methods: Between 11/2011 and 12/2018, a total of 146 pts where treated for skull base chordoma and 135 patients were analyzed. Pts with follow-up <6 months were excluded.. Pts and tumors characteristics are summarized in Table 1. Prescription dose for PT is 74 Gy(RBE) delivered in 37 fractions of 2 Gy(RBE), CIRT prescription dose is 70.4 Gy(RBE) delivered in 16 fractions. Clinical outcome (3-5 year LC and OS rate) and toxicity profile (according to CTCAE V4.03- scale) were evaluated. Recurrent cases were retrospectively evaluated: the follow-up MRI sequences were the recurrence was detected were fused with the planning CT scans and data analyzed.

Results: Sixty-five pts were treated with CIRT, 70

patients with PT. Median follow-up was 44 months (range 6-87 months). For the CIRT pts group, the 3-year and 5-year LC rates were 77% and 71% respectively, relapsed occurred in 13 of 65 patients in close proximity to brainstem or optic chiasm. The 3-year and 5-year OS rates were 90% and 82% respectively. In PT cohort the 3-year and 5-year OS rates were 90% and 82% respectively, relapse occurred in 8 of 70 patients, all but one next to brainstem. The 3-year and 5-year OS rates were 93% and 83% respectively. In univariate analysis the LC was significantly influenced by brainstem/optic pathway involvement and GTV volume: GTV <10 $cm^3$ for PT and GTV<23 cm3 for CIRT were unfavorable prognostic factor for LC. High grade (G3-G4) late toxicity occurred in 16 pts (12%): 2 case of complete visual loss (G4) expected because of optic nerve in field. Median time to G ≥ 3 toxicity was 21 months (8 – 44, range).

Conclusions: Particle therapy is the most innovative and conformal RT for treatment of skull base chordomas. It allows to deliver higher (biologically effective) dose levels and to obtain high tumor control rates, with a low rate of radiation-related side effects. Brainstem/optic pathway involvement and irradiation tumor size is recognized as prognostic factors.

**Table 1.**

| | TOT n (%) 135 patients | CIRT cohort n (%) 65 patients | PT cohort n (%) 70 patients |
|---|---|---|---|
| KPS | | | |
| ≤ 80 | 22 (16) | 11 (17) | 11 (16) |
| 90-100 | 113 (84) | 54 (83) | 59 (84) |
| Sex | | | |
| Male | 82 (61) | 42 (65) | 40 (57) |
| Famale | 53 (39) | 23 (35) | 30 (43) |
| Age (years): median (range) | 57 (13-81) | 58 (13 - 81) | 53 (17- 81) |
| Treatment | | | |
| Primary | 107 (79) | 46 (71) | 61 (87) |
| Recurrent | 28 (21) | 19 (29) | 9 (13) |
| Surgery (n) | | | |
| 1 | 77 (57) | 34 (52) | 43 (61) |
| >1 | 58 (43) | 31 (48) | 27 (39) |
| Brainstem abutmnet/compression | | | |
| Y | 31 (23) | 14 (22) | 17 (25) |
| N | 103 (77) | 51 (78) | 52 (75) |
| Not evaluated * | 1 | | 1 |
| Optic patway abutmnet/compression | | | |
| Y | 11 (8) | 58 (89) | 64 (94) |
| N | 123 (92) | 7 (11) | 4 (6) |
| Not evaluated * | 1 | | 1 |
| GTV ($cm^3$): median (range) | 7 (0-99.3) | 13 (0.4-87.4) | 3.5 (0-99.3) |
| Dose: median (range) | - | 70.4 (70.4) | 74 (72-74) |

*Only CT imaging.

## CO017

## A LARGE, MULTICENTER, RETROSPECTIVE STUDY ON EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC OVARIAN CANCER (MITO RT1 STUDY): A COLLABORATION OF MITO, AIRO GYN, AND MANGO GROUPS

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Aims: The aim of this retrospective, multicenter study (MITO RT-01) was to define activity and safety of Stereotactic Body Radiotherapy (SBRT) in a very large, real life dataset of metastatic/persistent/recurrent ovarian cancer (MPR-OC) patients. Clinical and SBRT parameters have been analyzed in order to identify predictors of outcome.

Methods: The endpoints of the study were the rate of complete response (CR) to SBRT, and the 24-month actuarial local control (LC) rate on "per lesion" basis. The secondary end-points were acute and late toxicities, and the 24-month actuarial late toxicity free survival. Objective response rate (ORR) included CR and partial response (PR). Clinical benefit (CB) included ORR and stable disease (SD). Toxicity was evaluated by

RTOG/EORTC and CTC-AE scales, according to center policy. Logistic and Cox regression were used for the uni- and multivariate analysis of factors predicting clinical CR and actuarial outcomes.

Results: Fifteen Radiation Oncologist Institutions participated to the study; after evaluation of inclusion/exclusion criteria, 261 OC patients, carrying a total of 449 lesions treated by SBRT between May 2005 and November 2018, were selected for the enrollment.

CR, PR and SD were observed in 291 (65.2%), 106 (23.8%), and 33 (7.4%) lesions, giving a rate of CB of 96.4%. Patient age <60 years, PTV <18 cm3, lymph node disease, and BEDα/β10 >70 Gy were associated with higher chance of CR in the multivariate analysis. With a median follow-up of 22 months (range: 3-120), the 24-month actuarial LC rate was 81.9%. Achievement of CR and total dose >25 Gy were associated with better LC rate in the multivariate analysis. Mild toxicity was experienced in 54 (20.7%) patients: of 63 side effects, 48 were grade 1, and 15 were grade 2. The 24- month late toxicity free survival rate was 95.1%.

Conclusions: This study confirms the activity and safety of SBRT in MPR-OC patients and identifies clinical and treatment parameters able to predict CR and LC rate.

## CO018

### RECURRENCE PATTERN OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC PROSTATE CANCER: A MULTI-INSTITUTIONAL ANALYSIS

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Purpose: For patients with oligometastatic/oligorecurrent/oligoprogressive lymph node metastases from PCa, metastases-directed therapy is an emerging strategy. The aim of this retrospective study was to evaluate the oncological outcome and pattern of recurrence of patients treated with stereotactic body radiation therapy (SBRT) on lymph node metastases.

Methods: In this multi-institutional analysis, patients with maximum 5 lymph node metastases from PCa treated with SBRT were included. Primary endpoints of the analysis were local control (LC), out-of-field nodal progression-free survival (NPFS), overall progression-free survival (PFS) and overall survival (OS).

Results: 109 patients and 155 lymph node metastases were evaluated. Patients' median age was 70.8 years (range, 51-84) and median PSA before SBRT was 1.88 ng/ml (range, 0.3-45.5 ng/ml). The dose delivered to the target ranged from 25 to 48 Gy in 4-7 fractions; median BED1.5Gy was 198 Gy (range 108.3 – 432 Gy). With a median follow-up of 16 months, LC rates at 1- and 3-years were 93% and 86%, respectively. In-field progression of disease was observed in 11 (7%) lesions. One and 3-years NPFS was 59% and 29% and median NPFS was 15 months. Rates of OS at 1- and 3-years were 100% and 95%. The median time to the administration of a systemic treatment after SBRT was 7.8 months (1.7-54.8).

Conclusions: SBRT is an effective and well tolerated treatment option in the management of lymph node metastases from PCa. Prospective trials are necessary to better select patients who benefit the most from this ablative focal treatment, and better define the recurrence patterns.

## CO019

### EXTENDED OR FOCUSED RADIOTHERAPY IN OLIGO-METASTATIC/OLIGO-RECURRENT PROSTATE CANCER: LONG TERM CANDIOLO EXPERIENCE

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Aims: Recent technology advances in diagnostic and radiotherapy (RT) field have allowed to early detect and early treat oligo-metastasis/oligo-recurrences prostate cancer (OMPC) paients (pts). The aim of this paper is to present our experience in RT of OMPC pts focusing on local-locoregional control, toxicity and time to recurrence.

Methods: From October 2010 to December 2018, we treated 61 pts [mean age (min-max): 61 (45-77), Karnofsky: 80-100] with node and/or bone recurrences from prostate cancer. All patients received functional imaging (by 68Ga-PSMA ligand /CT-PET in 21 patients, 18 choline /CT-PET in 40 pts and also multiparametric MRI in 6 patients). Pts were treated according our Internal protocol and they signed an informed consent form. The recurrence sites were nodal in 57 (pelvic in 36 pts, lumbar aortic in 21 pts), bone in 4 pts. For each pts number of metastases ranged between 1 and 5 (mean 2.5) for group 1 (extended RT) and between 1 and 2 lesions for group 2 (focused RT) . Thirty-nine pts (group 1) were treated by IMRT-SIB-IGRT with Tomotherapy on regional node with prophylactic doses (range 51-54 Gy – 1.7-1.8 Gy per fraction) and on positive nodes from 66Gy (2.2 Gy per fraction) to 70,5 Gy, (2.35 Gy per fraction). Twenty-two pts (group 2) were treated with targeted RT on lesions by Tomotherapy (18 pts) (doses: 24-30 Gy in 4-5 fractions) or SBRT LINAC-based (4 pts) (doses 18-24 Gy in single fraction).

Results: No GU/GI acute or late toxicity >G2 (RTOG scale) were observed in both groups. All constraints for normal tissues were respected according to QUANTEC. The mean follow up was 51 months (range 10-91) in the group 1 and 18,4 months (range 6-29) in the group 2. In the group 1, 6 pts dead for progression disease and 5 were lost at follow up; local control (LC) and loco-regional control (LRC) were 96.7% and 75% respectively, and the average time to recurrence was 24 months (range 3-91); the site of recurrence was loco-regional in 15 pts, bone in 3 pts and both in 2 pts; 4 pts developed visceral and nodal metastases. In the group 2, LC was 100% and average time to recurrence was 6.7 months (range 1-13). The sites of recurrence in this group was loco regional (pelvic) in 7 pts; to date, 3 pts showed biochemical relapse.

Conclusions: To date, our data show better results in terms of time to recurrence in the group of extended RT compared to targeted RT, despite similar LC and treatment tolerance, suggesting that targeted RT do not always translates into a good oncological results and that each case needs a multidisciplinary evaluation. Moreover, two groups are not comparable in terms of follow-up time, and a longer follow up is necessary for group 2.

## CO020

### SBRT FOR OLIGOMETASTATIC PATIENTS ON THE LUNG. A MONO-ISTITUTIONAL EXPERIENCE ON 987 TREATED LESIONS

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Aims: Patients with oligometastases to the lung from solid tumors are now considered candidates for curative therapy. Uncertainties on the patients selection and the relationship with systemic therapies are still not well defined. We study the results in terms of LC, OS, toxicity and progression modality in 409 pts treated whit SBRT for pulmonary oligometastases from different primary tumors.

Methods: Between December 2010 and December 2018, 456 pts were treated with SBRT on 987 lesions. Primary cancer was lung in 42%, colorectal in 27%, breast in 6%, H&N in 3%, Kidney in 4% and 18% others. All lesions was contured on CT scan data sets acquired in supine position using wing board and dual legs. CT was acquired in breath hold using Active Breathing Coordinator device in 354 pts, for 48 pts was used a 4D CT. Treatments were planned using MONACO TPS with Montecarlo optimization algorithm. Median target volume was 3,24 cc. The median dose of 33,2 Gy was prescribed to 70% isodose with median BED at the isocenter of 118Gy in 1 to 3 fx (median 3fx). Treatment was delivered by 6MV Linac . Set-up and isocenter position assessed by CBCT. Toxicity was evaluated using CTCAE v 4.0

Results: With median follow up of 22 months, median OS was 56m, DFS was 16m and median LC 18m. 38 pts relapsed in the treatment field, 91 pts in the chest and 246 showed extra pulmonary recurrences. Statistically significative differences on OS was observed between patient with primary controlled or not (2y, OS 88% vs 60%), with metachronous vs synchronous metastases (2y, OS 97% vs 63%), chemotherapy or not after SBRT (2y, OS 86% vs 52%). 5y OS for patients treated for breast metastases was 87%, for colorectal cancer 51% and for NSCLC 61%. No significant differences on LC was detected between different primary tumors. LC rates appears relate only to BED value. Toxicity was mild and not exceeded the grade 2.

Conclusions: SBRT appears as safe and effective therapy showing high rate of LC of pulmonary metastases using BED value exceeding 100Gy. The influence on OS appears to be related to the time of metastases appearance (synchronous vs metachronous), primary tumor controlled or not and the use of chemotherapy after SABR. The rate of OS, confirms the possibility to use of SABR with curative intent in well selected oligometastatic patients. The better rates of OS occurs in pts treated for breast and lung cancer. The majority of failures was represented by extra thoracic spread, leading to necessity of more effective systemic therapies.

## CO021

### STEREOTACTIC FRACTIONATED RADIOTHERAPY IN CHOROIDAL METASTASIS

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Aim: The purpose of this study is to demonstrate safety and feasibility of Stereotactic Fractionated Radiotherapy[SRT] in choroidal metastatic patients and to evaluate clinical outcomes in terms of local control and toxicity.

Materials and Methods: Thirty-six pretreated patients [pts] were evaluated: one had histological confirmation, the others had a clinical and/or radiological diagnosis. Eye examination, Ultrasound and Ocular Computed Tomography were performed in every patient to evaluate visus. All of them received SRT + Photo-Dynamic Therapy between November 2009 and August 2017. Thirteen patients were males (36%), 23 were female (64%); 15 of 36 had bilateral localizations (42%), with 51 eyes overall treated. Nine patients (25%) received a boost on small volumes. Median age is 61,5 (34-85), median follow-up 11,5 months (2-64). Primary tumor site was breast cancer (17/36, 47%) and lung carcinomas (12/36, 33%); the remaining were esophageal, HCC, kidney, bladder, prostate and pancreatic carcinomas. All pts were pretreated with chemotherapy; 31/36 (86%) had also extraocular metastasis. CT scan was performed in every pts and 4/36 (11%) underwent MR. Localization was performed with Leksell Type relocatable Stereotactic Frame (BrainLab, Germany). The CTV included all choroid and macro-

scopical lesions; 3mm isotropic expansion was added to CTV to define PTV. Omolateral lacrimal glands was partially, if possible, excluded from PTV. Acute radiation-induced toxicity was assessed according to RTOG scales; as Organ at Risk, conjuntival mucosa, lacrimal glands, brainstem, brain and lens were evaluated. RT treatments were non-coplanar 3D Conformal RT (21/36,58%), Step-and-shoot Intensity Modulated RT [IMRT] (10/36, 28%) and Arc-Therapy (5/36, 14%).

Results: All pts completed the prescribed treatment. Total dose ranged from 12 to 36 Gy (median 30 Gy), number of fractions was between 5 and 18; boost was from 0,75 to 12 Gy. Median BEDGy10 was 35.01Gy10 (15,6-44,8), Median BEDGy3 was 50Gy3 (24-60). Response rate resulted in: Complete Response 4/36 (11%), Partial Response 15/36 (42%), Stable Disease 12/36 (33%), Progression Disease 5/36 (14%). Toxicity was low: G3 adverse event, consisting in severe conjuntival hyperemia, has occurred in 1/36 pts(3%).

Conclusions: Stereotactic Fractionated Radiotherapy in choroidal metastases is a feasible and safe procedure, characterized by low toxicity and by the possibility to spare most of the optical nerves and the whole brain.

## CO022

### SURGERY FOLLOWED BY HYPOFRACTIONATED RADIOSURGERY ON THE TUMOR BED IN OLIGO-METASTATIC PATIENTS WITH LARGE BRAIN METASTASES. RESULTS OF A PHASE II STUDY

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Aims: This prospective phase II study assessed safety and feasibility of surgery followed by hypofractionated radiosurgery (HSRS) on the tumor bed in oligometastatic patients with single large brain metastases (BMs).

Methods: Between June 2015 and May 2018 101 patients were enrolled. Oligometastatic disease was defined by a maximum of 5 metastatic lesions. Hypofractionated radiosurgery on the tumor bed inplaced of WBRT. HSRS was performed within 1 month from surgery and consisted of 30 Gy/3 fractions.. Local control, occurrence of new BMs, overall survival, and treatment related toxicities were assessed.

Results: At a median follow up time of 26 months local recurrence occurred in 6 (5.9%) patients. Six-month, 1, 2-year local control rates were 100%, 98.9%±1.1%, 85.9%±0.6%. New BMs occurred in 39 (38.6%) patients; median brain-distant-progression time, 6-month 1, 2-year brain-distant-progression rates were 39 months (95%CI 19-39months), 17%±3.7%, 31.4%±4.8%, and 42.5%±5.9%. At the last observation time 50 (49.5%) patients are alive and 51 (50.5%) dead; 10 patients died for neurological cause and 40 for systemic progression. Median overall survival time, 6-month 1, 2-year OS rates were 22 months (95%CI20-30months), 95%±2.1%, 81.9%±3.8%, and 46.6%±6%. Infratentorial site, residual-tumor-volume, longer interval time between primary diagnosis and occurrence of BMs, and oligometastatic disease status significantly influenced outcome. Grade 2-3 radionecrosis occured in 26 patients. Neurocognitive functions remained stable or in some cases improved.

Conclusions: Surgery followed by HSRS on the tumor bed, is a safe and effective approach, affording good brain control with negligible toxicities. BMs does not always define a disease with worse prognosis, provided that a really ablative local treatments is carried out.

## CO023

### RADIOSURGERY (SRS) REIRRADIATION OF BRAIN METASTASIS (BM) FROM BREAST CANCER

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Purpose: To assess the clinical outcome and toxicity of reirradiation with SRS after prior WBRT, as a salvage treatment for progressive BM in patients with metastatic breast cancer.

Methods: From December 2001 to December 2017, 128 patients with 259 recurrent BM after WBRT were reirradiated with SRS. In this report, we have retrospectively analyzed only patients with brain metastatic breast cancer (BMBC).

Results: 35 BMBC patients with 79 BM were studied. Median age was 55 years (range, 35-82). 21 (60%) patients were HER +, of which 7 (33%) and 14 (67%) were ER- and ER+, respectively. 5 (14%) patients were triple-negative while the remaining 9 (26%) had a luminal-like breast cancer. 15/21 (71%) of HER+ patients, received trastuzumab between WBRT and SRS, in all cases targeted therapy was stopped at least 7 days before reirradiation. The median KPS was 100 (range, 60-100), 30 (86%) patients had a Neurological functional status (NFS) of 0, 4 (11%) and 1 (3%) a NFS of 1 and 2, respectively. 29 (83%) patients had a controlled extracranial disease. Median time between WBRT and SRS was 16 months (range, 2-92). The median number of reirradiated BM was 2 (range, 1-4) and the median tumor volume was 0.9 cc (range, 0.1-18.6). Prior WBRT doses ranged from 10 fractions of 3 Gy (66%) and 5 fractions of 4 Gy (34%), SRS re-treatment median dose was 18 Gy (range, 15-25). Three months after reirradiation, 9 (11%) BM were in complete remission, 19 (24%) in partial remission, 49 (62%) were stable and only 2 (3%) progressed, resulting a brain control of 97%. 17 (48.5%) patients had an out-field relapse after a median time of 12 months (range, 3-34): 5 (29%), 2 (13%), 5 (29%) and 5 (29%) patients received SRS, WBRT, chemotherapy, and supportive care, respectively. Among patients with out-field relapse: 9

(53%) were HER+, 3 (18%) triple-negative and 5 (29%) Luminal-like. At the time of analysis, all patients have died: 15 (43%) for brain progression, 10 (28.5%) for systemic progression and 10 (28.5%) for both cranial and systemic progression. The median OS from reirradiation with SRS was 14 months (range, 3-82), 12, 14 and 15 months in HER+, triple-negative and luminal-like patients, respectively. No acute and/or late toxicities were registered.

Conclusions: Reirradiation with SRS is an effective and a safe treatment for selected BMBC patients. Patients selection should be based on good KPS and NFS, controlled extracranial disease and 1 to 4 BM.

## CO024

### HYPOFRACTIONATED STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN THE TREATMENT OF PULMONARY METASTASES: A SINGLE INSTITUTION EXPERIENCE FROM A TERRITORIAL HOSPITAL

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Aims: To retrospectively analyze the feasibility and the efficacy of Stereotactic Body Radiation Therapy (SBRT) in the treatment of pulmonary metastases from multiple primary cancers.

Methods: Between January 2010 and December 2018, 146 patients (54 female, 92 male) were treated with SBRT (169 lesions). Median age was 72 years (range 43-90) and Karnofsky PS ≥ 70. Different doses and fractionation were used, based on patient's status, respiratory conditions, volume and site of the lesions. Irradiation was performed with 6 to10 MV X-ray beams from a LINAC Trilogy by Varian Medical Systems. Used techniques were conformal dynamic arcs, IMRT or VMAT. From 2016, a Maximum Intensity Projections (MIP) was performed for target volume generation in 4D CT scans. Used Treatment Planning System was Ray Station 4.5 or Pinnacle 9.10. Toxicity was evaluated using the CTCAE 4.03. Response, progression or stable disease (SD) were defined according both to RECIST criteria and respiratory function.

Results: Treated sites were metastases from primary lung cancer (93), colorectal (22), kidney (9) and others (22). Twenty five (17,1%) patients were treated on more than one lesion. The patients reported in this analysis were considered unfit for surgery due to medical contraindications. Median SBRT dose was 40 Gy (range 16-50 Gy) mainly in 5 fractions (range 1-8). Median follow-up was 12 months (range 1-86). No patients presented complete radiological response. A radiological partial response and stable disease (SD) were documented in 46 (31,5%) and 49 (33,6%) patients respectively. A respiratory improvement was observed in all of them. Disease recurrence or progression after SBRT occurred in 51 (34,9%) patients. A median disease-free interval from SBRT to recurrence or progression was 13 months (range 2-52). No patients experienced acute toxicity of grade ≥2 or other late adverse events. When the dose/fraction was higher than 8 Gy a prophylactic therapy with steroids was proposed. The 2-years OS was 64%.

Conclusions: Hypofractionated SBRT is an effective tool in the management of patients with pulmonary metastases. Even if lesions from different primaries were treated using various fractionation schedules and modalities, SBRT achieved acceptable tumor control with minimal toxicities. Our results suggest that a careful patient selection would be desirable in to determine the benefit of this treatment option.

## CO025

### ABSTRACT WITHDRAWN

## CO026

### THE DOSIMETRIC IMPACT OF AXILLARY NODES CONTOURING VARIATION IN BREAST CANCER

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Aims: To investigate the dosimetric impact of axillary nodes contouring variation in breast cancer (BC).

Methods: 19 radiotherapy (RT) centres were asked to create the planning target volume (PTV), named as Single Centre PTV (SCPTV) from the clinical target volume (CTV) they had delineated in a previous investigation, (Single Center CTV,SCCTV) and to plan the locoregional treatment. The SCCTV comprised the axillary nodes of 3 BC patients with different anatomy, candidate to receive RT. The 3 corresponding gold standard (GS) CTVs (GSCTV) were created from a consensus using the STAPLE algorithm. For each patient, the GS PTV (GSPTV) was obtained by applying each single centre's CTV to PTV margins to the GSCTV. The following Dose Volume Histogram (DVH) parameters for each centre's SCCTV, GSCTV, SCPTV and GSPTV of the 3 patients were compared: dose delivered to 99%, 98%, 95%, 2% and 1% of the volume (D99, D98, D95, D2, D1, respectively), the mean dose delivered (Dmean) and the volume receiving 95% of the dose (V95). Statistical analysis included mean value, standard deviation (SD), 95% confidence intervals (95% CI) and p-value.

Results: Data are available for 18 out of 19 centres. Seventeen centres used Intensity Modulated RT. The CTV to PTV margins ranged from 0 to 10 mm (median, 5 mm). Each centre's DICOM dose distribution, structure set and corresponding computed tomography (CT) data were imported into MIM v6.1.7 [MIM Software Inc.]. Results are shown in Table 1. GSPTV Dmean was on average 4% of prescribed dose lower than that of SCPTV. Considering all patients, the mean difference in D99, D98 and D95 between the SC-PTV and GS-PTV was statistically significant, ranging from 22.24% to 34.30%. Mean D2 was always lower than 107%, both for GSPTV and SCPTV, while mean D1 was higher than 105% only in one patient. SCPTV V95 was always higher than 90%, whereas GSPTV V95 was always lower than 90%. By analyzing results related to CTV, it has been found that, on average, the GSCTV coverage was better than the GSPTV coverage, as the GSCTV V95 was respectively 12.18%, 10.57% and 10.95% higher than GSPTV V95.

Conclusions: Axillary nodes CTV delineation variation led to significant reductions in dose delivered to GSPTV. No plans achieved acceptable GSPTV coverage, as V95 was always lower than 90%. The poor ideal plan coverage outlined the dosimetric impact of axillary nodes contouring variability and the need for delineation training and standardization.

**Table 1. Dosimetric results for the axillary nodal SCPTV and GSPTV of the three patients analysed**

| | | PTV | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D99 | | D98 | | D95 | | D2 | | D1 | | V95 | | Dmean | |
| | | SC | GS | SC | GS | SC | GS | SC | GS | SC | GS | SC | GS | SC | GS |
| Patient 1 | Mean | 89,76% | 50,47% | 92,15% | 57,22% | 94,87% | 69,46% | 104,13% | 103,93% | 104,59% | 104,44% | 92,77% | 73,40% | 99,78% | 94,94% |
| | SD | 8,28% | 19,04% | 5,80% | 18,55% | 3,87% | 15,06% | 2,16% | 2,16% | 2,29% | 2,30% | 9,93% | 12,56% | 1,83% | 3,11% |
| | Difference | **39,29%** | | **34,93%** | | **25,41%** | | **0,20%** | | **0,16%** | | **19,37%** | | **4,84%** | |
| | 95% CI | 27,84% | 50,75% | 24,37% | 45,49% | 17,21% | 33,61% | 0,09% | 0,30% | 0,05% | 0,26% | 13,68% | 25,06% | 3,30% | 6,39% |
| | p-value | 0,000001 | | 0,000002 | | 0,000005 | | 0,001118 | | 0,005817 | | 0,000002 | | 0,000004 | |
| Patient 2 | Mean | 90,07% | 63,96% | 92,36% | 70,08% | 94,99% | 80,02% | 104,39% | 104,35% | 104,97% | 104,99% | 94,11% | 79,48% | 99,83% | 96,84% |
| | SD | 8,67% | 14,67% | 6,18% | 13,24% | 3,65% | 10,23% | 2,59% | 2,77% | 2,85% | 3,08% | 6,76% | 10,65% | 1,79% | 2,62% |
| | Difference | **26,12%** | | **22,28%** | | **14,98%** | | **0,03%** | | **-0,02%** | | **14,63%** | | **2,99%** | |
| | 95% CI | 18,51% | 33,72% | 15,96% | 28,60% | 10,26% | 19,69% | -0,20% | 0,27% | -0,28% | 0,23% | 10,64% | 18,62% | 1,89% | 4,09% |
| | p-value | 0,000002 | | 0,000001 | | 0,000005 | | 0,760137 | | 0,865542 | | 0,000001 | | 0,000028 | |
| Patient 3 | Mean | 88,28% | 50,78% | 90,94% | 56,60% | 94,22% | 67,90% | 104,93% | 104,79% | 105,50% | 105,42% | 91,38% | 77,28% | 99,93% | 95,57% |
| | SD | 9,58% | 21,87% | 7,59% | 22,71% | 4,83% | 22,24% | 3,26% | 3,25% | 3,50% | 3,51% | 10,43% | 11,10% | 2,29% | 3,56% |
| | Difference | **37,50%** | | **34,34%** | | **26,32%** | | **0,14%** | | **0,08%** | | **14,10%** | | **4,35%** | |
| | 95% CI | 24,35% | 50,65% | 20,89% | 47,79% | 13,54% | 39,10% | -0,04% | 0,32% | -0,19% | 0,34% | 9,53% | 18,67% | 2,48% | 6,22% |
| | p-value | 0,000021 | | 0,000068 | | 0,000527 | | 0,127789 | | 0,543155 | | 0,000009 | | 0,000170 | |

## CO027

## SURVEY IN RADIATION ONCOLOGY CENTRES OF TUSCANY AND UMBRIA REGIONS ON ADJUVANT RADIOTHERAPY IN BREAST CANCER: INDICATIONS, VOLUMES, FRACTIONATION

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Aims: On behalf of the Italian Association of Radiation and Clinical Oncology (AIRO), the Tuscan - Umbrian Section conducted a survey to evaluate the management of drainage lymph nodes in breast cancer (BC) patients, in order to identify practice patterns.

Methods: an electronic questionnaire was sent to all Radiation Oncology Centers in Tuscany and Umbria,

with three clinical cases, which could be included in the so-called "gray areas", asking for: 1. whether radiotherapy (RT) was indicated or not 2. if drainage lymph nodes (supra/infraclavicular and/or axillary nodes) should be included in treatment volume 3. which dose/fractionation should be advisable.

Results: A total of 15 questionnaires were returned. For case 1, RT after mastectomy and lymph node dissection (LND) for infiltrating lobular carcinoma pT1c (m) pN1a (2/4), G3 ER 98%, PgR 100%, Ki 67 45%, cerB2 negative, was proposed in only 7/15 cases (46.6%). The majority would irradiate wall and drainage lymph nodes excluding the axillary nodes (AN). Conventional fractionation was chosen by all the Centers except for one that would prefer hypofractionation (40 Gy/15 fractions). The bolus was used only by 2 Centers. For case 2, RT after breast conservative surgery (BCS) and sentinel node biopsy (SNB) for infiltrating ductal carcinoma with neoplastic diffusion at 3 of the 5 removed sentinel lymph nodes (SNs), of which 1 macro and 2 micrometastatic SNs, pT1cpN1a (3/5), G2 ER95%, PgR 30%, Ki 67 18%, cerB2 negative, was proposed in all cases. Six over 15 Centers would include in RT volume the supra/infraclavicular nodes (S/I Ns) and of these, 5 would also irradiate the AN. Conventional fractionation was chosen by all the Centers except for 4. For case 3, RT after neoadjuvant chemotherapy, BCS and LND for multifocal infiltrating ductal carcinoma with 1 macrometastatic and 1 micrometastatic lymph node out 18, ypT2 ypN1a (2/18), G2 ER 100%, PgR 60%, Ki 67 15%, cerB2 negative, was proposed in all cases. The majority (12 Centers) would include in RT volume the S/I Ns and of these, 4 would also irradiate the AN. Conventional fractionation was chosen by all the Centers except for 3.

Conclusions: This survey illustrates the very different current practice patterns for management of drainage lymph nodes in 15 Radiation Oncology Centers in Tuscany and Umbria. This difference reflects an important limit that exists today due to the lack of consolidated data. More clinical trials and collaboration are needed.

**CO028**

## PRE-SPECIFIED INTERIM ANALYSIS OF THE SAFE TRIAL: A 4-ARM RANDOMIZED, DOUBLE-BLIND, CONTROLLED STUDY EVALUATING THE EFFICACY AND SAFETY OF CARDIOTOXICITY PREVENTION IN NON- METASTATIC BREAST CANCER PATIENTS TREATED WITH ANTHRACYCLINES WITH OR WITHOUT TRASTUZUMAB

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Aims: SAFE trial (NCT2236806) is a phase 3 study comparing the effect on subclinical heart damage of bisoprolol (B), ramipril (R), or both drugs (R+B), as compared to placebo (P), in breast cancer treated with (neo)adjuvant anthracyclines +/- trastuzumab.

Methods. Primary endpoint is subclinical cardiotoxicity measured with echocardiography and global linear strain (GLS). This interim analysis was pre-specified on the first 120 patients who had completed cardiological assessments at 12-mos. Stopping rules per arm were: dose reduction >15%, study withdraw rate >5%, and no significant impact on 3D-left ventricular ejection fraction (3D-LVEF) as compared to T0 at 12-mos assessment.

Results: A total of 191 out of 480 patients have been enrolled; overall 123 patients were available for the analysis (P=34; R=28; B=31; R+B=30). GLS increased at 3-mos (5.7%; $p<0.001$), at 6-mos (7.8%; $p<0.001$) and at 12-mos (7.1%; $p<0.001$) respect to T0 in P; at 3-mos (2.7%; $p=0.002$), at 6-mos (3.2%; $p=0.014$), but not at 12- mos in R; no significant changes at 3-mos, a significant increase at 6-mos (2.7%; $p=0.035$), at 12-mos (3.2%; $p=0.008$) in B; no significant changes at 3-, 6-, and 12-mos in R+B. Arm differences were significant ($p=0.002$). Both R+B and the R arms showed a withdraw rate of 7%, with a dose reduction rates of 21% and 17%, respectively. 3D-LVEF decreased at 3-mos (-3.3%; $p<0.001$), at 6-mos (-5.2%; $p<0.001$) and at 12-mos (-3.7%; $p=0.004$) respect to T0 in P; at 3-mos (-2.4%; $p=0.001$), at 6-mos (-1.9%; $p=0.010$), at 12-mos (-2.2%; $p=0.045$) in R. In B and R+B patients no significant changes were observed at 3- and 12-mos, with a decrease at 6-mos (-2.5% and 3.0%, respectively; $p=0.002$). Arm differences were significant ($p=0.038$). R arm showed a significant decrease on 3D-LVEF at 12-mos as compared to T0 and will be evaluate for closure.

Conclusions: At the interim analysis, a cardiopreventive treatment significantly decrease subclinical heart damage; definitive results will be useful to define the most effective treatment.

## CO029

### ABSTRACT WITHDRAWN

## CO030

### FEASIBILITY RESULTS OF PHASE II CLINICAL STUDY FOR THE PREOPERATIVE TREATMENT OF OPERABLE OR BORDERLINE OPERABLE PANCREATIC ADENOCARCINOMA WITH CHEMOTHERAPY AND CARBON ION HADRONTHERAPY (PIOPPO TRIAL)

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Background: PIOPPO is a prospective, phase II, multicentre, single-arm study started at CNAO to assess the efficacy and the feasibility of the neoadjuvant administration of 3 cycles of FOLFIRINOX followed by a short-course of carbon ion radiotherapy (CIRT) for resectable (Rpc) or borderline resectable pancreatic adenocarcinoma (BRpc).

Aim: Primary endpoint is local progression free survival and secondary endpoints are overall survival, R0 resectability rate and treatment toxicity.

Methods: Thirty patients will be enrolled in the study, the sample size being defined with an expected probability of success proportion of success at 24 months of 60% vs 35% (H0: p <= 0.35-H1: p> 0.35). Enrolled patients will undergo the scheme FOLFIRINOX for 3 cycles of FOLFIRINOX followed by CIRT. CTV is defined as GTV with a 5-mm margin and the locoregional elective lymph node and neuroplexus region according to Japan Pancreas Society classification. PTV includes the CTV with a 5-mm margin to account for set up uncertainties and residual tumor motion. The Anzai system will be used to acquire the patient breathing signal for retrospective 4D CT reconstruction and treatment plans will be optimized on the CT scan corresponding to the maximum expiration phase. Treatment is performed combining gating and rescanning with a ≈1s gating window centered around the maximum expiration phase. Patients will receive CIRT at the dose of 38.4 GyRBE carried out in 8 fractions, 4 fractions per week. Before surgery, restaging CT scans will be performed to evaluate resectability and absence of systemic progression. 4 to 6 weeks after the completion of CIRT, patients will undergo pancreaticoduodenectomy (for tumors of the pancreatic head) or distal pancreatectomy and splenectomy (for tumors of the body/tail). Tumor regression grade will be evaluated according to Evans score. Adjuvant chemotherapy will be expected from 30 to 40 days after surgery as expected in clinical practice.

Results: Since January 2018 six patients have been so far enrolled and five have completed the surgical phase. No significant acute toxicities, including surgery-related were observed.

Conclusions: Our preliminary results suggest that CIRT does not affect negatively the surgical approach. Our results provide initial evidence of the feasibility of the combined chemotherapy and CIRT in the neoadjuvant setting for Rpc or BRpc.

## CO031

### PREOPERATIVE SHORT-COURSE RADIOTHERAPY FOLLOWED BY DELAYED SURGERY IN ELDERLY PATIENTS WITH ADVANCED RECTAL CANCER: RESULTS AND TOXICITY

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Aims: Preoperative radiotherapy (RT), plus chemotherapy (CT) is associated with significant improvement in local control and better tolerance in advanced rectal cancer (RC), compared to postoperative RT. Many experiences have been conducted with short course RT (25 Gy/5), followed by immediate or delayed surgery. This schedule demonstrated favorable toxicity profile and comparable efficacy to "long" course radiochemotherapy. Purpose of this analysis is to evaluate the clinical outcomes of short-course RT followed by delayed surgery for elderly patients with advanced RC, unfit for long course therapy.

Methods: From 2009 to 2018, ninety patients with locally advanced middle-lower RC were treated with short-course RT. Fifty six (31 male and 25 female)

underwent to delayed surgery and the others were treated with palliative intent. Median age of the surgical patients was 77 (r. 65-88). The characteristics of patients and tumors are summarized in Table 1. Acute and late toxicities were assessed according to CTCAE 4.03.

**Table 1. Patients and Tumor characteristics.**

| Characteristic | N (%) |
|---|---|
| Median Age | 77 (range: 65-88) |
| **Gender** | |
| Female | 25 (45) |
| Male | 31 (55) |
| **Tumor distance from anal verge** | |
| ≤ 5 cm | |
| 6-10 m | |
| >10 cm | |
| **Clinical Stage** | |
| cT3 | 42 (75) |
| cT4 | 14 (25) |
| cN+ | 26 (46.4) |
| cN0 | 30 (53.6) |
| **Pathological stage** | |
| pT0 | 1 (1.8) |
| pT1 | 3 (5.3) |
| pT2 | 22 (39) |
| pT3 | 30 (53.9) |
| cN0 | 36 (64) |
| cN1 | 14 (25) |
| cN2 | 6 (11) |

Results: Clinical and pathological stages are reported in Table 1. The median follow-up was 70 months (r. 6-115). A 3D conformal RT was performed in a prone position. The clinical target volume (CTV) included the primary tumor, the mesorectal space and pre-sacral, internal iliac (up to the promontory) and obturator lymph nodes. The time to surgery was in a range of 6-22 weeks (mean 8) after RT end. The surgical resection was: low anterior in 41 patients (73,2%), abdomino-perineal in 12 (21,4%) and trans-anal in 2 (5,3%). Adjuvant CT (5-FU or capecitabine-based regimen) was administered to 15 patients (26,7%) on the basis of pathological stage. T and N histological down staging was reported in 35 patients (62,5%) and in 19 of the 38 cN+ (50%) respectively. One patient achieved pathologic complete response. Grade 1-2 acute gastrointestinal and genitourinary toxicity were found in 26% and 5.3% respectively. Early and late severe toxicities were not reported. Thirty four patients (60,7%) are alive without disease, Cancer related mortality and local recurrence rate were 17,8% and 21,4%, respectively.

Conclusions: Short-course RT with delayed surgery in unfit elderly patients may be a valid option in locally advanced RC. This analysis showed a considerable down staging of both T and N, with high rates of conservative surgery. The toxicity was acceptable, with low cancer related mortality and low local recurrence rate.

## CO032

## IMPACT OF MUSIC THERAPY INTERVENTION ON OXIDATIVE STRESS AND DEPRESSION IN BREAST CANCER PATIENTS UNDERGOING POSTOPERATIVE RADIOTHERAPY: A RANDOMIZED STUDY

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Aims: To evaluate the role of psychotherapy intervention with music therapy elements in early stage (pT1-2 N0-1) breast cancer patients (pts) during postoperative radiotherapy (RT).

Methods: This is a monocentric randomized perspective study involved Radiotherapy, Psychiatry and Physiology Institute of University Hospital "Maggiore della Carità" of Novara approved from our ethical committee. Since March 2018, 56 pts, candidates for adjuvant radiotherapy, were enrolled. Five patients left the protocol due to poor compliance. Pts were randomized in two arms: treatment as usual (TAU) or music psychotherapy group (PSY). Forty-nine patients received hypofractionated RT (40.5 Gy, 2.7 Gy/fx in 3 weeks or 45 Gy, 2.25 Gy/fx plus boost in 4-5 weeks) for pT1-2 and seven received conventional RT (50 Gy 2 Gy/fx in 5 weeks) for in situ carcinoma. PSY group also received psychoterapy with music therapy elements that consisted in a weekly session conducted by an experienced psychiatrist. Music therapy intervention was performed in small groups of 4-5 pts. At T0 (CT-simulation day), T1 (last RT day) and T2 (3-4 months after the end of RT) all pts performed blood samples to investigate GSH, MDA, TNF-α, IL-6, PCR, phospholipase A2, gamma tocopherol, lycopene levels. Psychometric evaluation was performed by Beck Depression Inventory, Montgomery-Asberg Depression Rating Scale, State-Trait Anxiety Inventory 1-2, Resilience Scale for Adults and Short Form-36 to assess depression, anxiety and resilience. Data of the two groups (TAU and PSY) were analyzed and compared by t-Student test.

Results: Twenty-seven pts were enrolled in the TAU and twenty-four pts in the PSY group. At T1, lipidic peroxidation markers were significantly reduced in PSY group ($p<0.05$). At T2, IL-6 levels resulted significantly lower than T0 in the PSY group, while an increasing trend at T1 and T2 was observed in TAU group. A reduction trend of gamma tocopherol/cholesterol and lycopene/cholesterol was observed at T2 in both grou-

ps. No significant difference of GSH and PCR levels was found between two groups. Psychometric tests are still under analysis.

Conclusions: Music therapy elements was a feasible and well accepted psycotherapy intervention in early stage breast cancer pts during postoperative RT. A significant reduction in lipidic peroxidations markers at T1 and in IL 6 at T2 was observed in the PSY group. Psychometric data are expected soon to complete the pts assessment.

## CO033

### AIEOP LH-2004 PROTOCOL FOR CHILDREN AND ADOLESCENTS WITH HODGKIN LYMPHOMA: RADIATION FREE AND LOW DOSE INFOLVED FIELD RADIOTHERAPY ARE SUFFICIENT IN COMPLETE REMISSION LOW AND STANDARD RISK PATIENT

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Aims: Low risk (GR1): to reduce treatment toxicity avoiding RT in pts with CR after CT. Standard risk (GR2) and high risk (GR3): to reduce RT dose delivered after 4/6 cycles of CT in pts in CR (complete disappearance, or ≥75% reduction of bulky masses, and metabolic response) or PR (<75% reduction at conventional imaging).

Methods: GR1, stages I-IIA without M/T >0.33 or >4 nodal regions or lung hilar adenopathy; GR2, pts not included in GR1 and GR3; GR3, stages IIIB-IV or pts with bulky disease (M/T>0.33). GR1 pts received 3 ABVD and 25,2 Gy only to PR pts after CT. GR2 pts received 4 COPP/ABV + 14.4 Gy to involved nodal regions if CR achieved; pts in PR received 2 further cycles of IEP (Ifosfamide, Etoposide and Prednisone) and RT (14,4 Gy if CR, 25.2 if PR). GR3 pts received 4 COPP/ABV and 2 additional COPP/ABV+RT if CR was achieved; in PR pts, 2 cycles of IEP were administered and 14.4 Gy if CR was obtained. If not, pts received 2 additional COPP/ABV and RT according to the quality of response. The response was evaluated after the 2nd and the 4th cycle and at the end of CT in GR3, by conventional imaging and with PET in pts with mediastinal mass.

Results: From June 2004 to April 2017, 1115 pts were eligible and 948 pts were evaluable for this analysis (M/F 1,24; median age 13 yrs; range 1,2-17,9) with a diagnosis by the end of December 2014. The median observation time is 56 months. NS is the most frequent histological subtype (78%); 158 (17%) pts were in GR1, 206 (22%) in GR2 and 584 (61%) in GR3 (41% of them due to bulky disease). The OS, EFS and FFP at 10 years are 93.8%, 76.7% and 80.5% respectively. The EFS at 10 yrs of GR1, GR2, GR3 are 84.4%, 80.3% and 74.1%. The FFP at 10 yrs is 87.8% for GR1, 88.2% for GR2 and 75.4% for GR3. GR1: 69% of pts achieved CR after CT and spared RT, with no statistical difference in FFP rates with pts who received RT because in PR (87,9% vs 87,8% at 10 yrs). GR2: 75,7% of pts received 14,4Gy because in CR at the end of CT, without any differences in FFP (88% vs 90% at 10 yrs) compared to pts treated with higher dose of RT because in PR at the end of CT. In GR3, in PR pts additional CT and RT dose did not succeed in overcome the gap (FFP 91,6% in CR pts vs 74,8% in PR pts at 10 yrs).

Conclusions: This HL trial shows that GR1 or GR2 pts in CR after CT may be successfully treated with a RT-free regimen (11%) or with low dose IF-RT (45%) respectively. In GR3 pts the additional CT and RT did not overcome the gap between CR e PR.

## CO034

### CARDIAC SUBSTRUCTURES DOSE SPARING IN PEDIATRIC HODGKIN'S LYMPHOMA

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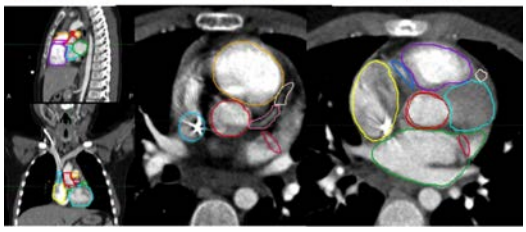
Aim: Pediatric Hodgkin's Lymphoma (HL) survivors represent a group of patients at high risk for clini-

cal and subclinical cardiovascular (CV) disease. The incidence of CV events increases over time from the diagnosis. Both chemotherapy and radiotherapy (RT) are responsible for cardiotoxicity. Often RT target is located near critical cardiac substructures (CS) such as origin of coronary arteries and cardiac valves. Thus, became important to assess the risk of long-term CV complications after therapy. In this study, we analyzed the dose received by different CS using intensity-modulated radiation therapy (IMRT) "butterfly" technique (BT).

Materials: Four pediatric HL (mean age 13) with stage II-IV and mediastinal bulky disease at diagnosis were treated with involved-site radiotherapy (IS-RT). Treatment plans were performed with TPS Pinnacle, planning a total dose range from: 14,4Gy in 8 fractions for patients enrolled in AIEOP LH 2004 protocol, and 28.8Gy in 16 fractions for patients enrolled in Euronet PHL C2 protocol. We use Contrast CT (cCT) for segmentation of CS, than we performed deformable image registration (DIR) in MIM Software to adapt organs at risk between cCT and Simulation CT. The following CS were contoured: right and left atrium, right and left ventricle, aortic, pulmonary, mitral and tricuspid valves, left main, left anterior descending, left circumflex and right coronary arteries. IMRT plans were generated using 5 co-planar beams (3 anterior 330°- 0°- 30° and 2 posterior 160°-210°) BT. We analyzed PTV coverage (mean dose -Dmean- and V95% -percentage volume receiving 95% of prescription dose-), and doses to CS (Dmax, Dmean).

**Table 1 and Figure 1.**

| ORGAN AT RISK | Maximum dose (Gy) ± SD | Mean dose (Gy) ± SD |
|---|---|---|
| Heart | 19,62 ± 5,47 | 5,18 ± 3,37 |
| Left ventricle | 12,11 ± 7,64 | 4,58 ± 4,24 |
| Right ventricle | 11,42 ± 6,71 | 3,50 ± 3,09 |
| Left atrium | 18,92 ± 7,58 | 8,02 ± 3,74 |
| Right atrium | 18,46 ± 6,00 | 5,24 ± 2,96 |
| Aortic valve | 10,14 ± 7,01 | 8,72 ± 6,47 |
| Pulmonary valve | 11,92 ± 6,20 | 9,63 ± 6,33 |
| Mitral valve | 3,78 ± 3,11 | 3,20 ± 2,39 |
| Tricuspid valve | 3,78 ± 3,26 | 3,24 ± 2,69 |
| Left main coronary a. | 17,63 ± 8,01 | 15,93 ± 7,89 |
| Left anterior descending a. | 16,29 ± 9,61 | 7,05 ± 4,43 |
| Left circumflex coronary a. | 16,02 ± 8,53 | 11,26 ± 6,76 |
| Right coronary a. | 11,61 ± 6,95 | 8,92 ± 6,55 |



Results: Dose sparing of CS, especially origin of coronary arteries and cardiac valves, is achievable with IMRT BT. In in case of overlap with target, priority is assigned to target coverage. We met following PTV coverage: V95%= 97±2% and Dmean =19Gy. Dose for CS are reported in table. Image represents an example of CS contouring.

Conclusions: Mediastinal radiation dose is the most important risk factor for the appearance of late CV disease in pediatric HL. Lower radiation doses for current protocols and IMRT BT treatment planning increase dose sparing for CS so that further reduction of cardiac late effects may be expected.

## CO035

## ADAPTIVE PROTONTHERAPY FOR PEDIATRIC PATIENTS WITH HEAD AND NECK PARAMENINGEAL RHABDOMYOSARCOMA

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Introduction: Protontherapy (PT) is an established treatment for pediatric malignancies because of the optimal target coverage and surrounding normal tissue sparing that can be achieved. This advantage can be lost if anatomical target changes occur, leading to alteration of the initial dose distribution. Our purpose was to monitor with scheduled re-planning Ct scans, initial plan dose alterations in selected complex pediatric malignancies such as parameningeal head and neck (H&N) rhabdomyosarcoma (PM-RMS).

Material and methods: At the Trento Protontherapy Center, from February 2018 to April 2019, 6 patients (pts) (3 male, 3 female) affected by H&N PM-RMS ( 3 embryonal, 3 alveolar) were studied. Median age was 9 years (range: 4-16); 2 pts had localized disease, 4 had neck lymph nodes metastases. Three pts required general anesthesia. PT was definitive for all of them. Staging was IRS III N1 for 4 pts and IRS III N0 for 2. Chemotherapy was administered according to the EPSSG 2005 protocol. PT dose to the low risk clinical target volume (CTV) was 50.4 Gy(RBE) delivered in 28 fractions of 1.8 Gy(RBE), followed by a boost of 5.4 Gy(RBE) in three fractions of 1.8 Gy(RBE) to the high risk CTV. Neck CTV mean dose was 43.6 Gy(RBE) (range: 41.4-50.4). Treatment plan was multifield optimization (MFO) for low risk CTV and single field optimization (SFO)for high risk CTV and neck CTV. Pts were monitored with a CT-on-rail sited in the treatment room. The nominal treatment plan was recalculated on the re-planning CT and if significant variations were found it was optimized again. The decision to re-optimize was taken in a case-by-case scenario considering dosimetric and clinical parameters. Pts were re-scanned regularly once a week for the first three weeks than accordingly to the clinical situation and to the findings of the re-calculation.

Results: All pts completed their treatment as scheduled without unplanned breaks due to side effects. The

total number of re-planning CT was 27, mean number for pt was 4 (range: 3-6). Two out of 6 ps had their plan optimized again 2 times each. Reason for re-optimization was paranasal sinuses mucous filling; in one case important weight loss contributed as well.

Conclusions: Our study demonstrate the feasibility and safety of prototherapy for pediatric H&N PM-RMS and the need for plan robustness close evaluation.

## CO036

### INCIDENCE OF SECOND MALIGNANCIES AMONG PEDIATRIC PATIENTS TREATED WITH HELICAL TOMOTHERAPY

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Aims: IMRT delivered with helical Tomotherapy (HT) has been increasingly applied in young patients with cancer. Concerns about a potential increase of radiation-induced malignancies (SMN) exist. The aim of this study was to determine the incidence of SMN among pediatric patients treated with HT.

Methods: We analyzed the incidence of SMN among 153 patients less than 24 yrs of age treated with HT since its introduction in 2006 to May 2014 at our Institution.

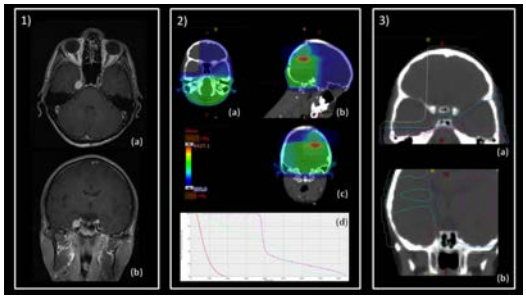

**Figure 1.**

1) Axial (a) and coronal (b) MR images demonstrating a right trigeminal neurinoma. The patient was completely asymptomatic. The lesion was found 12 years after HT for recurrent supratentorial ependymoma of the left parieto-occipital lobe. The patient was previously treated with 3DCRT 2 years earlier. The child was 11 years old at the time of the first treatment and 13 at the time of re-irradiation with HT. At the time of the study, the secondary benign tumor had just been totally resected and the patient was still in complete remission for ependymoma 14.5 years after diagnosis.
2) Axial (a), sagittal (b), coronal (c) images and DVHs (d) showing the dose distributions of HT and 3DCRT plan sum. 3DCRT-prescribed dose was 50.4 Gy in 33 fractions to the PTV (cyan). HT-prescribed dose was 36 Gy in 20 fractions (magenta). Radiation-induced trigeminal neurinoma is contoured in red.
3) Axial (a) and coronal (b) images showing radiation isodose 20 Gy (magenta), 18 Gy (blue), 7 Gy (cyan) and 2 Gy (white) generated by the plan sum. Radiation-induced trigeminal neurinoma is contoured in red. The delineated red volume recieved a maximum dose of 19.2 Gy, a minimum dose of 2.3 Gy and a mean dose of 7.8 Gy. The radiation-induced benign tumor arose within a low-dose region.

Results: Eighty-seven patients with a follow-up of at least 5 yrs after HT were included. The median follow-up was 7.6 yrs (5-12.7). The median age at HT was 14 yrs (1.5-24). Patients were irradiated with HT alone or in combination with other radiation techniques for CNS tumors (n=39), lymphomas (n=23), sarcomas (n=17), H&N cancers (n=5), or other histologies (n=3). Treatment sites were brain (n=25, 2 whole ventricular), mediastinum (n=22), craniospinal (n=14), H&N (n=7), pelvis (n=6), thorax (n=5, 2 total pleural), limbs (n=4), abdomen (n=3, 1 whole abdomen), spine (n=1). Median prescribed doses were 54 Gy for CNS tumors, 25.2 Gy for lymphomas, 50.4 Gy for sarcomas, 66 Gy for H&N cancers, and 15-21 Gy for the remaining cases. The cumulative incidence of SMN and radiation-induced benign tumors was 1% (1/87) and 2% (2/87), respectively. At a median follow-up of 7.6 yrs (5.2-12.7), 68 patients (78%) were alive in complete remission. Among these long-term survivors, a 13-y-o patient developed a secondary fifth cranial nerve schwannoma 12 yrs after HT for recurrent supratentorial ependymoma (Figure 1). A 17.5-y-o female affected by Hodgkin lymphoma developed a recurrent fibromatosis of the soft tissues of the breast region close to the central venous catheter insertion site within the irradiated area 5 yrs after HT (14.4Gy/8fr). At a median follow-up of 7.2 yrs (5-8.9), 10 patients (12%) were died of disease. One patient died because of esophageal cancer 7 yrs after total pleural irradiation for Ewing sarcoma of the thoracic wall (36Gy/20fr). The tumor arose within the high-dose volume. Nine patients (14%) were alive with disease without evidence of SMN at the time of the study.

Conclusions: This is the first report of SMN risk in children undergoing HT. With a follow-up of up to 12 yrs, HT resulted not associated with an increased risk of SMN due to low-doses to normal tissues as previously reported. Longer follow-up is required to determine how this risk compares to other IMRT techniques and proton therapy.

## CO037

### PITUITARY DEFICITS AFTER RADIOTHERAPY IN PEDIATRIC PATIENTS AFTER LONG TERM FOLLOW-UP

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Aims: To evaluate the risk of developing pituitary deficits in pediatric patients (pts) with CNS tumors treated with radiotherapy

Methods: We retrospectively analyzed patients with brain tumors, younger than 16 years, treated between 1996-2015 with a minimum follow up of 2 years after the end of radiotherapy. In this study, we evaluated three deficits: GH deficiency (GHD), ACTHD and TSHD. We registered the dose to the target and the mean dose to the organs at risk (OARs) analyzing the results related to hypothalamus and pituitary gland. Cumulative dosage for medulloblastoma, germinoma, glioma and ependymoma was calculated by the sum of

the cranio-spinal dosage and the dose received from the boost. The population was divided into four (4) groups depending on the dose of radiotherapy given: Group 1: 0-14 Gy, Group 2: 15-29 Gy, Group 3: 30-39 Gy and Group 4: ≥40 Gy.

Results: 88 patients have been identified: 20 pts were excluded because they presented hormone deficiency before starting radiotherapy, and 4 pts because they had an endocrinological follow-up of lower than 2 years. Therefore, 64 patients were evaluated: 32 medulloblastomas (50.0%), 17 gliomas (26.5%), 7 germinomas (10.9%), 3 ependymomas (4.6%), and 5 other histological types (7 8%) (2 Ewing sarcomas, 1 PNET, 1 pinealoblastoma, 1 AT/RT). 61 pts also underwent to chemotherapy and 42 to surgery. The mean pituitary dose in patients with GHD was 36.5±9.78 Gy (p 0.01), TSHD 38.0±6.0 Gy, ACTHD 34.6±10.5 Gy. Patients treated with 3DRT had a higher risk of developing GHD, ACTHD, and TSHD if compare with IMRT techniques (p<0,05).The "safe dose" under which no patient has shown GH deficiency is <10 Gy while for TSH and ACTH deficit is <20 Gy.

Conclusions: The data of our study underline the role of the dose delivered to the pituitary in the different radiotherapy techniques in the development of neuroendocrine late toxicity.

**CO038**

## RADIOTHERAPY IN A PLEURO-PULMONARY BLASTOMA OCCURING IN A 2-YEAR OLD MALE: A CLINICAL CASE REPORT

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Aims: Pleuro-pulmonary blastoma (PPB) is a malignancy of the lungs that accounts for 0,5% of all pediatric malignancies. It occurs in children less than 6 years of age. PPB is classified into three main types: type I is cystic, type II is mixed cystic and solid, and type III is solid and aggressive sarcoma. Tipe I has the best prognosis; type II and III have a 5-years survival rate of 53% , because of frequent relapse and distant metastases (brain, bone, liver, pancreas, kidney and adrenal gland). The patients with PPB usually develop respiratory symptoms: dyspnea, chest pain, cough, respiratory distress, pneumotorax, fever, persistent pneumonitis, , atelectasis.

Materials and Methods: A 2 year old male was admitted to the hospital Pediatrico Bambin Gesù (Rome) because of a hemorrhagic shock due to rupture of a right pulmonary mass. A chest computed tomography (CT) scan revelead a solid mass in the right lung, compression of the heart, ptosi of liver and right kidney and two subpleural micronodules on the left. He underwent a thoracotomy and biopsy that showed PPB type III. The patient received chemotherapy according to the EpSSG-RMS high risk protocol (with ifosfamide, vincristine, actinomycin, doxorubicine –IVaDo-for three cycles). Restaging chest CT showed a residual right disease and disappearance of the two micronodules.He underwent second gross total resection of the superior and medium lobe of the right lung and biopsy of the supraclavear pleura. Histological study confirmed residual PPB on the pleural tissue and necrosis on the lung. He received adjuvant chemotherapy ( for five cycles with regimen IVA-ifosfamide, vincristine, actinomycin D) that was well tolerated with no dose reduction. Restaging TC didn't show residual disease.

The colleagues of hospital Bambin Gesù contacted U.O. Radioterapia Oncologica Ospedale Policlinico San Martino of Genova to ask a comparison between their VMAT treatment plan and a plan elaborated with tomotherapy Hi-Art tecnology. The last one showed best results in term of target coverage and of organ at risk saving . So we decided together to treat the patient with tomotherapy. He received radiotherapy to the pleural cavity of the right hemythorax with 50,40 Gy in 28 Fractions (1,8 Gy/fx) with IMRT-IGRT technique using Tomotherapy Hi-art system in helical modality (treatment of 45 days). Plan was delivered in 650 seconds and the patient was under anesthesia. Tomotherapy plan was created with Field width 1,05, fixed and Pitch 0,287. The volume of PTV was 320 cc. The 95% of PTV is covered by 92% of dose.The difference between right lung and the PTV has an average dose of 35 Gy. To decrease left lung dose the "directional block" was applied.

Results: Radiotherapy was well tolerated: he only had G1 erythema according to RTOG tox. Last brain and chest TC didn't show recurrence of disease. The patient today is alive in complete remission (10 months after radiotherapy) and he is in maintenance chemotherapy. He didn't develop late side effects; he has a good respiratory function.

Conclusions: PPB is a rare and aggressive malignant tumor that arises from mesenchymal cells of the lung. The treatment is multimodal and includes surgery, chemotherapy and radiation therapy. In PPB the volumes that must be irradiated are large: with the help of the new technologies (such as the tomotherapy) we can treat the patients even if they are young.

## CO039

### IMPLEMENTATION OF A METHOD FOR HEART IRRADIATION: A CASE REPORT OF INTERATRIAL EWING'S SARCOMA

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Aims: Primitive neuroectodermal tumor and Ewing's Sarcoma of cardiac origin are rare entities among primary cardiac neoplasm.Ewing's Sarcoma occurs between the ages of 5 and 30. The tumor initially develops most frequently in bone, particularly in the pelvis.The disease has a high potential for metastases.

Methods: A 9 years old child went to the hospital for orsening asthenia, loss of appetite and low-grade fever in May 2018.A chest X-ray showed a significant increase in cardiac shadow associated with severe pleuric and pericardial effusion, with a "Swimming Heart" situation. The histological examination, performed at the Giannina Gaslini Institute in Genoa, of cardio-surgery in extra-corporeal circulation with the implant of pacemaker, showed the presence of a Sarcoma of the Ewing/PNET family, with negativity for neoplastic cell research in pleural and pericardial effusions. The child was initiated into the EW1 protocol (modified arm A). After chemotherapy, the child was given Radiotherapy at our Ospedale Policlinico San Martino. On the same day she underwent CT-scan with personalized thoracic-abdominal immobilization system (Orfit) and heart CT at Radiology at our Institute, with images fusion in order to plan treatment with maximum accuracy and minimise cardiac toxicity.The exam was done with CT Definition Flash (128x2 layers) before and after rapid somministration iodinate contrast agent, with performed on a Dual-Flash perspective spiral technique in diastole and systole and subsequent retrospective acquisition with perspective beam modulation and reconstructions in multiple phases of the RR range (0-100%) with an average heart rate of 93bpm. After collegial discussion we decide to give the child radiotherapy of the interatrial septum, evaluating during and after each session the heart rate. The child received 59.40 Gy in 33 fractions, 5 times/week with daily IMRT-IGRT technique using Tomotherapy, from 08/04/2019 to 30/05/2019 due to residual lesion after unradical surgery and Chemiotherapy.The PTV was defined with the Heart-CT considering the excursion of the right coronary., (systo-diastolic movement 7.5 mm in the longitudinal axis at the proximal tract, 9 mm at the medium tract and 9.5 mm at the distal tract) Table 1.

Results: Radiation therapy was well tolerated, with no evidence of acute toxicity.

Conclusions: This is a very rare localization of the Ewing's Sarcoma, but with the use of specific Heart CT could be possible give Radiation therapy to a moving organ.

**Table 1.**

| STRUCTURE | MAX DOSE (Gy) | MIN DOSE (Gy) | MEDIAN DOSE (Gy) | AVERAGE DOSE (Gy) |
|---|---|---|---|---|
| PTV | 61.37 | 54.85 | 59.22 | 59.17 |
| PTV-PRV | 60.59 | 54.85 | 58.43 | 58.21 |
| LEFT LUNG | 14.13 | 0.09 | 0.42 | 2.03 |
| RIGHT LUNG | 29.06 | 0.08 | 0.89 | 3.28 |
| VERTEBRAL COLUMN | 15.66 | 0.14 | 0.49 | 2.45 |
| RIGHT CORONARY ARTERY | 57.85 | 8.21 | 37.36 | 35.33 |
| RIGHT ATRIUM | 52.44 | 0.61 | 2.24 | 7.42 |
| RIGHT VENTRICLE | 60.03 | 0.53 | 2.85 | 10.51 |
| LEFT ATRIUM | 60.56 | 4.66 | 19.64 | 23.18 |
| LEFT VENTRICLE | 47.89 | 0.26 | 0.80 | 4.30 |
| SPINAL CORD | 11.47 | 0.17 | 0.45 | 2.36 |
| PRV-SPINE | 13.16 | 0.15 | 0.43 | 2.23 |
| LEFT CORONARY ARTERY | 12.23 | 7.37 | 10.76 | 10.24 |

## CO040

### USE OF AUTOMATIC FEATHERING ALGORITHM (ECLIPSE V.15) IN THE VOLUMETRIC-MODULATED ARC THERAPY (VMAT) PLANNING OPTIMIZATION FOR CRANIOSPINAL IRRADIATION

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Aim: Craniospinal irradiation (CSI) is often the treatment of choice for pediatric tumors like medulloblastoma or leukemia and lymphoma affecting the central nervous system (CNS). However, matching the cranial and spinal fields requires careful technical planning taking into account intra-fraction patient position inaccuracies that may cause cold and/or hot spots where the treatment fields overlap. The aim of this study is to compare the sensitivity of VMAT cranio-spinal technique to set-up errors between Eclipse v.13 and Eclipse v.15 with its new Automatic Feathering (AF) algorithm for craniospinal treatment planning.

Methods: AF algorithm was retrospective tested on two pediatric patients (1 medulloblastoma e 1 acute lymphatic leukemia affecting CNS) treated in our Institute, in supine position, with standard VMAT technique using Eclipse v.13. Both treatments had 3 isocenters (1 cranial and 2 spinal) and 2 junctions of 5 cm. Each plan was re-optimized using Eclipse v.15 with AF algorithm. The sensitivity of AF feature was evaluated

by shifting the isocenters of the brain plan closer towards the second isocenter by 1mm, 3mm and 5 mm simulating different set-up errors. The impact of AF algorithm was then evaluated by comparing maximum doses at fields junction. In order to asses field junction dose more accurately, single and total field dose profiles in CC direction were also compared for each simulated set-up error.

Results: For both patients we compared average maximum doses of Eclipse v.13 and Eclipse v.15 for different simulated setup errors (shifts) at the field junction. Respect to Eclipse v.13, Eclipse v.15 with AF algorithm reduced the average maximum dose for 3 mm shift of about 14% and for 5 mm shift of 22%. Figure 1 shows the dose profiles across the junction as a function of the different shifts for the most representative patient. Eclipse v.13 yields in an high and sharp peak that falls outside of the junction, while Eclipse v.15 yields in a slight increase that spreads over the entire junction.

Conclusions: This study proved that AF algorithm is able to effectively optimize the dose distribution where the treatment fields overlap avoiding cold and hot spots due to intra-fraction setup errors. Future developments of this study will concern about the possibility of further reducing hot and cold spots due to setup errors considering different junction extensions and a greater number of patients.

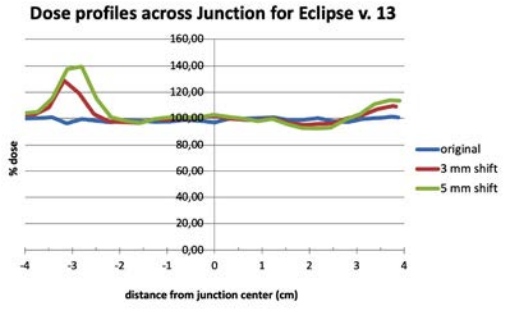


**Figure 1a**. Dose profiles across the junction for different simulated setup errors (shifts) with Eclipse v.13

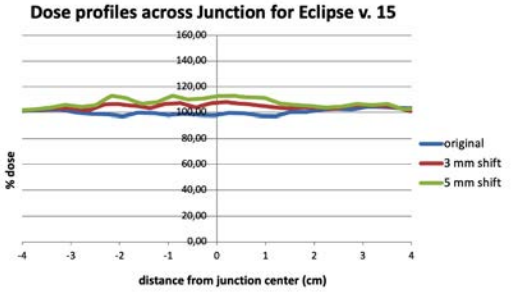


**Figure 1b**. Dose profiles across the junction for different simulated setup errors (shifts) with Eclipse v.15

**Figure 1.**

**CO041**

## THE FAST APPROACH AS ADJUVANT WHOLE BREAST IRRADIATION FOR FRAIL BREAST CANCER PATIENTS

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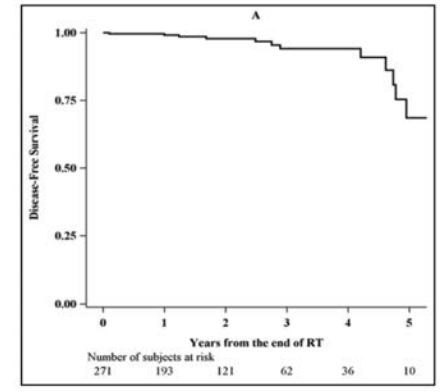
Aim: To evaluate the outcome in terms of toxicity, local control and survival of elderly breast cancer (BC) patients treated with adjuvant once-weekly hypofractionated radiotherapy (RT).

Methods and Materials: From 7/2011 to 7/2018, 271 BC patients were given received 5.7 Gy once a week for 5 weeks to the whole breast, without boost to the tumor bed (total dose 28.5 Gy), after breast conserving surgery. Patients were eligible if affected by T1-T3 invasive BC, with no or limited axillary involvement. The scheme was offered to elderly women (age threshold of 65 years) and to those with commuting difficulties or disabling diseases.

**Table 1. Disease free survival for all the patients.**




| | Events * | 1-yr DFS (95% CI) | 3-yr DFS (95% CI) | HR univariate (95% CI) |
|---|---|---|---|---|
| All patients | 13/257 (5.1%) | 99.1 (96.4-99.8) | 94.2 (87.4-97.4) | - |

* Local, locoregional and distant recurrence, second tumor, death

Results: Median age was 76 (45.5-86.4) years. Median follow-up was 24.6 (6.2-65.7) months. Most of BC were T1 (77%), while the remaining were T2 (22.2%), T3 (0.4%). Axillary status was negative in 68.3%, minimally involved in 14.4% (pN1) and not assessed in 17.3% of the cases (Nx). Most of the

women received hormonal therapy (84%), while 10.7% received chemotherapy. The schedule was delivered either with three-dimensional conformal RT (n=133) or with intensity modulated RT (n=138). No statistically significant difference was observed between the two techniques in terms of toxicity and efficacy. Maximum acute toxicity at the end of RT for 271 patients was as follows: grade (G) 1, 2 and 3 erythema in 63%, 7% and 0.4% of patients, respectively. G2 edema was detected in 10% of patients. Desquamation occurred in 4.4% as G1 and 1.5% as G2 of cases. At median 2-year follow up, LENT-SOMA assessment was available for 137 patients. Fibrosis (G1 and G2 in 46.7% and 9.5%, respectively) and skin changes (G1 and G2 hyper- or hypo-pigmentation in 29.2% and 2.2% respectively, G1 and G2 telangiectasia in 3 patients) were observed. A minority complained pain of G1 (n=26) and G2 (n=2) intensity. Two-year oncologic outcome was assessed for 257 patients. At the last follow-up examination, 244/257 patients were alive and free from any event (Table 1). There was a total of 5 (1.9%) isolated locoregional recurrences: 4 involved the breast and 1 the axillary lymph nodes. At 3 years, disease-free survival and overall survival were 100% and 99%. Predictive factors for toxicity were breast volume >500 cm3 for acute toxicity, while none was correlated with severe late toxicity.

Conclusions: Toxicity was mild and acceptable with high patients' satisfaction. Local control was acceptable, none died of BC and overall survival was 99% at 3 years.

## CO042

### OLDER AGE AND COMORBIDITY IN BREAST CANCER: IS RADIOTHERAPY ALONE THE NEW THERAPEUTIC FRONTIER?

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Aims: To assess the impact of age, comorbidities and hormonotherapy (HT) use in elderly breast cancer (BC) patients (pts) treated with hypofractionated radiotherapy (Hypo-RT).

Methods: From June 2009 to December 2017, 734 ER-positive BC pts (stage pT1-T2, pNx-1, M0 and age over 65 years) receiving Hypo-RT and followed until September 2018, were analyzed. Hypo-RT consisted of 42.4 Gy in 16 daily fractions, a sequential boost was administered in cases of grade 3 tumor and close or positive margins. Baseline comorbidities included in the hypertension-augmented Charlson Comorbidity Index (hCCI) were retrospectively retrieved. Baseline pts and tumour characteristics were analyzed in relation to HT status (never/discontinued, ongoing) at last contact by chi-2 test. Five-year disease-free survival (DFS) and overall survival (OS) were estimated by Kaplan-Meier method. The log-rank test was used to compare groups. Adjusted hazard ratios (HRs) were estimated by Cox proportional hazards models. In survival analysis, HT use was treated as time-dependent variable. A subgroup analysis was performed on pts aged ≥70 with a pT1 luminal A BC.

Results: The comorbidity was present in about 70% of pts (median age: 74 years).HT has been prescribed in 88.9% pts. Most of them assumed the prescribed HT and 7.8% discontinued the treatment. Current HT use was less frequent for pts aged ≥80 ($p<0.001$) and pts with high comorbidity burden (hCCI≥2) ($p=0.001$). At the time of the analysis, 91.7% pts were still alive and 4.5% pts experienced a disease progression (local or nodal recurrences and metastases). At a median follow-up 46.8 months (range 4-115 months), the overall 5-year DFS was 86.8% varying between 89.5% for current HT use and 76.6% for no/discontinued HT use ( $p<0.001$). The prognostic effect of HT was confirmed for pts aged≥70 with a pT1 luminal A BC: 5-year DFS were 91.3% and 79% for ongoing HT user and no/discontinued HT user, respectively ( $p<0.018$). The hazard of disease progression was significantly increased for pts with hCCI≥2 and with tumour size ≥1 cm and strongly decreased for currently ongoing HT users. HT did not impact on OS in any of the analyzed groups.

Conclusions: This study shows that disease progression was strongly increased for pts with hCCI≥2 and tumor size>1 cm and decreased for HT users. In elderly pts, HT assumption did not showed a benefit in terms of survival. Further studies (RT alone versus RT+HT versus HT alone) are needed on elderly women with BC.

## CO043

### PROMOTER METHYLATION OF MGMT ASSOCIATED WITH NEGATIVE EXPRESSION OF EPIDERMAL GROWTH FACTOR RECEPTOR SELECTED A SUB-GROUPS OF LONG SURVIVAL GLIOBLASTOMA PATIENTS CANDIDATE TO A DE-INTESIFICATION OF RADIOTHERAPY TREATMENT

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Aim: To explore therapeutic results of de-escalated radiotherapy (RT) dose schedules combined to Temozolomide (TMZ)-RT treatment in sub-group of patients with very favourable prognosis based on MGMT and EGFR expression in newly diagnosed glioblastoma (GB).

Methods: Patients with newly diagnosed GB received either standard (SDRT: 60-59.4 Gy) or reduced (RDRT: 54-52 Gy) dose radiation therapy (RT) with concomitant and adjuvant TMZ between June 2010 and October 2016. We retrospectively evaluated the therapeutic effectiveness of the RT ranges schedules in terms of overall survival (OS) with univariate and multivariate analysis, after analyzing the MGMT methylation status and EGFR protein expression.

Results: One hundred patients were selected for the present analysis. Clustering survival analysis for the methylation status of MGMT (methMGMT/unmethMGMT) and EGFR expression (High EGFR: H-EGFR; Low EGFR: L-EGFR), identified three different prognostic groups($p = 0.001$), as follows. Patients with unmethMGMT/H-EGFR had the shortest survival time (median OS: 5months) and patients co-expressing methMGMT/L-EGFR had a very long prognosis (median OS: 35 months),as compared to the other two sub-groups (methMGMT/H-EGFR; unmethMGMT/L-EGFR), which had respectively median OS of 11 and 12 months. Twenty-seven patients were methMGMT/L-EGFR in which 17 patients received the standard RT-TMZ course (SDRT-TMZ) whereas the remaining ten underwent the reduced dose schedule (RDRT-TMZ). The survival analysis showed that in this sub-group of patients, SDRT-TMZ and RDRT-TMZ groups did not show different median OS (p=ns). Instead, a difference in survival outcomes was confirmed in all others MGMT-EGFR expressed patients with better survival for patients undergoing to SDRT,

Conclusions: In our experience, a reduction of radiation dose schedule should be investigated in this subgroup of patients and could deserve prospective trials for validation.

**CO044**

## PALLIATION OF ADVANCED HEAD AND NECK (H&N) CANCER IN ELDERLY PATIENTS: A REPEATED SHORT-COURSE ACCELERATED RADIATION THERAPY (SHARON) REGIMEN

M. Ferro[1], M. Boccardi[1], A. Ianiro[2], G. Macchia[1], A. Re[1], V. Picardi[1], C. Romano[2], A. Zamagni[3], M. Ferioli[3], A. Arcelli[3], S. Cammelli[3], M. Ferro[1], M. Missere[4], S. Mignogna[5], M. Buwenge[3], C. Pozzo[5], S. Cilla[2], V. Valentini[6], A.G. Morganti[3], F. Deodato[1]

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Aims: To assess the feasibility and safety of a repeated SHort-course Accelerated RadiatiON therapy (SHARON) regimen in the palliative setting of H&N locally advanced or metastatic cancer in elderly patients.

Methods: Patients with histological confirmed H&N cancers, age ≥80 years, expected survival >3 months and Eastern Cooperative Oncology Group (ECOG) performance status of ≤3 entered the study. Patients were treated in cohorts of six patients: a total dose of 20 Gy was delivered in 2 consecutive days with a twice daily fractionation (5 Gy per fraction) and at least 6-8 hour interval. If no Grade 3 toxicity was registered within 3 months from treatment, a second enrollment started with another cohort of six patients to whom were administered two cycles for a total dose of 40 Gy, with an interval between cycles of about one month. Primary endpoint was to evaluate feasibility of two cycles. Secondary endpoint was to assess symptoms-free progression time and survival.

Results: Nineteen consecutive patients (male/female: 11/8; median age: 84 years; range: 80-97) were treated. ECOG performance status was 3 in 9 patients (48%). Primaries different cancer were included: oral cavity (N°=4; 21%), larynx (N°=4; 21%), oropharynx (N°=4; 21%), paranasal sinus (N°=3; 16%), lip (N°=2; 11%), salivary gland (N°=1; 5%), nasal cavity (N°=1; 5%). Eleven patients were treated with one cycle. No experience of Grade 3 toxicity was registered: only one patient (10%) reported a pharyngeal G2 toxicity. The dose was then escalated to 40 Gy and other 8 patients were treated: three G2 toxicity (38%) were reported (one pharyngeal, one mucosal and one skin G2 toxicity). No G3 toxicity was reported. With a median follow-up time of 3 months, the symptoms free progression-time in the first group was 3,8 months, whilst in second cohort was 8 months (Figure 1). The median overall survival time was 8 months. Overall palliative response rate was 99%. Moreover, among 13 symptomatic patients for pain, 8 showed an improvement or resolution with an overall pain response rate of 62%.

Conclusions: Repeated short-course accelerated radiotherapy in palliative setting of Head & Neck cancers is safe and well tolerated even in elderly patients. A phase II clinical trial will be necessary to verify whether an increase in the number of cycles can safely prolong the symptom-free progression time.

CO045

## UNCONVENTIONAL RADIOTHERAPY SBRT-PATHY VS. STANDARD OF CARE FOR INOPERABLE BULKY LUNG CANCER

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Aim: to report on the improved therapeutic ratio by newly developed SBRT exploiting the bystander (BE) and abscopal effects (AE) for the treatment of either inoperable or unsuitable for radical radiotherapy bulky lung cancer compared with standard of care. In a pre-clinical phase of this translational research was proven that the hypoxic tumor cells show higher potential for tumoricidal BE and AE compared with normoxic tumor cells. In order to improve the radiotherapy outcome by generating BE and AE those findings were translated to the clinic, and new SBRT-based PArtial Tumor irradiation targeting HYpoxic segment (SBRT-PATHY) but sparing tumor immune-microenvironment was developed. The hypothesis is that SBRT-PATHY can improve the local and distant tumor control inducing major regression of partially irradiated bulky due to BE but also of unirradiated metastases due to AE. The primary endpoint was bulky response rate. The secondary endpoints included: distant tumor control, survival, safety, symptom control.

Materials and Methods: 60 patients stage IIIB/IV bulky lung cancer considered inoperable or unsuitable for radical radiotherapy were treated (Aug. 2013 - Aug. 2018) with: 1. Conventional RT only: 3Gy x 10 to the bulky (20 patients), 2. Standard CHT only (20 patients), 3. SBRT-PATHY only: 10 or 12Gy x 1-3 to 70% (based on bulky site and volume) to a so called Bystander (hypoxic) Tumor Volume (BTV) defined using PET-CT as a hypovascularized-hypometabolic (SUVmax<3) junctional zone between the central necrotic and peripheral hypervascularized-hypermetabolic bulky segment, avoiding the tumor microenvironment (20 patients). Immunohistochemistry was performed on the available tissue samples to explore for the modifications within the tumor microenvironment.

Results: 3 treatment groups were comparable in terms of performance status, histology and disease stage. Table 1 summarizes the results. Median follow up was 12.7 months (range: 4-27), mean bulky diameter: 8.1 cm (range: 6-13.5). Histology: 39% squamous, 51% adenocarcinoma, 10% other.

Conclusions: Exploitation of the tumoricidal radiation-hypoxia-induced BE and AE by SBRT-PATHY may potentially enhance the radiotherapy therapeutic ratio.

**Table 1. Summary of the results.**

| TREATMENT GROUP | BULKY RESPONSE RATE (CR or PR) | DISTANT TUMOR CONTROL | OVERALL SURVIVAL | CANCER SPECIFIC SURVIVAL | PROGRESSION FREE SURVIVAL | TOXICITY (G1-4) | SYMPTOM CONTROL |
|---|---|---|---|---|---|---|---|
| 1. | 20% | 0% (abscopal effect) | 5% | 10% | 0% | 15% | 25% |
| 2. | 20% | 55% (chemo effect) | 60% | 60% | 15% | 65% | 15% |
| 3. | 95% | 46% (abscopal effect) | 55% | 80% | 55% | 5% | 80% |

CO046

## SBRT WITH SIMULTANEOUS INTEGRATED BOOST AND PROTECTION: INCIDENCE AND PATTERN OF RECURRENCE IN BORDERLINE RESECTABLE AND LOCALLY ADVANCED PANCREATIC CANCER

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Aims: To analyze incidence and pattern of recurrence and to define a dosimetric map of loco-regional failure (LRF) after Stereotactic Body Radiation Therapy (SBRT) with Simultaneous Integrated Boost (SIB) and Protection (SIP) for pancreatic cancer (PC) patients (pts).

Methods: We retrospectively reviewed 51 consecutive pts (26 borderline resectable and 25 locally advanced disease) treated from November 2016 to August 2018. All the pts received induction chemotherapy prior to SBRT. SBRT was delivered over 5 consecutive fractions using a SIB technique, prescribing 10 Gy/fraction to the region of vessel abutment/encasement and 6 Gy/fraction to the remaining Planning Target Volume (PTV) tumor. SIP was generated prescribing 25 Gy on the overlap area between the PTV and the Planning Organ at Risk Volume. Elective Nodal Irradiation (ENI) was not performed. 27 pts underwent surgical tumor resection after SBRT. For the analysis we defined 3 different site of failure: in field (inside the isodose 30 Gy), out field (area corresponding to the ENI) and distant failure. We realized for each location of LRF a dosimetric evaluation matching the computed tomography (CT) that showed LRF with the SBRT treatment plan CT. A deformable image registration (DIR) was performed to better compare the CT anatomy.

Results: Median follow up time after SBRT was 10.1 months (range 4.2-27.6 months). Overall, a Local Control Rate (LCR) of 80% was obtained (85%, 23/27 in surgical vs 75%, 18/24 in nonsurgical pts; p=0.32). Tumor relapse occurred in 30 pts (59%): distant alone in 20 pts, LRF only in 6 pts and a combination of distant and LRF in 4 pts. Concerning LRFs, 7 were exclusively in field and 3 a combination of in and out field failure. Median Local Progression Free Survival from SBRT was 9 months (8.5 vs 9.7 months in surgical vs nonsurgical pts; p=0.78). The dosimetric evaluation showed that all in field failures occurred inside the area covered by 95% of the prescribing isodose, with extent in the area immediately close to the PTV. Interestingly, we didn't observe isolated nodes recurrences in the ENI area. At the last follow-up 34 pts (67%) were alive, with a median Progression Free Survival of 16.3 months and a median Overall Survival of 18.6 months from the time of diagnosis.

Conclusions: SBRT for PC pts pretreated with chemotherapy was able to provide an acceptable LCR and the lack of ENI didn't significantly increase the rate of failure in the regional nodes area.

## CO047

### THE PROGNOSTIC ROLE OF FDG PET/CT BEFORE COMBINED RADIO-CHEMOTHERAPY IN ANAL CANCER PATIENTS

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Aims: FDG PET/CT could be useful in the prognostic stratification of anal cancer patients. Therefore, we retrospectively assessed the prognostic value of FDG PET/CT parameters, including MTV and TLG measured within the primary tumour and the involved lymph nodes, before definitive RCT in anal cancer patients.

Methods: Anal cancer patients with positive baseline FDG PET/CT who underwent combined RCT treatment with curative intent from May 2011 to February 2018 were included. PET parameters were measured within the primary tumours and the involved nodes: primary tumour (T)-SUVmax, T-SUVpeak, T-SUVmean, T-MTV, T-TLG, whole body (WB)-MTV and WB-TLG. Kaplan-Meier curves, Cox-regression analysis, Mann-Whitney U test and logistic regression machine learning technique were used to test for associations between clinical data, metabolic parameters and outcomes as overall survival (OS), disease specific survival (DSS), metastatic free survival (MFS), disease free survival (DFS), local relapse free survival (LRFS) and colostomy free survival (CFS).

Results: Fifty-nine patients were included in the study. Median follow-up was 28 months. Higher pre-treatment WB-MTV, T-TLG and WB-TLG were associated with worse OS (p=0.025, 0.021 and 0.02 respectively). PET parameters resulted also statistically significant for DSS, DFS and CFS (p=0.032, 0.043, $9\times10^{-4}$ for WB-TLG). Cox analysis showed that PET parameters are significant predictors of OS (for this outcome also age is significant), DSS, DFS, CFS and LRFS. On multivariate analysis, age, stage, T-SUVpeak, WB-MTV and T-TLG resulted significantly related to OS. In addition, a further stratification for patients with advanced stage (cT3-T4 any N or any T N+) showed that MTV and TLG, measured within the primary tumour and the involved nodes, are significantly higher in patients dead for cancers in patients with relapse or colostomy.

Conclusions: Pre-treatment metabolic parameters measured within the primary tumour and the involved nodes may represent additional new biomarkers for estimating prognosis in anal cancer patients and for modulating the treatment.

Legend of acronyms
maximum Standardized Uptake Value (SUVmax)
metabolic tumour volume (MTV)
total lesion glycolysis (TLG)

## CO048

### ARE WE READY FOR A PARADIGM SHIFT FROM HIGH-DOSE CONVENTIONAL TO MODERATE HYPOFRACTIONATED RADIOTHERAPY IN INTERMEDIATE-HIGH RISK PROSTATE CANCER? A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS WITH TRIAL SEQUENTIAL ANALYSIS

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Aim: To evaluate efficacy and late toxicity of moderate hypofractionated (HFRT) over high-dose (>76 Gy) conventional radiotherapy (CRT) in a non-inferiority perspective.

Methods: The study inclusion criteria were RCTs involving patients with localized intermediate and high-risk PCa and treated with moderately hypofractionated regimens (HRT) or high-dose CRT. High-dose CRT was defined as a cumulative dose of 76 Gy or greater delivered in conventional fractionations. The treatment volumes had to be the same for both arms and had to include the whole prostate, with or without the seminal vesicles or pelvic lymph nodes. All RCTs using dose per fraction greater than 4 Gy were excluded. HFRT regimens were deemed non-inferior to high-dose CRT if the computed CI for the overall RR did not exceed the non-inferiority margin of 7%.

Results: A total of 2481 men were enrolled in the four RCTs included in this systematic review with 1249 men receiving HFRT and 1232 receiving high-dose CRT, respectively. When the prespecified margin, corresponding to a critical RR of 0.930 for CCS, OS and BFS, was used all efficacy outcomes satisfied the criteria for the non-inferiority analysis indicating the non-inferiority of HFRT regimens over high-dose CRT in the medium term period. The analysis of the CIs boundaries of the computed RRs indicated that they exceeded the pre-specified margin indicating that the evidence concerning the non-inferiority of HFRT regimens over high dose CRT was inconclusive. We deemed our meta-analysis conclusive, in demonstrating that HRFT regimens were non-inferior over high-dose CRT, when the required sample size is reached and the cumulative Z-curves cross the futility boundaries constructed by TSA. The required sample size to consider meta-analysis conclusive was based on an alpha error 5%, a beta error 0.20-0.10 (study power in the range of 80%-90%) and a non-inferiority margin 7%. TSA analysis indicated that the accrued sample size (2481 patients) exceeded the required sample size (2007 patients for OS, 2464 patients for CSS and 2416 patients for BFS) need

to confirm the non-inferiority of HFRT regimens in terms of efficacy parameters.

Conclusions: Noninferiority analysis indicates that moderate HFRT regimes are non-inferior over high-dose CRT in the medium-term. Inconclusive is the evidence for the late toxicity. Longer follow-up will provide a more clear answer concerning the non-inferiority of HFRT regimens in the long-term period.

**CO049**

## RESULTS FROM THE TTIRS TRIAL: A RETROSPECTIVE MULTICENTER ANALYSIS OF THE ASSOCIATION BETWEEN CONCOMITANT TARGETED THERAPY OR IMMUNOTHERAPY AND RADIOSURGERY FOR THE TREATMENT OF BRAIN METASTASES FROM NON SMALL CELL LUNG CANCER ON BEHALF OF BRAIN AND THORACIC ONCOLOGY NATIONAL GROUP OF AIRO

S. Scoccianti[1], E. Olmetto[1], R. Di Franco[2], P. Anselmo[3], G. Beltramo[4], C. Mantovani[5], M.F. Osti[6], V. Pinzi[7], N. Giaj-Levra[8], A. Bruni[9], P. Matteucci[10], S. Pedretti[11], E. Giudice[12], P. Tini[13], M. Krengli[14], P. Ciammella[15], F. Pascqualetti[16], M. Trignani[17], A. Merlotti[18], V. Borzillo[2], D. Franceschini[19], C. Delli Paoli[1], E. Maranzano[3], U. Ricardi[5], P. Navarria[19], V. Scotti[1]

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Aims: To investigate the association between concomitant RadioSurgery (RS) and Immunotherapy (IT) or Targeted Therapy (TT) for the treatment of brain metastases (BM) from Non Small Cell Lung Cancer (NSCLC). Aims of the study were Local Progression free Survival (L-PFS), Distant Progression Free Survival (D-PFS), Overall Survival (OS) and Safety. This a multicenter study by Brain and the Thoracic Oncology Group of Airo (Italian Association of Radiation Oncology).

Methods: Data about patients treated with concomitant IT or TT and RS were retrospectively collected. Concurrent time was considered a period of 4 weeks. L-PFS and D-PFS were defined as the time from RS to local progression of the treated lesions and to the appearance of new BM, respectively. Patients should have at least a follow up of 3 months. Safety results were reported according to the CTCAE v4.1. Kaplan Meyer analysis of survival was performed.

**Table 1. Patients and treatments characteristics.**

| Patient's Characteristics | Number 254 (%) |
|---|---|
| **Gender** | |
| M | 140 (55%) |
| F | 114 (45%) |
| **Age** | |
| Median | 65 years |
| Range | 33-86 years |
| **Smoke (p/y)** | |
| Unknown | 164 (64.5%) |
| 0 | 14 (5.5%) |
| <10 | 8 (3%) |
| 10-20 | 6 (2%) |
| >20 | 62 (25%) |
| **Histology** | |
| Adenocarcinoma | 232 (91%) |
| Squamous Cell Carcinoma | 22 (9%) |
| **Molecular Biology** | |
| EGFR+ | 77 (30%) |
| ALK+ | 41 (16%) |
| PDl-1> 1% | 53 (21%) |
| **Stage at diagnosis** | |
| Unknown | 5 (2%) |
| M0 | 94 (37%) |
| M1 | 155 (61%) |
| Brain M1 | 72 (28%) |
| **Primary Disease controlled at RS** | |
| Yes | 156 (61%) |
| Not | 98 (39%) |
| **RPA Class** | |
| 1 | 57 (22.5%) |
| 2 | 196 (77.2%) |
| 3 | 1 (0.3%) |
| **molGPA Score** | |
| 0-1 | 17 (7%) |
| 1.5-2 | 105 (41%) |
| 2.5-3 | 109 (43%) |
| 3.5-4 | 23 (9%) |
| **Concomitant Treatment** | |
| **IT** | **113 (44%)** |
| Nivolumab | 56 (49.5%) |
| Pembrolizumab | 41 (36%) |
| Atezolizumab | 4 (3.5%) |
| Unknown | 12 (11%) |
| **TT** | **141 (56%)** |
| Erlotinib | 39 (28%) |
| Gefitinib | 33 (23%) |
| Afatinib | 14 (10%) |
| Osimertinib | 4 (3%) |
| Crizotinib | 30 (21%) |
| Certitinib | 2 (1.5%) |
| Alectinib | 2 (1.5%) |
| Others | 6 (4%) |
| Unknown | 11 (8%) |

Results: Data of 254 NSCLC patients from 19 Italian radiotherapy centers were analyzed. Patients were treated from 05/01/2007 to 29/11/2018. Median age was 65 years (range 33-86). A total of 499 BM were treated: 184 (72%) patients were treated in a single fraction while 70 (28%) with Hypo-Fractionated radiotherapy. The most used drugs were Nivolumab (22%), Pembrolizumab (16%), Erlotinib (15%), Gefitinib (13%) and Crizotinib (12%). Patients and treatments characteristics are summarized in Table 1. Eleven

patients were lost during follow up (FUP). After a median FUP of 7 months L-PFS, D-PFS and OS were 48 months (range 30m-69m), 12 months (range 9m-16m) and 7 months (range 2m-15m) respectively. Nivolumab compared to Pembrolizumab seemed to show a better L-PFS (HR: 0.7 CI 95%: 0.14-3.04), D-PFS (HR 0.79 CI 95% 0.35-1.77) and OS (HR: 0.5 CI 95% 0.2-1.7) without reaching a statistical significance. Among TT Erlotinb compared to Gefitinb and Crizotinib showed a better OS while D-PFS showed a trend in favor of Gefitinib. Grade 2 and 3 Radionecrosis were reported in 10 (4%) and 2 (1%) patients, respectively. No other severe neurological toxicity were described.

Conclusions: Our data suggest that RS and IT or TT for the treatment of BM from NSCLC is feasible and safe. Among IT Nivolumab seems to be associated with a better intracranial control and OS compared to Pembrolizumab, while there is not a clear difference in terms of outcomes between different targeted agents. Prospective data are needed to confirm our results.

## CO050

### PRELIMINARY EVALUATION OF NIVOLUMAB LONG RESPONDING NSCLC PATIENTS: A REAL-LIFE DATA COLLECTION FROM 14 TUSCAN CENTERS

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Aims: Two randomized phase III trials showed improved overall survival (OS) for Nivolumab (N) versus Docetaxel in pre-treated advanced NSCLC. A subset of these patients (pts) benefits of N for long term, with an impressive durable response. Aim of current analysis is to describe a selected series of these pts.

Methods: We collected the data of advanced NSCLC pts treated with N for at least 24 months, after a first-line therapy. Baseline characteristics, responses to treatment and adverse events were described. Data related to subsequent lines of therapy, previous and/or concurrent treatments, including radiotherapy (RT), were available.

Results: From June 2015 to the time of analysis, 53 advanced NSCLC pts were selected. Median age was 68.2 years; males were 74%, females 26%; the majority of pts (92%) were current or former smokers and 55% had metastatic disease at diagnosis. Squamous histology was 47%, while non-squamous one 53%; none oncogene-addicted disease. 59% of pts had ≥2 metastatic sites at the start of N. Median number of N administrations was 62 (range 35-89). Median time to best response was 6.4 months (range 2-20): 3 complete responses, 34 partial responses and 16 disease stabilizations were observed. A half of pts (27) underwent RT: in 9 pts (17%) radical doses to locally-advanced thoracic disease, in two pts post-operative RT, in 6 pts (11%) radical doses to metastases, in 15 pts (28%) palliative RT. RT was concomitant to N in 7 pts (13%): in all of these N is still ongoing. At the time of the analysis, 90% of pts are alive and 70% of pts are still on treatment with N. N was interrupted in 16 pts for disease progressions (7 pts), pulmonary or pancreatic severe adverse events (2 pts) and for other causes in 7 patients. No treatment-related deaths were observed. Median progression free survival was 30.7 months (range 16.8-42.4). Median OS from the start of N was 31.9 months (range 18.9-42.4). Median OS from the diagnosis of metastatic disease was 44 months (range 14.3-71.2). After disease progression, 6 pts received further therapies.

Conclusions: The present series of pts treated with N for at least 2 years confirm the efficacy of this drug, showing durable responses in a subset of pts, mainly current or former smokers, without oncogene addiction, squamous and non-squamous NSCLC. The half of pts needed RT. RT was delivered safely during immunotherapy.

## CO051

### TOLERANCE AND SAFETY OF STEREOTACTIC RADIOTHERAPY (SBRT) IN STAGE IV NON SMALL LUNG CANCER (NSCLC) PATIENTS DURING IMMUNOTHERAPY (IT): A MULTICENTRIC RETROSPECTIVE ANALYSIS ON BEHALF OF AIRO THORACIC ONCOLOGY STUDY GROUP

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Aims: IT has recently enhanced the treatment armamentarium for stage IV NSCLC as well as SBRT. Radiobiological studies and initial clinical reports suggest a potential synergistic effect of SBRT and IT even if the mechanism is not yet completely clear. Aim of this study is to retrospectively analyze the safety, tolerance and clinical outcome of SBRT plus IT (Nivolumab [NIVO], Pembrolizumab [PEM] or Atezolizumab [ATE]) in advanced NSCLC patients (pts).

Methods: We retrospectively analyzed 49 consecutive pts affected by stage IV NSCLC treated with SBRT given concurrently with IT from 2015 to January 2018. Twenty-nine pts were male and 20 female. Mean age was 66. Adenocarcinoma was diagnosed in 79% of pts, while squamous cell carcinoma in 21%. At diagnosis, 16 pts had locally advanced NSCLC, while 33 stage IV. Thirty-three pts were submitted to chemotherapy before receiving IT, while 16 pts received IT as first line. NIVO was administered to 26 pts, PEM to 19 and Ate to 4 pts. Twenty six pts received SBRT concomitantly to IT, 15 before starting IT (within 30 days from first cycle) and 8 after progression during IT (within 30 days from the last cycle) due to oligoprogression. SBRT was delivered to brain metastases in 38 pts, to bone lesions in 6, to the mediastinum in 2 and to other sites in 3.

Results: All pts were submitted to SBRT using different doses and schedules: 22 pts received 12-25 Gy in single fraction (Fx), 16 pts received 24-54 Gy in 3-5 Fx and 1 pt received 40 in 8 Fx. Overall response rate was 78.7%. At a median FUP of 17 months 1- and 3 year-Overall Survival were 80.5%±5.5%ES and 42.4%±8.5%ES respectively, Cancer Specific Survival 86.6%±ES5.1% and 45.7%±8.9%ES respectively and progression free survival 67.7%±6.1%ES and 28.5±8.1%ES. During FUP 30 pts experienced disease progression with a mean duration time of IT of 6.1 months (range 1-24,1); mean time to progression was 5.1 months. No pt had to interrupt systemic therapies and no severe toxicities (>G2) were found due to SBRT treatment. Known systemic side effects from IT were observed in 10 pts: 3 pts had diarrhea, 1 pulmonitis, 2 liver toxicity, 2 pneumonitis and 2 thyroiditis.

Conclusion: SBRT and IT with the checkpoint inhibitor represent a safe, well tolerated and efficient multimodal treatment, with the available data suggesting also potential, synergystic effects on local and systemic disease in stage IV NSCLC pts. Ongoing studies set out to understand the optimal timing, RT doses and ideal combination between RT and IT in this setting.

**CO052**

## THE PROGNOSTIC SIGNIFICANCE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN THE ERA OF HPV STATUS FOR OROPHARYNGEAL CANCER PATIENTS: SOMETHING WE NEED TO FINALLY CONSIDER?

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Aim: To evaluate the role of baseline neutrophil-to-lymphocyte ratio (NLR) and other haematological biomarkers such as neutrophil, lymphocyte, platelet and monocyte count as prognostic markers in locally advanced squamous cell carcinoma of the oropharynx (OPC) treated with definitive chemo-radiotherapy (CRT) in the era of HPV status.

Patients and Methods: A retrospective analysis of 125 patients (pts) affected with locally advanced OPC and treated between 2010 and 2015 at two tertiary cancer centres in Northern Italy (European Institute of Oncology, Milan and Centro di Riferimento Oncologico di Aviano, Aviano) was performed. Inclusion criteria were: age>18 years, stage III or IV (TNM 7th ed.), definitive CRT. Multivariate Cox proportional hazard models were applied to assess the independent role of haematological markers of for progression-free survival (PFS) and overall survival (OS), adjusting for other prognostic factors and confounders. Logistic models were used to assess the association with downstage in TNM 8th ed.

Results: Median age was 61 (42-77) years and 94

(75.2%) pts were male. HPV status was available in 102 (81.6%) pts and among them 77 (61.6%) pts had HPV/p16+ related OPC. Therapeutic choice consisted in sequential and concurrent chemo-radiotherapy as well as induction followed by concurrent CRT schedule, and it was delivered to 43 (34.4%), 71 (56.8%) and 11 (8.8%) pts, respectively. Median follow-up was 50 months (range 5-95 months). All haematological biomarkers significantly changed after CT/RT. A value of NLR≥3 was associated with poorer OS with more than double increased risk of death: HR=2.5 (95%CI: 1.1, 5.5; p=0.03, adjusted for age, stage and HPV status). Two-year OS was 91% and 81% in pts with NLR<3 and ≥3, respectively. No correlation was found between other haematological parameters and prognosis. Prognostic value of NLR has been confirmed restaging our cohort of pts with the new TNM staging (8th ed.).

Conclusion: In our cohort, a baseline NLR≥3 at treatment initiation represented a negative prognostic marker for OPC treated with definitive CRT. Our results are in line with literature data and are confirmed after re-staging with last TNM. Therefore, this inexpensive and readily available marker could be considered for risk stratification of pts with locally advanced OPC.

**CO053**

## IMMUNOLOGICAL PROGNOSTIC BIOMARKERS IN RELATION TO HPV STATUS AND CLINICAL OUTCOMES IN OROPHARYNGEAL CANCER PATIENTS: PRELIMINARY RESULTS OF A PROSPECTIVE INVESTIGATION

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Background: To perform a comprehensive analysis of the circulating and intratumoral T cell compartments in patients affected by Oropharyngeal Squamous Cell Carcinoma (OSCC) to search for new prognosticators and to get insights on new possible immunotherapeutic strategies.

Methods: From May to October 2018 we prospectively enrolled 20 patients (pts) affected by locally advanced OSCC and treated by radiotherapy or chemo/bio-radiotherapy. Peripheral blood and tumor biopsies were collected before treatment and evaluated by multiparametric flow cytometry panels to delineate: tumour-infiltrating lymphocytes (CD4+ and CD8+ TILs), frequency of CD4+ T regulatory cells (Treg), expression of immune checkpoints (IC) (CD39, PD-1, CTLA-4, TIM3). These parameters were correlated with response to treatment, also in the context of the p16 status.

Results: Median follow up was 8 months (range: 2-18). Median age was 65 years (range: 35-83). 11 (55%) and 9 (45%) pts had a HPV + and HPV – tumors, respectively. Four pts (20%) underwent radical radiotherapy, while 16 (80%) pts received a combined treatment (12 CDDP, 4 Cetuximab). At last re-evaluation, 13 (65%) pts presented a complete response, 1 (5%) pt a progression disease (PD) and 6 (30%) pts were dead (3 PD, 2 toxicity and 1 for non-cancer related causes). CD3 TILs were more represented in tumor biopsy compared to peripheral blood. There was no significant difference among TILs in responders vs non responders pts (p=0.10- Figure 1A) but there was a higher CTLA-4 expression on TILs of HPV+ vs HPV – pts (median value: 30% vs 10% - Figure 1B). Interestingly, categorizing TILs according to PD1 expression (PD1-, PD1 intermediate, PD1 bright) we observed a significant higher expression of other IC (TIM-3, CD 39) in those cells with the highest PD1 level (Figure 1C-1D). Intratumoral CD4+ Treg frequency resulted statistically increased in cancer specimens with respect to blood (Figure 1E) and Treg exhibited an active functional phenotype (high FoxP3, CTLA-4 and CD39 expression and high expression of immune checkpoints as PD1 and TIM3); moreover CD4+ Treg were more represented in HPV – tumours compared to HPV + tumours (p=0.02- Figure 1F).

Conclusions: The results highlight the co expression of different IC on a subset of TILs that might suggest the develop of new combinatorial protocols in selected pts. The higher expression of Treg cells in HPV – tumours might explain the worse prognosis but further investigation is recommended.

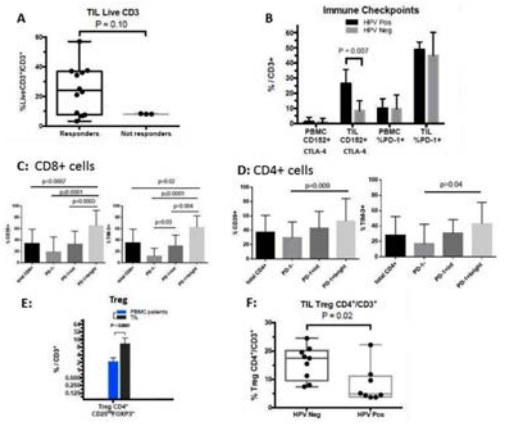


**Figure 1.**

## CO054

### DEVELOPMENT OF OVERALL SURVIVAL PREDICTIVE NOMOGRAMS IN PATIENTS WITH LOCALLY ADVANCED OROPHARYNGEAL CANCER COMING FROM ITALIAN PRO.M.E.THE.O. GROUP

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Aims: Treatment of oropharyngeal cancer is moving toward a tailored treatment based on stratification of risk group, which requires patient-specific estimates of survival outcomes. Aim of this study is to develop a predictive model of overall survival (OS) for patients (pts) with locally advanced oropharyngeal cancer (LAOC) treated with radiotherapy (RT) in association with Cetuximab (Cet), coming from PRO.M.E.THE.O. (PRedictiOn Models in Ent cancer for anti-EGFR based THErapy Optimization) italian multicentric dataset.

Methods: Pts with LAOC treated with RT-Cet coming from 6 centres (Cuneo, Firenze, Genova, Modena, Roma, Torino), were considered for this analysis. We take into account different variables: age at diagnosis, gender, PS ECOG, TNM stage, total dose at CTV High Risk, fractionation, overall treatment time, RT interruption days. Follow-up times (2, 3, and 5 years) for the OS were used as the model outcome. Pts were randomly divided into a training set (group A) corresponding to 80% of dataset and validation set (group B) representing the remaining 20%. A binary logistic regression model was trained on group A with stepwise feature selection based on Akaike's information criterion (AIC). The model was then performed on testing set. ROC AUC and confusion matrix statistics at 5 threshold were used as performance criteria. Nomograms were performed at 2, 3 and 5 years.

Results: Overall 218 pts were collected and 183 had the selected variable and were analyzed in this study. OS predictive models were developed and represented by nomograms at 2,3 and 5 years. Figure 1 represent the 2 years OS nomogram. Covariates that show negative impact on 2y OS were positive nodal status, presence of metastasis, PS ECOG >1, Age, dose < 66Gy and interruption days of radiotherapy >3. ROC AUC for training set, testing set and whole dataset for OS at 2, 3 and 5 years are shown in Table 1.

Conclusions: A large multidimensional database allow the creation of a multifactorial OS prediction model in LAOC treated by RT-Cet. An external validation should be needed to confirm the robustness of the model for a possible clinical application for a personalyzed approach.

**Table 1.**

| AUC | Train | Test | Overall |
|---|---|---|---|
| 2 years | 0.787 | 0.763 | 0.793 |
| 3 years | 0.763 | 0.706 | 0.767 |
| 5 years | 0.741 | 0.852 | 0.771 |

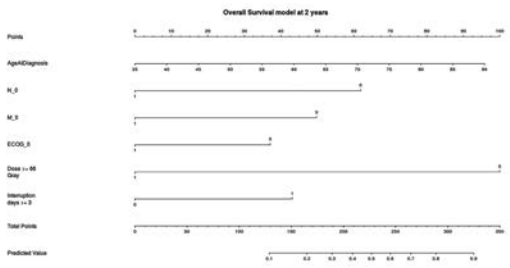


**Figure 1.**

## CO055

### OCCURRENCE OF SYMPTOMATIC CARDIAC EVENTS IN EARLY BREAST CANCER PATIENTS RECEIVING CHEMOTHERAPY, TRASTUZUMAB, OR THEIR COMBINATION WITH OR WITHOUT RADIOTHERAPY: AN ANALYSIS OF REAL WORLD DATA

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Aims: To assess symptomatic cardiac events (SCEs) in a large and unselected cohort of early breast cancer (BC) patients (pts) treated with Trastuzumab (T)+/-chemotherapy (CT)+/-radiotherapy (RT).

Methods: Starting from healthcare administrative database, ie clinical discharge records and drug prescriptions available in the Lombardy region (Italy), we surveyed a cohort of pts diagnosed with BC between 01/2008 and 12/2011, treated with T+/-CT+/-RT, and monitored until 12/2016. The effect of RT on the occurrence of SCEs, including heart failure and cardiomyopathy as per ICD9-CM codes, in pts treated with CT or T+/-CT with or without RT was estimated using the Kaplan-Meier (KM) method, and RT independent predictive value was assessed by the Cox regression model.

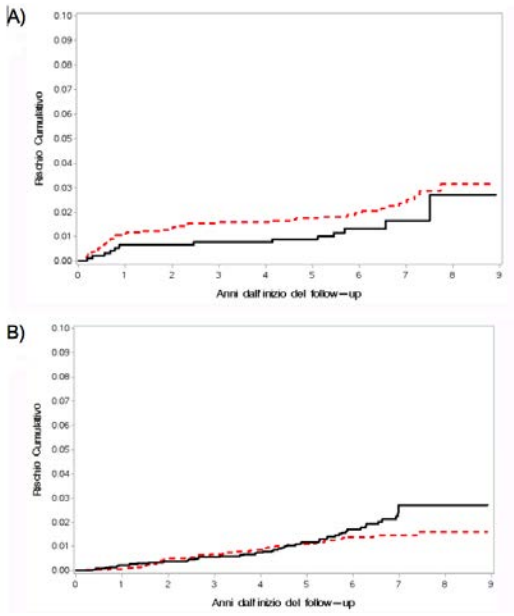


**Figure 1.**

Results: RT was not associated with increased risk of SCEs among 2,927 BC pts treated with T+/-CT and 7,908 pts treated with CT alone, Hazard Ratio (HR) 1.00, 95% Confidence Interval (CI) 0.74-1.34. After 1:2 matching for age, date of treatment start, and pre-existent cardiovascular risk factors (CRFs), we found that pts treated with T+/-CT (T-users=2,809) were less likely to receive RT as compared to those treated with CT alone (non T-users=5,618), 69% versus 72.3%, p= 0.002. A total of 140 pts experienced a SCE, 52 (1.8%) and 88 (0.2%) were T- and non T-users, respectively. Most of these events occurred during the first year from starting treatment with T+/-CT. RT-adjusted HR for SCEs versus non SCEs in the whole patient cohort was 1.32, CI 0.35-4.92 during the first year of F/U. KM of SCEs during the 9-year observational period in T- and non T-users treated or not with RT during the first year from starting treatment with T are reported in the Figure 1.

Conclusions: Pts receiving T+/-CT are less likely to be irradiated. Nevertheless, RT does not affect the occurrence of early SCEs, which are instead associated with T+/-CT exposure. The occurrence of late SCEs in irradiated T- and non T-users deserve further analysis.

## CO056

## DEFINITIVE DATA OF TOGETHER STUDY TREATMENT OUTCOME OF METASTATIC LESIONS FROM RENAL CELL CARCINOMA UNDERGOING EXTRA-CRANIAL STEREOTACTIC BODY RADIOTHERAPY

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Aims: stereotactic body radiation therapy (SBRT) use has increased overtime for metastatic renal cell carcinoma (mRCC) patients management, with a likely good control of irradiated lesions. Recently, a wide range of retrospective reports contributed to configure the landscape of the current clinical practice in this field. We planned a retrospective multicenter Italian study, with the aim of investigating the outcome of treatment with SBRT for non-brain secondary lesions in mRCC patients. Methods: all consecutive metastatic non-brain and non-only-bone lesions from mRCC underwent SBRT at five Italian institutions from January 2015 to June 2017 were considered. The primary endpoint of the study was the lesion-PFS, calculated from SBRT initiation to the local progression of the irradiated lesion. The techniques used for treatment planning and delivery of SBRT were quite homogeneous, according to the local clinical practice of each center. To execute simulation patients were accommo-

dated in setup position using specific personalized immobilization systems. CT scan was performed using 2 mm slice thickness with or not intravenous contrast. Gross Tumor Volume (GTV) and regional Organs at Risk (OaR) were delineated by a Radiation Oncologist. GTV was defined using simulation CT scan fused with MRI and/or PET-CT. PTV was created with an expansion around the GTV that depends by the lesion's characteristic and the patient's compliance. A 5 to 10 mm isotropic or not margin was added to the GTV. The dose prescription was to the PTV or to an isodose line, making an inhomogeneities inside the target. RT technique was Intensity Modulated Radio Therapy (IMRT), mainly Arc Therapy. RT schedules used by the five treating centers were quite homogeneous. Patient position was evaluated daily with cone beam CT before each treatment session.

Results: 57 extracranial metastatic lesions from 48 patients with primary mRCC underwent SBRT. The 72.4% of lesions were progression-free at 40 months, with significantly better lesion-PFS for small metastatic lesions. SBRT was safe and the local disease control was 87.7%. After SBRT 37.5%of patients permanently interrupted systemic therapy.

Conclusions: consistently with the previous literature, our findings support the use of SBRT in selected mRCC patients.

**CO057**

## A 13 YEAR EXPERIENCE OF PROSTATE HDR BRACHYTHERAPY: ANALYSIS OF OUTCOME AND TOXICITY

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Aim: To evaluate clinical outcomes, toxicity and dosimetric aspects in patients affected by localized prostate cancer treated with 3D conformal high dose rate (HDR) brachytherapy (BRT) as monotherapy (1,2,3). Materials and Methods: From March 2004 to October 2017, 277 patients with prostate cancer (T1c-T2cN0M0) were treated in our institute using 3D conformal HDR brachytherapy as monotherapy with a temporary implant. The mean age was 67 years with a range of 47-81 years. Of them, 116 patients were low risk, 145 at intermediate risk, and 15 at high risk. Overall, 154 patients received 38 Gy in 4 fractions (2 fractions/day in 2 days), 36 patients received 27 Gy in 2 fractions (1 fraction/day), and 87 patients received 19 Gy in 1 fraction. The treatment plan was elaborated using CT based software to perform 3D conformal dose planning aided by an inverse planning algorithm using these dosimetric constraints for organ at risk (OAR): dose received by 2 cc of rectum (D2cc) <75% of prescription dose (PD); D2cc of bladder <80% PD. For the urethra: the dose received by 1% of volume (D1%) <115% PD and D10% <110% PD. The prescription for the target was D90% >95% PD. Results: After a median follow-up of 6 years (range=6-160 months) overall survival and cancer-specific survival rates were 90% and 97% respectively. Biochemical disease-free rate resulted 78%; for low and intermediate risk biochemical free disease rate was 85%, whereas for high risk disease was 62%. Regarding dosimetric aspects, we obtained satisfactory dose distributions in terms of planning target volume (PTV) coverage (D90%>100% PD), with a strict respect of OAR constraints. Genitourinary (GU) and gastrointestinal (GI) acute toxicity > G2 was observed in 28% of patients. Late toxicity > G2 was very low (2.2 %), while only 3 patients reported G3 late toxicity (0.8%), which consisted in GU toxicity. Conclusions: With a median follow-up of 6 years, HDR BRT was shown as a valid treatment modality for patients with localized prostate cancer in terms of both biochemical and local control, as well as toxicity. Future studies can be addressed to evaluate the quality of life in this subset of patients.

**CO058**

## EFFICACY AND TOXICITY FOLLOWING SALVAGE HIGH-DOSE-RATE BRACHYTHERAPY FOR LOCALLY RECURRENT PROSTATE CANCER AFTER RADIOTHERAPY: A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aims: According to the NCCN guidelines, Salvage Brachytherapy is a treatment option for pathologically confirmed local recurrence after EBRT or brachytherapy. We retrospectively evaluated the feasibility and the toxicity of high dose rate (HDR) brachytherapy at our institution.

Methods: Between November 2013 and February 2018, 30 consecutive patients with biopsy proven intraprostatic recurrence of cancer after definitive radiation therapy underwent a salvage re-irradiation using HDR brachytherapy. Treatment regimen was 24 Gy delivered to the whole gland in 2 implants of 12 Gy performed 2-4 weeks apart. All patients had had no severe side effect of the previous radiotherapy course and underwent a rectoscopy to ascertain the absence of radiation proctitis prior to salvage procedure. Biochemical control was assessed according to the Phoenix definition. Secondary outcomes included survival and toxicities.

Results: Median age at the salvage brachytherapy was 68.5 years (range 61.3-83.2). The median Gleason score at diagnosis was 7 (7-7) and at the time of brachytherapy 8(7-9). The median interval between salvage HDR brachytherapy and the first radiotherapy course was 9.1 years (range 0.8-22.4). The median PSA at salvage brachytherapy was 4.9 ng/mL (range 1.3-40) , 14 pts (38,9%) had hormone therapy after EBRT, 8 pts (22,2%) had hormone therapy during brachytherapy and 6 pts (20%) were castration-resistant. After a median follow-up of 1.7 years, a total of 19 pts (63%) presented a biochemical relapse with a median time of 1.3 years (range 0.2-3.9) and 16 a clinical relapse (4 local only, 2 local and regional, 5 regional and metastatic and 5 metastatic only). Local relapses occurred after a median time of 2.7 y (range 0.9-4.7). Overall toxicity profile was good, with no severe grade 3 or higher acute or late gastrointestinal or genitourinary toxicity recorded.

Conclusions: Salvage HDR brachytherapy for locally recurrent prostate cancer after radiotherapy is feasible and associated with an acceptable toxicity profile. The high rate of clinical relapse warrants further investigation to define the subgroup of patients who will benefit from salvage local therapy.

## CO059

### EFFICACY AND TOXICITY OF HIGH-DOSE-RATE SINGLE FRACTION BRACHYTHERAPY FOR LOCALIZED PROSTATE CANCER: A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aims: To report the efficacy and toxicity of high-dose-rate (HDR) brachytherapy (BRT) delivered as a single fraction of 19 Gy for men with localized prostate cancer.

Methods: From October 2015 to march 2018, 30 patients with histologically proven and clinically localized prostate cancer were treated in our institution with 19Gy single fraction HDR-BRT. Patients were classified into risk group according to the NCCN guidelines. All patients had a staging MRI. Treatment was delivered using transrectal Ultrasound (TRUS) planning, with 19Gy prescribed to the prostate with no margins. Follow up (FU) was performed at 1, 3 and 6 months after implantation, and every 6 months afterwards. Biochemical failure was defined according to the Phoenix definition. Toxicity was reported according to the Common Toxicity Criteria for Adverse Event, Version 4.0 (CTAE v4) by the National Cancer Institute.

Results: The median age was 73.5 years. The median gland volume was 39 cm3. Of the 30 patients, 22(73.3%) had a T2 disease, 28(93.3%) had a Gleason score ≤7, the median pre-treatment prostate-specific antigen level was 8.31 ng/mL. 10 pts (33.3%) were classified at high risk, 17(56.7%) intermediate and 2(6.7%) low risk. A total of 17 patients (56.7%) received hormonal therapy of whom 8(26.7%) were classified at high-risk, 6(20%) were favorable intermediate and 3(10%) unfavorable intermediate, for a median duration of 3 months. All pts tolerated the implantation procedure very well with minimal discomfort. No intraoperative or perioperative complications occurred. The median Follow up was 20 months (range: 2-31) after treatment. 1 patient (pt) died for causes unrelated to prostate cancer. Acute genitourinary toxicity grade 1 (hematuria) was observed in 4 (13.8%) patients. Acute Grade 2 urinary retention requiring the temporary use of a catheter in the immediate postoperative period was observed in 1 (3.4%) pt. No acute or late toxicity in term of gastrointestinal toxicity such as anal pain, rectal bleeding, diarrhea, anal ulcer and/or rectourethral fistula has been observed after treatment. Four patients had a biochemical relapse, with a median time of 20 months (range: 16-28), representing a 2-years actuarial relapse rate of 82,6%. No clinical relapse or death from prostate cancer occurred.

Conclusions: In our series, 19Gy HDR-BRT demonstrates low rates of toxicity, and encouraging efficacy but longer follow-up is warranted before this treatment can be recommended more widely.

## CO060

### IMPLEMENTATION OF COMBINED INTRACAVITARY AND INTERSTITIAL BRACHYTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Aims: To improve target volume coverage with the implementation of combined intracavitary and interstitial brachytherapy (ICIS-BT) in the locally advanced cervical cancer treatment.

Methods: Traditionally intracavitary brachytherapy in addition to external-beam radiotherapy (EBRT) is a standard treatment for locally advanced cervical cancer. In patients with large-volume tumors at the time of brachytherapy, with minor parametrial response, and/or in the case of unfavorable topography, intracavitary technique is not optimal choice. In these situations additional interstitial brachytherapy has been applied to improve target coverage. In our department, from October 2017 to October 2018, eleven patients were treated using combined ICIS-BT for primary cervical cancer. The morphological and/or dimensional features of the

target volume (i.e. ≥30 cc) drove our choice. All patients received EBRT (VMAT) with concomitant chemotherapy and sequential brachytherapy boost. The prescribed dose was 45 Gy in 25 fractions over 5 weeks. Chemotherapy regimen was weekly Cisplatin (40 mg/m$^2$). Image-guided adaptive brachytherapy (IGABT) based on magnetic resonance imaging (MRI) was performed for all 11 patients. Imaging technique and volume definition were in accordance to the recommendations from the Gynecological (GYN) GEC ESTRO working group. GTV, High Risk CTV (HR-CTV), Intermediate Risk CTV (IR-CTV), bladder, rectum and sigmoid were delineated at the time of each brachytherapy fraction on para-axial MR images with the applicator in place. Dose-volume histograms were calculated to evaluate doses to tumor target and organs at risk. The total dose prescribed was 28 Gy in 4 fractions. EBRT and brachytherapy cumulative doses were evaluated by calculation of a biologically equieffective dose in 2 Gy per fraction (EQD2) using the linear-quadratic model with $\alpha/\beta = 10$ Gy for tumor effects and $\alpha/\beta = 3$ Gy for late normal tissue damage. Acute genitourinary, gastro-enteric and vaginal toxicity was monitored at each fraction and recorded according to the CTCAE criteria version 4.03. The planning aims, according to the EMBRACE II protocol, have been achieved for all 11 patients (i.e. D90 for the HR-CTV should be between 90 and 95 Gy and for D98 for the GTV above 95 Gy). Also the hard constraints for the organs at risk were never exceeded (D2cm$^3$ of the bladder below 80 Gy, D2cm$^3$ of the rectum below 65 Gy, D2cm$^3$ of the sigmoid/bowel below 70 Gy). To demonstrated that the implementation of interstitial component was essential to improve target dose coverage, the treatment of the 11 patients were rescheduled avoiding interstitial needles dose contribution. The D90 to HR-CTV obtained with ICIS-BT and without the use of needles were compared.

Results: Brachytherapy treatment was well tolerated by all 11 patients. Patients didn't show G3 toxicities or higher. Figure 1 shows the variation of the D90 CTV-HR for each of the eleven patients and one treatment fraction, with and without the contribution of the interstitial needles. The average gain in terms of target coverage was of 25% in favor of the ICIS-BT treatments.

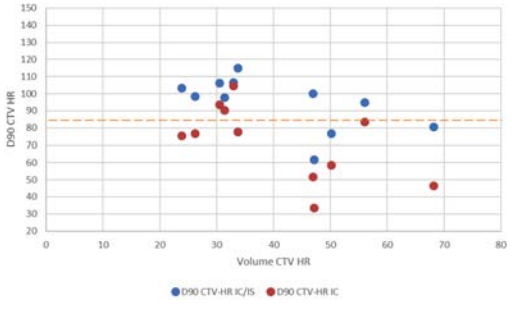


Figure 1.

Conclusions: Brachytherapy is a part of the standard treatment for cervical uterine cancers in the locally advanced stage. In patients with large-volume tumors at the time of brachytherapy, with minor parametrial response, and/or in the case of unfavorable topography, the implementation of the interstitial technique alongside the intracavity technique allows to guarantee an adequate coverage of the target, with a consequent better local control of the disease.

**CO061**

## ACTINIC VAGINITIS IN PATIENTS TREATED WITH VAGINAL HDR BRACHYTHERAPY IN POST-OPERATIVE ENDOMETRIAL CANCER FIGO STAGE I: ROLE OF HYALURONIC ACID AND AMINO ACID VAGINAL CREAM

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Aims: Actinic vaginitis is the most common Vaginal Brachytherapy (VBT) related toxicity, often heavily affecting women's sexual QoL due to additional alterations as symptomatic inflammation and dyspareunia. A hyaluronic acid and aminoacids (HA+AA) vaginal cream is a medical device acting as anti-inflammatory, recommended in prevention of actinic vaginitis caused by the radiotherapy of the pelvic district. Aim of this work was to evaluate the efficacy of HA+AA vaginal cream in prevention of vaginal mucositis after adjuvant HDR-VBT.

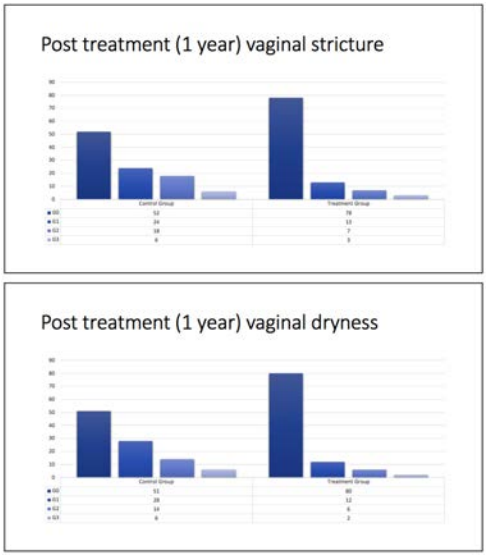


Figure 1.

Methods: A prospective observational study was conducted over a 26-month accrual period. From January 2014 to March 2016 we enrolled 120 women (aged 53-80 years) who underwent surgery for endometrial carcinoma stage I and adjuvant HDR-VBT (30 Gy/5 fractions), divided in 2 groups. Treatment Group: 60 women treated with HA+AA vaginal cream twice daily for 4 weeks, starting simultaneoulsy to VBT. Control Group: 60 patients did not undergo any treatment during and after VBT. No concomitant medication was allowed over the period of treatment and observation. Patients were examined at the time of admission (T0), one month, 3 months and 1 year after treatment. Subjective parameters, including CTCAE 4.03 scale for AEs and objective assessment, including inflammatory signs inspected by the physician, were investigated.

Results: 3 months after VBT, the treated group showed a statistically significant improvement ($P<0.05$ vs. control) on subjective symptoms of inflammation, dryness and pain. One year after VBT, further statistically improvement was observed, especially in the subset of patients evaluated for stricture. Rates of G0 vaginal stricture were 78% vs 52%, respectively in the treatment group vs control and 3% vs 6% G3. G0 dryness was 80% (vs 51%) in the treatment group and G3 was only 2% (vs 6%). We observed 83% G0 vaginal pain in the treatment group (vs 65%) with 0 G3 (vs 1%).

Conclusions: Application of HA + AA vaginal cream on the irradiated vagina during VBT was shown to postpone the first signs of acute vaginal discomforts and reduce the severity of mucosal reactions. Moreover, time to recover was longer, especially for exudative epithelises, in the control group. This indicates that HA was effective as a prophylactic but also as a therapeutic measure. The results of this prospective study suggest an interesting role of the HA+AA vaginal cream as supportive treatment to improve compliance and QoL in patients undergoing VBT.

## CO062

## ACCELERATED PARTIAL BREAST RE-IRRADIATION USING INTERSTITIAL HIGH-DOSE-RATE BRACHYTHERAPY FOR LOCAL RECURRENCE: 5-YEAR RESULTS

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Background and Purpose: BALESTRA (Brachytherapy as Adjuvant Local rE-irradiation for Salvage Treatment of Recurrent breAst cancer) is a prospective study with the purpose of evaluate feasibility, acute and late toxicity and preliminary outcome of a single institution experience of accelerated partial breast re-irradiation with adjuvant interstitial HDR brachytherapy (BT).

Material and Methods: Between January 2011 and September 2015, 31 consecutive patients with histologically confirmed recurrent breast cancers after conservative surgery and conventional whole breast radiotherapy were retreated with a second conservative surgical resection and reirradiated by adjuvant HDR-BT. A dose of 34 Gy in 10 fractions, 2 fractions per day with a minimal interval of 6h was delivered.

Results: Follow-up is available for 29 patients. The procedure was well tolerated in all patients. No acute epidermitis or soft tissue side effects higher than grade 2 were recorded, with good cosmetic results in all patients. Local recurrence occurred in 2 patients (6.8%) after 32 and 42 months from BT, distant metastases were observed in 10.3% of women. After a median follow-up of 59.8 months (range, 17.3-96.8) the overall survival was 100%. 5-years local control and 5-years progression free survival rate is 91% and 84%, respectively.

Conclusions: Our preliminary analysis showed that HDR-BT is a feasible treatment for partial breast reirradation offering very low-complications rate and a fast procedure. Higher patient number are warranted in order to define the role of this treatment modality in the breast conservative management of local recurrence.

**Table 1. Patient characteristics.**

| Characteristic (31 pts) | Classification | number (%) |
|---|---|---|
| Age at the time of BT | <50 years | 7 (23) |
| | 50-60 years | 9 (29) |
| | >60 years | 15 (48) |
| Time to IBTR | < 5 years | 4 (13) |
| | 5-10 years | 9 (29) |
| | 10-20 years | 14 (45) |
| | > 20 years | 4 (13) |
| Recurrence site | Same quadrant of primary cancer | 11 (35) |
| | Other quadrant of primary cancer | 16 (52) |
| | Missing data | 4 (13) |

*BT: brachytherapy; IBTR = ipsilateral breast tumor recurrence.*

## CO063

### LONG-TERM OUTCOMES USING ELECTRON IORT APBI FOR EARLY STAGE BREAST CANCER: THE VERONA UNIVERSITY HOSPITAL EXPERIENCE

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Purpose/Objective(s): Intraoperative radiotherapy (IORT) it is a type of accelerated partial breast irradiation (APBI) and consists in the administration of radiation therapy on the tumour bed at the time of surgery. Patients deemed at low risk of locale recurrence (LR) or those deemed suitable for partial breast irradiation, according to the GEC-ESTRO and ASTRO recommendations,could be considered as ideal candidates for IORT. Several published studies of electron intraoperative radiation therapy, when delivered as APBI, have demonstrated low recurrence rates (1.5-2.5%) at 5-year follow-up in ASTRO Suitable or ESTRO Good women. We evaluated our patient cohorts treated with IORT APBI, with follow-up up to 10 years, to answer the question of long-term control.

Materials/Methods: From July 2006 to December 2015, 295 patients suitable for breast-conserving therapy entered a single-arm phase II study and were treated with IOERT, as radical treatment, immediately after surgical resection using a single dose of 21 Gy to Dmax. Patient inclusion criteria were mostly ASTRO Suitable Group except for G3 grade. All patients received IOERT with a mobile electron linear accelerator.

Results: With a median follow-up of 84 months, 6 women (2.03%) experienced a true local recurrence (reappearance of the tumor in the same quadrant). None of the patients had a new ipsilateral carcinoma (reappearance of cancer in another quadrant of the same breast). In addition, 5 women (1.69 %) developed distant metastases, 2 (0.67%) a contralateral breast cancer, and 9 (3%) other cancers. 22 patients (7.46%) died. Patients that recurred underwent mastectomy. 5-year overall survival (OS) was 96% (95% CI 92.9;97.8). We analyzed characteristics associated with a high risk of local relapse such as: age, grading, hormone profile. In univariable analysis, age > 70 years (HR 2.40, 95% CI 2.40;17.71 p 0.002), grading G2 (HR 9.93, 95% CI 1.25;69.16 p 0.0294), and negative hormone testing (HR 2.29, 95% CI 1.00;5.93 p 0.0602) have been associated with a lower 5-year OS. In multivariable analysis no statistically significant value were reported except age >70 (p 0.0004). 5-year disease free survival (DFS) was 94.3% (95%CI 90.6;96.6). Even in this case we analysed characteristics associated with a high risk of local relapse such as age, grading, hormone profile. In univariable analysis, age > 70 years (HR 4.18, 95%CI 1.96;8.91 p 0.002), grading G2 (HR 9.93, 95% CI 1.30;14.14 p 0.0167), and negative hormone testing (HR 2.06, 95% CI 0.94;4.54 p 0.0602) have been associated with a lower 5-DFS.

Conclusions: Data from our trial suggest that single-dose IOERT in early stage breast cancer can be delivered safely and with excellent results. Our long-term recurrence rates are very low. 5 OS and DFS rate are results comparable with literature data on EBRT thus encouraging the use of IOERT in subset of low risk patients with early stage breast cancer.

## CO064

### IORT FOLLOWED BY ACCELERATED HYPOFRACTIONATED WHOLE-BREAST IRRADIATION VERSUS ACCELERATED HYPOFRACTIONATED WHOLE-BREAST IRRADIATION FOLLOWED BY SEQUENTIAL BOOST: PROPENSITY MATCHING ANALYSIS OF LONG-TERM TOXICITY AND COSMETIC OUTCOME

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Aims: To compare the 6-years late toxicity and cosmetic outcome in women treated by Intraoperative Radiotherapy (IORT), as anticipated boost, followed by hypofractionated radiotherapy (HRT) versus HRT followed by sequential boost (SB) in women with stages I-II breast cancer.

Methods: Two-hundred and ninety-four women were retrospectively studied. HRT (42.40 Gy in 16 daily fractions of 2.65 Gy) was delivered in all patients. Ninety-eight of them underwent IORT (10 Gy in single fraction) during surgery and before HRT. These subjects were matched by propensity analysis with 196 women treated by HRT followed by SB (10 Gy in four daily fractions of 2.5 Gy). Late skin and subcutaneous toxicity as well as cosmetic outcome were measured at 3 and 6 years after treatments. The acute and the late skin and subcutaneous toxicity were rated according to the Radiation Therapy Oncology Group (RTOG) scale for early and late side effects. The cosmetic outcome, was assessed with the European Organization for Research and Treatment of Cancer (EORTC) Cosmetic Rating System. Differences in the incidence of toxicities between the two groups were evaluated by the Fisher's exact test. The analysis significance level was adjusted by the Bonferroni method. According to this correction an $\alpha$ error <0.0125 was considered statistically significant.

Results: Acute Grade 2 (G2) or greater skin toxicity was 31.6% in the HRT+SB group and 11.2% in the

IORT+HRT group (p=0.001). Three-years after radiation treatments, G2 or more skin late toxicity were observed in 1% vs. 10.8% (p=0.01) women treated by IORT+HRT and HRT+SB, respectively. The rate of late subcutaneous toxicity was 16.7% in the HRT+SB group and 18.4% in the IORT+HRT group (p=0.72). At 6 years after radiotherapy, women treated by IORT+HRT experienced a comparable rate of G2 or greater skin and subcutaneous late toxicity with respect to women treated by HRT+SB (0% vs. 2.4% and 3.7% vs. 6.5% with p=0.57 and p=0.74). The percentage of women with a fair or poor cosmetic outcome was 15.8% in the IORT+HRT group and 15.7% in the HRT+SB group at 3 years (p=1.0) and was 5,6% vs. 5,4% (p=1.0) at 6 years.

Conclusions: IORT as anticipated boost seems not adversely affect 6-years late toxicity and cosmetic outcome compared with HRT followed by SB. Randomized controlled trials will be necessary to confirm our findings.

**Table 1. Acute Toxicity assessed by the RTOG–EORTC Acute Radiation Morbidity Scoring Criteria.**

| | | IORT+HRT | | HRT+SB | | p value |
|---|---|---|---|---|---|---|
| | | Patients (Number) | % | Patients (Number) | % | |
| ACUTE TOXICITY | G0 | 45/98 | 45.9% | 60 /196 | 30.6% | 0.0139 |
| | G1 | 42/98 | 42.8% | 74/196 | 37.8% | 0.448 |
| | G2 | 11/98 | 11.2% | 45/196 | 22.9% | 0.0178 |
| | G3 | 0 /98 | 0% | 17/196 | 8.7% | 0.001 |
| | G4 | 0 /98 | 0% | 0/196 | 0% | 1.0 |
| PATIENTS WITH ACUTE SKIN TOXICITY < G2 | | 87/98 | 88.8% | 134/196 | 68.4% | 0.001 |
| PATIENTS WITH ACUTE SKIN TOXICITY ≥ G2 | | 11/98 | 11.2 % | 62/196 | 31.6% | |

IORT= Intra-Operative Radiotherapy; HRT= Hypofractionated Radiotherapy; SB= Sequential Boost.

## CO065

### RETROSPECTIVE ANALYSIS OF INTEGRATED CHEMORADIATION TREATMENT OF HNSCC WITH IMRT-SIB: LONG TERM TOXICITY AND OUTCOME

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Aims: to evaluate the long term results in terms of toxicity, response rate and survival in patients (pts) with advanced head and neck squamous cell cancer (HNSCC), treated with intensity-modulated radiotherapy with simultaneous integrated boost (IMRT-SIB) schedule with concurrent chemotherapy (CHT).

Methods: Between April 2010 and December 2017, 143 consecutive pts (109 males and 34 females; mean age 62 years) with HNSCC (88 oropharynx, 12 larynx, 31 hypopharynx, 12 nasopharynx) were treated at our institute with concurrent chemoradiotherapy (CTRT). AJCC/UICC stage was: III in 36 pts and IV in 107 pts. 54 pts received neoadjuvant CHT before CTRT (2 cycle with CDDP-5FU schedule in 10 pts, 2-3 cycles with TPF schedule in 44 pts) with partial response >50% of primary tumor (T) and Patological Nodal (PN) in 61% and 65%, respectively. IMRT-SIB dose prescription was 70 Gy, 63 Gy and 54 Gy in 35 daily fractions to the planning target volume (PTV) of Gross tumor volume (GTV T) and PN, high risk nodes (HRN), and low risk nodes (LRN), respectively. Concurrent CT was given for all pts: cisplatin (CDDP) 100 mg/m$^2$ i.v. per day every 3 weeks (wks) in 38 pts, CDDP 75-100 mg/m$^2$ i.v every 4 wks in 99, cetuximab 250 mg/mq i.v. wks in 6. During treatment, pts received pain therapy and nutritional support.

Results: The median treatment duration was 50 days. Mean delivered doses were: PTV GTV T and PN 71.2 Gy ± 1,8 SD; PTV HRN 64,4 Gy ± 2,3 SD; LRN 57.1 Gy ± 1,1 SD; controlateral parotid 22,2 Gy ± 4,24. Acute toxicity (according to RTOG/EORTC scales) consisted in: mucositis G2 in 52% of pts and G3 in 35%; Xerostomia G2 in 51% and G3 in 7%, dysgeusia in 90%, Dermatitis ≥ G2 in 62%. Mean weight loss was 3,6 Kg. RT was interrupted in 20 pts, mean 3.8 days (range 1-10). Toxicity 6 months (mos) after RTCT were: mucosal edema in 63% of the pts, Xerostomia G2 in 23%, dysgeusia in 30%, hearing loss in 7%. Late reactions, after ≥12 mos, were: Xerostomia G1-2 in 10%; hearing loss in 7%; dysphagia in 3%; mucosal edema in 12%. One pt underwent tracheotomy for edema post RT and another one needed PEG for pharyngeal necrosis. Complete response rate was 81.8% . Median follow up was 35 mos (range 2-108). At time of this analysis : 68 pts are alive free of desease; 15 are alive with desease; 60 are died. Median Disease free-survival and Overall Survival were 27 and 35 mos.

Conclusions: in our analysis IMRT-SIB concurrent to CT is feasible, well tolerated with a good clinical response.

## CO066

### LONGITUDINAL ASSESSMENT OF WEIGHT LOSS AND PATIENT'S REPORTED DYSPHAGIA AFTER RADIATION TREATMENT FOR HEAD AND NECK CANCER

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Aims: To analyze the factors associated with weight loss and "patient-reported dysphagia" after radical or adjuvant radiotherapy (with or without concurrent chemotherapy) treatment for Head and Neck Cancer (HNC).

Methods: 238 consecutive patients (pts) treated for HNC at a single Institution (from July 2015 to December 2017) were retrospectively analyzed. Disease was localized in oropharynx (63, 26.5%),

hypopharynx (21, 8.8%), larynx (38, 16%), oral cavity (53, 22.3%), nasopharynx ( 29, 12.2%), nose and paranasal sinuses (17, 7.1%) and salivary glands (10, 4.2%); thyroid, skin and tumors of unknown primitiveness (7, 2.9%) were. The longitudinal assessment of patient-reported dysphagia was performed only for those pts (58) that completed the Vanderbilt Head and Neck Symptom Survey - Italian Version 2.0 (VHNSS-IT) at 3, 6, 12, and 18 months after treatment. Maximum scores of the ""swallow-solid"" (SS), ""swallow-liquid"" (SL) and ""nutrition"" (N) subscales of the VHNSS-IT and the weight loss (WL) were correlated with clinical and therapeutic variables and acute and late toxicities (CTCAE v4).

Results: Of the 238 pts analyzed only 58 completed the VHNSS-IT throughout the follow up. The average WL at the end of treatment (EOT) was -4,54% of basal weight (p=0,000). Pts kept to lose weight up to 6 months after EOT (p=0,001 and p=0,062 at 3 and 6 months respectively). Basal weight was not reached until 18 months after EOT. Moreover WL was significantly higher in relation to concurrent chemotherapy (CC), enteral/parenteral (NET/NPT). In the same way acute (AD) and late (LD) high grade dysphagia, acute (AH) and chronic (CH) high grade hyposcialia affected WL. SL max scores were significantly higher in elderly pts and in those with alcohol consumption. Both SS and N were significantly higher in relation to NPT/NET use, to AD, to CD and to trismus. Moreover N value was significantly higher in relation to CC, to acute mucositis, to AH and CH and to chronic laryngeal edema. Table 1.

**Table 1. Weight, Swallow solid, Swallow liquid and Nutrition correlated to clinical and therapeutic variables and acute and late toxicities.**

| Weight | p value end of treatment vs start | p value 30-40 days vs start | p value 3 months vs start | p value 6 months vs start | p value 12 months vs start | p value 18 months vs start |
|---|---|---|---|---|---|---|
| Acute hyposcialia | 0,001 | 0,007 | 0,011 | 0,017 | 0,030 | 0,046 |
| Acute dysphagia | 0,009 | 0,113 | 0,591 | 0,340 | 0,266 | 0,990 |
| Chronic hyposcialia | 0,018 | 0,057 | 0,028 | 0,024 | 0,016 | 0,034 |
| Chronic dysphagia | 0,039 | 0,025 | 0,031 | 0,007 | 0,009 | 0,007 |
| NET or NPT | 0,003 | 0,021 | 0,215 | 0,050 | 0,053 | 0,483 |
| Concurrent chemotherapy | 0,005 | 0,009 | 0,021 | 0,068 | 0,043 | 0,018 |
| **Swallow solid** | | | **p value 3 month** | **p value 6 months** | **p value 12 months** | **p value 18 months** |
| NET or NPT | | | 0,327 | 0,063 | 0,205 | 0,033 |
| Acute dysphagia | | | 0,018 | 0,089 | 0,201 | 0,039 |
| Chronic dysphagia | | | 0,018 | 0,089 | 0,068 | 0,039 |
| Trismus | | | 0,066 | 0,076 | 0,013 | 0,028 |
| **Swallow liquid** | | | **p value 3 month** | **p value 6 months** | **p value 12 months** | **p value 18 months** |
| Elderly patiets (over 75 years) | | | | 0,030 | | |
| Alchool | | | | 0,014 | | |
| **Nutrition** | | | **p value 3 month** | **p value 6 months** | **p value 12 months** | **p value 18 months** |
| Concurrent chemotherapy | | | 0,008 | 0,534 | 0,360 | 0,200 |
| NET or NPT | | | 0,003 | 0,020 | 0,084 | 0,110 |
| Acute dysphagia | | | 0,011 | 0,080 | 0,024 | 0,204 |
| Chronic dysphagia | | | 0,049 | 0,080 | 0,024 | 0,002 |
| Trismus | | | 0,393 | 0,324 | 0,008 | 0,059 |
| Acute mucositis | | | 0,033 | 0,489 | 0,085 | 0,024 |
| Acute hyposcialia | | | 0,011 | 0,220 | 0,247 | 0,204 |
| Chronic hyposcialia | | | 0,023 | 0,563 | 0,044 | 0,096 |
| Chronic laryngeal edema | | | 0,553 | 0,562 | 0,141 | 0,025 |

Conclusions: Weight changes and subjective dysphagia were significant in relation to many clinical and therapeutic variables analyzed. Patients reported outcomes are inexpensive and easy to use in daily practice. They can help clinicians to identify pts who need early intervention. WL after EOT highlights the need of more intensive nutritional support in selected pts.

**CO067**

## PATTERNS OF FAILURE IN HIGH-RISK OROPHARYNGEAL CANCER PATIENTS TREATED WITH IMRT: COMPARISON OF TWO DIFFERENT CTV EXPANSION MODALITIES

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Aims: The aim of our work was to assess the impact of two different delineation approaches (anatomical vs geometric expansion) on the clinical outcome and patterns of failure of patients with oropharyngeal cancer (OPC).

Methods: We performed a retrospective analysis of consecutive patients treated at our institution for OPC between January 2010 and April 2018. In 2014, our local policy to delineate high risk CTV for both primary (CTV-p) and nodal (CTV-n) GTVs shifted from an anatomical expansion (AE) to a geometric expansion (GE) modality, described as follows: - AE: CTV-p consisted of the primary GTV plus the whole oropharyngeal anatomical compartment, edited for air cavities and anatomical barriers; CTV-n consisted of the nodal GTVs plus the corresponding lymph node level (delineated according to Gregoire's classification), including also the level immediately adjacent to it; - GE: CTV-p consisted of the primary GTV plus an isotropic 5 mm margin, manually edited for air cavities and anatomical barriers; CTV-n consisted of the nodal GTVs plus an isotropic 7 mm margin, manually edited to take into account anatomical barriers. Of note, an additional 5 mm margin to the CTV-p was not added. All patients received IMRT with 3 dose levels: the high, intermediate and low risk CTVs received 70, 60 and 50 Gy or 69.9, 59.4 and 52.8 Gy in 35 or 33 fractions, respectively, depending on whether a sequential or SIB technique was employed. A 3-5 mm PTV margin was added to CTV's (3 mm in case of daily image guidance). HPV status was not routinely available until 2015. Median locoregional control (LRC), PFS and OS were calculated. The relative estimates of LRC and PFS at 24 months were estimated by the Kaplan-Meier method.

Results: A total of 116 patients were included (table 1). At a median follow-up of 36 months (range: 5-108), 88 patients were alive (75.8%). The median PFS and OS for the whole group were 74 (95% CI: 45-74) and 72 (95% CI: 64-81) months, respectively. There was no

difference between the AE and GE cohorts in terms of 2-year LRC (86.9% *vs* 94.3%; median not reached; p= 0.28). 15 locoregional relapse were observed (13 in-field and 2 marginal) with no influence of contouring policy adopted.

Conclusions: The adoption of a GE expansion modality with resulting smaller high risk CTVs was not associated with a detrimental impact on outcome in OPC. Contouring approach did not influence the risk of marginal relapse.

**Table 1. Weight, Swallow solid, Swallow liquid and Nutrition correlated to clinical and therapeutic variables and acute and late toxicities.**

| Characteristic | No. of patients (%), n = 116 | AE (%), n = 43 | GE (%), n = 73 |
|---|---|---|---|
| Median age, years (range) | 62.5 (43-88) | 60 (43-81) | 63 (43-88) |
| Sex | | | |
| Male | 84 (72.4%) | 28 (65.1%) | 56 (76.7%) |
| Female | 32 (17.6%) | 15 (34.9%) | 17 (23.3%) |
| ECOG Performance Status | | | |
| 0 | 97 (83.6%) | 37 (86%) | 60 (82.1%) |
| 1 | 19 (16.4%) | 6 (14%) | 13 (17.9%) |
| Charlson Comorbidity Index (age-adjusted) | | | |
| <4 | 49 (42.2%) | 22 (51.2%) | 27 (36.9%) |
| 4-7 | 63 (54.3%) | 19 (44.1%) | 44 (60.3%) |
| ≥8 | 4 (3.5%) | 2 (4.7%) | 2 (2.8%) |
| Smoking history (pack/years) | | | |
| 0 | 23 (19.8%) | 6 (13.9%) | 17 (23.3%) |
| <10 | 19 (16.3%) | 12 (27.9%) | 7 (9.5%) |
| 10-20 | 27 (23.3%) | 5 (11.6%) | 22 (30.2%) |
| >20 | 47 (40.6%) | 20 (46.6%) | 27 (37%) |
| HPV status | | | |
| Positive | 52 (44.9%) | 7 (16.3%) | 45 (61.6%) |
| Negative | 20 (17.2%) | 7 (16.3%) | 13 (17.8%) |
| Unknown | 44 (37.9%) | 29 (67.4%) | 19 (26%) |
| AJCC stage (VIIth ed) | | | |
| II | 11 (9.5%) | 4 (9.3%) | 7 (9.5%) |
| III | 23 (19.8%) | 7 (16.3%) | 16 (22%) |
| IVA | 72 (62.1%) | 30 (69.7%) | 42 (57.6%) |
| IVB | 10 (8.6%) | 2 (4.7%) | 8 (10.9%) |
| Treatment modality | | | |
| RT alone | 23 (19.8%) | 16 (37.2%) | 7 (9.2%) |
| conc. cisplatin-RT | 88 (75.9%) | 25 (58.2%) | 63 (86.4%) |
| TPF followed by CRT | 5 (4.3%) | 2 (4.6%) | 3 (41.4%) |
| IMRT schedule | | | |
| sequential | 22 (18.9%) | 6 (14%) | 16 (22%) |
| SIB | 94 (81.1%) | 37 (86%) | 57 (78%) |

**CO068**

## CLINICAL OUTCOME IN LOCALLY ADVANCED HEAD AND NECK CANCER PATIENTS TREATED WITH MODERATE HYPOFRACTIONATED SIB-IMRT

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Aims: To retrospectively evaluate the clinical outcome in patients (pts) treated curatively with a moderate hypofractionated regime for locally advanced head and neck squamous cell carcinoma (HNSCC).

Methods: From 2011 to 2017, 70 pts were treated with simultaneous integrated boost intensity modulated Radiation Therapy (SIB-IMRT) in our radiation oncology centre. 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; 98% (69 pts) squamous cells cancer; PET-staged 67% IV a-b, 19% III, 10% II, 4% I (AJCC-7 th edition). 52 pts received SIB-IMRT with concurrent platinum-based chemotherapy or cetuximab (51 and 1 respectively), and 18 pts underwent SIB-IMRT alone. Levels of dose were 67.5Gy (2.25Gy/fr), 60 Gy (2Gy/fr), 54 Gy (1.8Gy/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). OS and PFS were estimated by using the Kaplan-Meier method.

Results: 67 pts (96%) completed the planned schedule. The median overall treatment time was 46 days (range 40-62). Response was assessed in 66 pts (94%). In according to the RECIST criteria, 60% of pts achieved a complete response (CR), 21% a partial response, 10% experienced a progression disease, 1% showed stable disease. 15/41 pts with CR had a progressive disease: 7 locoregional recurrences (4/7 underwent salvage surgery/radiotherapy), 8 distant recurrences. At the time of data analysis (May 2019), 21/70 were alive and with no evidence of disease. For all pts, the median OS was 5.5 years and the 3-years OS resulted 61%. The 3-years OS were 54.5% in oropharynx and hypopharynx, 75% oral cavity, 77% larynx, and 100% nasopharynx (Figure 1). The 3-years survival were 90%, 43%, 61% and 40% for stage I-II, III, IVa and IVb, respectively. Actuarial 3-years PFS was 41%, median PFS was 2.2 years. Meanwhile, 3 years Local Recurrence-PFS resulted 67%. No significant differences between the subgroups of pts were found; the primary cancer site and overall treatment time (more than 10 days over 40 days scheduled) do not correlate with OS and PFS.

Conclusions: In our analysis, moderate hypofractionated SIB-IMRT for locally advanced HNSCC not selected pts with or without chemotherapy produced good results in term of response rate, PFS and OS.

| Clinical results | |
|---|---|
| Median overall treatment time in days (range) | 46 (range 40-62) |
| Recist criteria | |
| - CR | 60% |
| - PR | 21% |
| - PD | 10% |
| - SD | 1% |
| 3 years OS (tumor site) | |
| - oropharynx | 54.5% |
| - larynx | 77% |
| - hypopharynx | 54.5% |
| - oral cavity | 75% |
| - nasopharinx | 100% |
| 3 years OS (stage) | |
| - IVa-b | 40% |
| - III | 61% |
| - II | 43% |
| - I | 90% |

**Figure 1.**

## CO069

### COMPARISON OF 3D-CONFORMAL RADIOTHERAPY (3DCRT) VERSUS SIB-IMRT ON PATTERN OF FAILURE IN PATIENTS AFFECTED BY LOCALLY ADVANCED ORAL CAVITY SQUAMOUS CELL CARCINOMA (LA-OCSCC)

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Aims: The main treatment modalities for LA-OCSCC are surgery and radio(chemo)therapy. Loco-regional relapse represent the predominant pattern of failure in this setting. The aim of our study was to analyze the impact different RT techniques on pattern of failure and outcome.

Methods: We performed a retrospective cohort analysis of consecutive patients treated at our institution for LA-OSCC between March 2010 and January 2018 with 3DCRT vs IMRT-SIB technique with adjuvant intent with or without chemotherapy. By definitions, 3DCRT consisted of sequential shrinking field technique (60-66Gy to high-risk CTV and 50Gy to low-risk CTV) whereas in IMRT-SIB cohort low-risk CTV was irradiated with 1,6-1,8Gy dose per fraction.

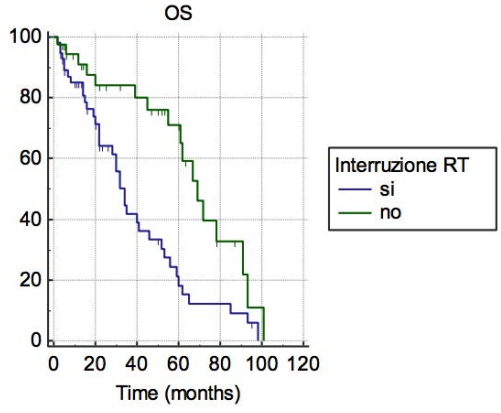


**Figure 1.**

Results: A total of 94 patients were included in the study (48 M, 46 F). Median age was 63,1 y. 62,8% of the study population had PS 0. 22,3% of patients had stage III, 67% had stage IVa and 3% had stage IVb. Primary tumour location was mobile tongue. 37 patients were treated with 3DCRT and 57 were treated with IMRT-SIB. Median interval between surgery and the start of adjuvant treatment was 77 days. The median number of days of interruption of RT treatment was 3.2. At a median F-UP of 2,5 years actuarial DFS and OS were 10.7 and 29.7 months respectively. In terms of pattern of failure, no difference between the two groups was observed. On univariate analysis, RT interruption had a negative impact on OS (P = 0,0011). This finding was confirmed on multivariate analysis (P =0,0262) (Figure 1)

Conclusions: Different RT techniques had no impact on patterns of failure and outcome in LA-OSCC patients. RT interruption remains a crucial prognosticator in this setting.

## CO070

### A MONO-INSTITUTIONAL ANALYSIS OF COMBINED MODALITY TREATMENT FOR OESOPHAGEAL CANCER

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Aims: To evaluate clinical outcomes, toxicity and postoperative complications of a consecutive series of patients affected with oesophageal cancer (both squamous cell - SCC and adenocarcinoma – ADK histology) treated with trimodality strategy (TM).

Methods: We describe a retrospective cohort of 53 patients who received multimodality treatment at our Institute (2014-2019). Radiotherapy (RT) was delivered employing volumetric-modulated arc therapy (VMAT). The more common RT schedules used were 41.4 Gy/23 fractions(fr) and 45 Gy/25 fr in ADKs and in SCCs, respectively. The protocol contemplated RT with concurrent chemotherapy (CT, mainly, Carboplatin/Paclitaxel and Cisplatin/5-fluorouracil in ADKs and in SCCs, respectively) and subsequently surgery.

Results: Detailed patients, tumor, treatment characteristics regarding both treatment volumes and organs at risk, toxicity profile and grade of postoperative complications are provided in Table 1. In ADK cohort (25 patients), tumors were mostly located in distal esophagus (22.7%) and gastroesophageal junction (22.7%). Middle (22.6%) and lower thoracic (20.7%) esophageal location were more common in SCC group. The most frequent stage at diagnosis was cT3(90%), cN2(48%) in ADK group and cT3(89.2%), cN1(64.2%) in SCC cohort. Maximum acute RT-CT toxicities were lymphopenia≥G3(83%), leukopenia≥G3 (22.5%), anorexia-G3(22.7%), esophagitis-G3(13.2%) and asthenia-G3(13.2%). Thirty-seven patients underwent surgery. Disease progression was the most frequent reason to deem patients as unoperable (21%). Subtotal esophagectomy was the most frequent surgical procedure performed (81%). Eighteen patients reported acute surgical complications and in 6 patients Clavien–Dindo≥G3 were observed. Globally, 22 patients had grade 1 and grade 2 pathological tumor regression (TRG) according to Mandard classification (18.9% in

ADKs and 40.5% in SCCs). A pN0-pN1 stage was reported among 32 patients (40.5% in ADKs and 46% in SCCs). Two-year overall survival was 48% in SCC group and 40% in ADK cohort, while 2-year cancer-specific survival was 58% and 42% in SCCs and in ADKs, respectively. For details regarding treatment-response and clinical outcomes see Figure 1.

Conclusions: Our clinical results support the TM approach, employing VMAT as RT technique, in oesophageal cancer patients. A mild toxicity profile was reported. Short-term oncological outcomes are in line with those reported in the literature.

**Table 1. Patients, tumor, treatment characteristics, radiotherapy toxicity profile and grade of postoperative complicationsand treatment response.**

| PATIENTS, TUMOR, TREATMENT CHARACTERISTICS | N (%) (n= 53) | *ADK* (n=25) | *SCC* (n =28) |
|---|---|---|---|
| ***Age*** | | | |
| Mean (years) | 63 | 62 | 64.6 |
| Range (years) | (40-83) | (40-83) | (51-79) |
| ***Sex*** | | | |
| Female | 15 (28.3%) | 4 (7.5%) | 11 (20.8%) |
| Male | 38 (71.7%) | 21 (39.6%) | 17 (32.1%) |
| ***Histology*** | | | |
| Adenocarcinoma | - | 22 (41.5%) | - |
| Squamous cell carcinoma | - | - | 28 (52.8%) |
| Undifferentiated carcinoma | - | 3 (5.7%) | - |
| ***Tumor Location*** | | | |
| Upper thoracic oesophagus | 5 (9.4%) | - | 5 (9.4%) |
| Middle thoracic | 13 (24.5%) | 1 (1.9%) | 12 (22.6%) |
| Lower thoracic | 23 (43.4%) | 12 (22.7%) | 11 (20.7%) |
| GEJ | 12 (22.7%) | 12 (22.7%) | 0 |
| ***Clinical Tumor Stage T*** | | | |
| T1 | 1 (1.9%) | - | 1 (1.9%) |
| T2 | 2 (3.8%) | - | 2 (3.8%) |
| T3 | 49 (92.4%) | 24 (45.2%) | 25 (47.2%) |
| T4 | 1 (1.9%) | 1 (1.9%) | - |
| ***Clinical Tumor Stage N*** | | | |
| N0 | 6 (11.4%) | 3 (5.7%) | 3 (5.7%) |
| N1 | 26 (49%) | 10 (18.9%) | 16 (30.1%) |
| N2 | 21 (39.6%) | 12 (22.6%) | 9 (16.9%) |
| ***Clinical Tumor Stage M*** | | | |
| M0 | 53 (100%) | 25 (47.1%) | 28 (52.9%) |

| | | | |
|---|---|---|---|
| ***Radiotherapy schedules*** | | | |
| Macroscopic disease and Elective volume: 41.4 Gy (1.8 Gy/die) | 26 (49%) | 24 (45.2%) | 2 (3.8%) |
| Macroscopic disease and Elective volume: 45Gy (1.8 Gy/die) | 19 (35.8%) | 1 (1.9%) | 18 (33.9%) |
| Macroscopic disease: 50 Gy (2 Gy/die) – Elective volume: 45 Gy (1.8/die) | 8 (15.2%) | - | 8 (15.2%) |
| ***Concurrent Chemotherapy*** | | | |
| CDDP + 5FU | 18 (33.9%) | 2 (3.8%) | 16 (30.1%) |
| CBDCA + PACLITAXEL | 30 (56.6%) | 22 (41.5%) | 8 (15.1%) |

| *ACUTE RT TOXICITY* | G0 | G1 | G2 | G3 | G4 |
|---|---|---|---|---|---|
| ***Anorexia*** | 11 (20.8%) | 21 (39.6%) | 9 (16.9%) | 12 (22.7%) | |
| ***Diarrhea*** | 48 (90.5%) | 4 (7.6%) | 1 (1.9%) | - | |
| ***Esophagitis*** | 1 (1.9%) | 22 (41.5%) | 23 (43.4%) | 7 (13.2%) | - |
| ***Asthenia*** | 12 (22.6%) | 16 (30.2%) | 18 (34%) | 7 (13.2%) | - |
| ***Nausea*** | 38 (71.6%) | 5 (9.4%) | 6 (11.4%) | 4 (7.6%) | - |
| ***Vomiting*** | 44 (83%) | 4 (7.6%) | 3(5.7%) | 2 (3.7%) | - |
| ***Hematological toxicity*** | | | | | |
| *Anaemia* | 10 (18.9%) | 28 (52.8%) | 13 (24.5%) | - | - |
| *Thrombocytopenia* | 21 (39.6%) | 25 (47.2%) | 5 (9.4%) | 0 | - |
| *Luekopenia* | 13 (24.5%) | 8 (15%) | 18 (33.9%) | 11 (20.9%) | 1 (1.9) |
| *Neutropenia* | 22 (41.4%) | 13 (24.5%) | 5 (9.4%) | 11 (20.9%) | - |
| *Lymphopenia* | 0 | 1 (1.8%) | 6 (11.4%) | 30 (56.6%) | 14 (26.4%) |

| Complications | N (%) n=37 | | | | |
|---|---|---|---|---|---|
| Number of patients with acute surgical complications | 18 (48.7%) | | | | |
| *SURGICAL COMPLICATIONS (CLAVIEN-DINDO CLASSIFICATION)* | *Grade I* | *Grade II* | *Grade III-a* | *Grade IV-a* | *Grade V* |
| Bleeding | - | 1 | 1 | - | 1 |
| Infection | - | 4 | - | 1 | 1 |
| Cardiovascular complications | - | 5 | 1 | - | 1 |
| Respiratory complications | 1 | 4 | 1 | 1 | 2 |
| Gastrointestinal complications | - | 1 | - | - | 1 |
| Psychiatric complications | - | 3 | - | - | 1 |
| Neurologic complications | - | - | - | - | - |
| Urologic complications | - | - | - | - | - |
| Chylothorax | - | 1 | - | 1 | - |
| Recurrent Laryngeal nerve paralysis | 1 | 1 | - | - | - |

| *TREATMENT-RESPONSE* | N (%) n= 37 | *ADK* (n=16) | *SCC* (n=21) |
|---|---|---|---|
| ***Tumor Regression Grading (Mandard)*** | | | |
| 1 | 12 (32.4%) | 5 (13.5%) | 7 (18.9%) |
| 2 | 10 (27%) | 2 (5.4%) | 8 (21.6%) |
| 3 | 7 (18.9%) | 3 (8.1%) | 4 (10.8%) |
| 4 | 8 (21.7%) | 5 (13.5%) | 3 (8.2%) |
| ***Pathological tumor stage T*** | | | |
| pTis | 1 (2.7%) | 1 (2.7%) | - |
| pT0 | 13 (35.1%) | 5 (13.5%) | 8 (21.6%) |
| pT1b | 5 (13.5%) | - | 5 (13.5%) |
| pT2 | 2 (5.4%) | - | 2 (5.4%) |
| pT3 | 16 (43.3%) | 10 (27.1%) | 6 (16.2%) |
| ***Pathological tumor stage N*** | | | |
| pN0 | 19 (51.4%) | 9 (24.3%) | 10 (27.1%) |
| pN1 | 13 (35.1%) | 6 (16.2%) | 7 (18.9%) |
| pN2 | 3 (8.1%) | 1 (2.7%) | 2 (5.4%) |
| pN3 | 2 (5.4%) | 0 | 2 (5.4%) |
| ***Pathological tumor stage M*** | | | |
| M0 | 35 (94.6%) | 15 (40.5%) | 20 (54.1%) |
| M1 | 1 (2.7%) | 0 | 1 (2.7%) |
| Mx | 1 (2.7%) | 1 (2.7%) | 0 |
| ***Grading*** | | | |
| G0 | 13 (35.1%) | 6 (16.2%) | 7 (18.9%) |
| G2 | 11 (29.7%) | 4 (10.8%) | 7 (18.9%) |
| G3 | 11 (29.7%) | 6 (16.2) | 5 (13.5%) |
| ***Vascular Invasion*** | | | |
| Yes | 7 (18.9%) | 3 (8.1%) | 4 (10.8%) |
| No | 25 (67.6%) | 13 (35.1%) | 12 (32.5%) |
| NA | 5 (13.5%) | 0 | 5 (13.5%) |
| ***Perineural Invasion*** | | | |
| Yes | 10 (27%) | 6 (16.2%) | 4 (10.8%) |
| No | 22 (59.5%) | 10 (27%) | 12 (32.5%) |
| NA | 5 (13.5%) | 0 | 5 (13.5%) |
| ***Margin Status*** | | | |
| R0 | 34 (91.9%) | 16 (43.2%) | 18 (48.7%) |
| R1 | 3 (8.1%) | 0 | 3 (8.1%) |
| ***ECE*** | | | |
| ECE+ | 5 (13.5%) | 3 (8.1%) | 2 (5.4%) |
| ECE- | 13 (35.1%) | 4 (10.8%) | 9 (24.3%) |

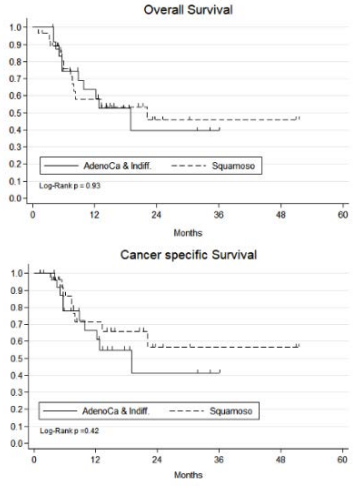


**Figure 1. Clinical outcomes.**

## CO071

### EVIDENCE FOR AN IMPROVED THERAPEUTIC INDEX WITH IMAGE GUIDED ADAPTIVE RADIOTHERAPY PLUS BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

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Aims: Traditional standard treatment for locally advanced cervical cancer (LACC) includes external beam radiotherapy (EBRT) with concomitant chemotherapy (CT) followed by intracavitary brachytherapy (BRT). Introduction of image guided adaptive radiotherapy has improved disease outcome and reduced toxicity in LACC. Aim of this study is to evaluate clinical outcome of chemoradiotherapy and acute and late toxicity in patients with LACC treated with EBRT+/-CT follow by BRT. The majority of treatment were planned using MRI for the best dose optimization to the target and OARs at time of treatment.

| | ACUTE | | | | | | | | LATE | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | G0 | | G1 | | G2 | | G3 | | G0 | | G1 | | G2 | | G3 | |
| | N | % | N | % | N | % | N | % | N | % | N | % | N | % | N | % |
| URINARY | 91 | 82% | 7 | 6% | 13 | 12% | 0 | 0% | 104 | 94% | 2 | 2% | 5 | 5% | 0 | 0% |
| RECTAL | 83 | 75% | 8 | 7% | 17 | 15% | 3 | 3% | 104 | 94% | 3 | 3% | 4 | 4% | 0 | 0% |
| INTESTINAL | 90 | 81% | 6 | 5% | 14 | 13% | 1 | 1% | 106 | 95% | 2 | 2% | 3 | 3% | 0 | 0% |
| HEMATOLOGICAL | 86 | 77% | 9 | 8% | 12 | 11% | 4 | 4% | 109 | 98% | 1 | 1% | 1 | 1% | 0 | 0% |

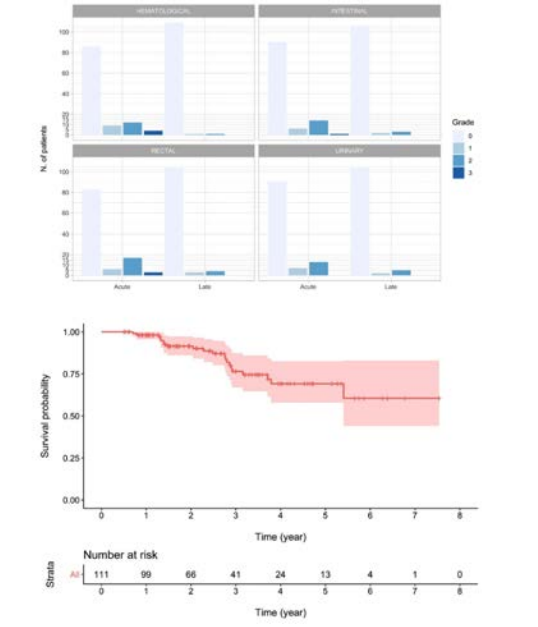


**Figure 1.**

Methods: From January 2011 to May 2018 we retrospectively analyzed 111 patients (pts) with LACC FIGO IB2-IVa. Pts treatments schedule were CT and EBRT with IMRT or Tomotherapy, followed by BRT. BRT treatment was planned with MRI or CT scan. Toxicity was scored according to CTCAE v4.0. Our primary end point is to evaluate clinical acute and late toxicity, secondary endpoint is overall survival.

Results: Pts treatments schedule were the following: concomitant CT with (only 16 pts didn't receive CT because of age or comorbidity) and EBRT with IMRT or Tomotherapy with median total dose 45 Gy (range 42-50.4) on pelvic +/- median dose 57.5 Gy (range 16-61.1) on node if there were positive, followed by BRT (median dose 28 Gy (range 28-30) in 4-5 fraction. Median follow up is 2,5 years (IQR 1,4-3,7 years), and OS is 87% (95% CI 80-95) at 2,5 yy.

Conclusions: As reported in literature we experienced that introduction of image guided adaptive radiotherapy has increased the therapeutic index (improved disease outcome and reduced toxicity) in LACC. In our experience symptoms score registered were low and the major of pts considered acceptable their QoL.

## CO072

### ADJUVANT VOLUMETRIC MODULATED ARC THERAPY (VMAT) COMPARED TO THREE DIMENSIONAL CONFORMAL RADIATION THERAPY (3DCRT) FOR NEWLY DIAGNOSED EXTREMITIES SOFT TISSUE SARCOMA PATIENT. OUTCOME AND TOXICITY EVALUATION

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Introduction and Purposes: To assess the impact of adjuvant volumetric modulated arc therapy (VMAT) compared with three dimensional conformal radiation therapy (3DCRT) in terms of toxicity and local control in patients with soft tissue sarcoma (STS) of the extremities treated with radical surgery and adjuvant radiotherapy.

Materials and Methods: From 2004 to 2016, 109 patients were treated, initially using 3DCRT and subsequently with VMAT. Clinical outcome was evaluated by contrast-enhanced MRI, thoracic and abdominal CT 3 months after treatment and then every 6 months. Toxicity was evaluated with Common Terminology Criteria for Adverse Events (CTCAE) scale version 4.3.

Results: The vast majority of patients had stage I-III STS disease (95%), liposarcoma (57%) histology, localized at the lower extremity (87%). Surgical resection was performed in all patients, followed by adjuvant 3DCRT in 38, and VMAT in 71. The median total dose was 66 Gy/33 fractions (range 60-70 Gy;25-35 frac-

tions). More successful bone sparing was recorded using VMAT ($p<0.01$). Median follow-up was 68 months. The 2,5-year LC were 95.3%±0.02, and 87.4%±0.03 for the whole cohort, 92%±0.05, 82.9%±0.06 for 3DCRT, 97.1%±0.02, 89.6%±0.04 for VMAT ($p=0.2$). On univariate and multivariate analysis the factors recorded as conditioning LC were the status of the surgical resection margins and the total dose delivered.

Conclusions: The availability of modern RT technique permits a better conformity on the target with maximum sparing of normal tissue and acceptable side effects. Our data underline that VMAT is a safe and feasible treatment with limited rate of toxicity, compared to 3DCRT. Results on local control of VMAT are encouraging.

## CO073

### ABSTRACT WITHDRAWN

## CO074

### DEFECOGRAPHY FOR ANAL SPHINCTER FUNCTION EVALUATION IN RECTAL CANCER PATIENTS TREATED WITH PELVIC RADIOTHERAPY

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Aims: Locally advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy (CRT) and sphincter saving surgery could suffer from sphincter function disorders when recanalised. Defecography (DRE) evaluates the transport of a semi-solid barium column to outside during a simulated defecation, investigating the two component of this process, both anatomically and functionally. The aim of this study was to evaluate the sphincter functionality with DRE.

Methods: Twenty-nine locally advanced rectal cancer patients (M:W=18:11) underwent neoadjuvant dose intensification treatment up to 5500 cGy (220 cGy/die) and sphincter saving surgery. DRE was performed evaluating the characteristics of contraction or inhibition of the pubo-rectal muscle and the type of incontinence (at rest/during Valsalva). The Memorial Sloan Kettering Cancer Center (MSKCC) Score was used to evaluate the number of evacuations per day, including incontinence. A comparison of both methods was reported.

Results: All patients completed the prescribed treatment and underwent anterior rectal resection with complete pathological response rate of 51%. With a median follow-up of 3.4 years, local control was recorded in all patients, with distant metastases reported in 6 (21%). Twenty-nine patients underwent DRE: 11 patients within 2 years, 18 after 2 years from the end of CRT. Anterior rectocele was observed in 15 patients, mostly in women (9 vs 6). A reduced or poor contraction or inhibition of the pubo-rectal muscle in DRE performed within 2 years was reported in the 73% whereas it resulted of 44% in DRE performed after 2 years (8 patients for each group). Regarding functional assessment, 5 (45%) and 7 (39%) patients showed incontinence at rest at DRE performed within or after 2 years, respectively. Overall, MSKCC score overestimated functional assessments in 5 (17%) patients. Table 1 reported DRE characteristics and the MSKCC score for each patient.

Conclusions: Despite the small number of analysed patients and the dose intensification schedule, sphincter dysfunctions rate was in line with literature. DRE resulted an important tool to evaluate anorectal function, giving information regarding not only sphincter morphology but also functionality. It resulted useful to evaluate incontinence during Valsalva, completing a qualitative evaluation of the MSKCC score. For an accurate evaluation both DRE and MSKCC could be considered.

**Table 1.**

DRE characteristics of contraction or inhibition of the pubo-rectal muscle and type of incontinence, and sphincter function score according to Memorial Sloan-Kettering Cancer Center (MSKCC) reported for each patient

| Patients | Age | Defecography (DRE) | | | MSKCC score |
|---|---|---|---|---|---|
| | | Contraction/inhibition of pubo-rectal muscle | Incontinence | | |
| | | | At rest | During Valsalva | |
| 1 | 68 | Low contraction/no inhibition | No | No | Good |
| 2 | 66 | Poor | Yes | Yes | Poor |
| 3 | 68 | Poor | No | No | Fair |
| 4 | 75 | Poor | Yes | No | Fair |
| 5 | 78 | Poor | Yes | Yes | **Excellent** |
| 6 | 75 | Poor | Yes | Yes | Fair |
| 7 | 70 | Normal | No | Yes | Good |
| 8 | 66 | Normal | No | Yes | Good |
| 9 | 56 | Severe incontinence | Yes | Yes | **Good** |
| 10 | 60 | Normal | No | No | Good |
| 11 | 69 | Reduced | No | Yes | Excellent |
| 12 | 79 | Normal | No | No | Good |
| 13 | 69 | Normal | No | Yes | Excellent |
| 14 | 57 | Normal | No | No | Excellent |
| 15 | 49 | Poor | Yes | Yes | **Good** |
| 16 | 46 | Normal | No | No | Good |
| 17 | 58 | Poor | Yes | Yes | **Good** |
| 18 | 58 | Poor | Yes | Yes | Poor |
| 19 | 77 | Poor | Yes | Yes | **Excellent** |
| 20 | 68 | Reduced | No | Yes | Fair |
| 21 | 75 | Reduced | Yes | Yes | Fair |
| 22 | 57 | Reduced | No | Yes | Poor |
| 23 | 70 | Normal | Yes | No | Poor |
| 24 | 57 | Poor | Yes | Yes | **Good** |
| 25 | 58 | Normal | No | No | Good |
| 26 | 69 | Normal | No | No | Good |
| 27 | 57 | Normal | No | Yes | **Fair** |
| 28 | 44 | Normal | No | No | Good |
| 29 | 66 | Normal | No | No | Good |

MSKCC: Memorial Sloan Kettering Cancer Center. Above the thick line: patients performing DRE within two years; under the thick line: after two years. In bold: patients with discordance between DRE and MSKCC score

## CO075

### ADJUVANT INTENSITY-MODULATED HYPOFRACTIONATED IMAGE-GUIDED RADIOTHERAPY (IGRT) CONCOMITANT TO CHEMOTHERAPY IN BILIARY TRACT CARCINOMA

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Background/Aims: Adjuvant (adj) radiotherapy (RT)/chemotherapy (ChT) is controversial in patients (pts) with bile duct carcinoma (ca) but suggested in R1, lymph nodes (LNs) positive or stage ≥ T2. We previously tested Hypo-IGRT in pts with locally advanced pancreatic ca (Int J Rad Onc Biol Ph, Vol. 87, 2013). We report our experience using the same RT schedule in adj

setting in biliary tract ca.

Methods: pts with intra, extra-epatic or gallbaldder ca were treated. Simulation consisted in contrast-enhanced computed tomography (c-e-CT) or FDG CTPET or 4D c-e-CT, CTV consisted in surgical bed and regional LNs considering tumor site. PTV was defined adding standard margins to CTV or 5 mm in pts who underwent 4D c-e-CT. Prescription dose was 40- 44.25 Gy (40-50 Gy) in 15 fr with SIB up to 50 Gy to R1 or positive CTPET sites respecting dose constraints to OAR delivered with VMAT or tomotherapy concomitant to capecitabine (cape).

Results: From 05/2009 to 04/2018, 40 pts (25 M; 15 F) were treated. Median age: 69 years (45-83). Twenty-one pts (52.5%) had Klatskin tumor, 11 pts (27.5%) common or distal bile duct ca, 5 pts (12.5%) intrahepatic ca and 3 pts (7.5%) gallbladder ca. After surgery 28 pts (70%) were R1, 12 pts (30%) were R0 (3: N+, 4: pT3N+, 2: pT4, 1: hepatic hilus infiltration, 2: after surgery for local relapse). Four pts were previously treated with neoadj ChT (3: GEM+CDDP, 1: cape). Fourteen pts received adj ChT (7: CDDP+GEM, 2: GEMOX, 2: PEXG, 1: GEM, 1: cape, 1: CBDCA+ VP16). Twenty-seven pts (67.5%) received concomitant ChT. Simulation was performed with c-e-CT and CTPET in 16 pts (40%), with 4D c-e CT in 6 pts (15%) and with c-e-CT in 18 pts (45%). Twelve pts (75%) were PET positive. Twenty-four pts (60%) were treated with tomotherapy and 16 (40%) with VMAT. All pts were evaluable for acute toxicity, it was G1-G2: 3 pts (7.5%) diarrhea, 19 (47.5%) nausea/vomiting, 8 (20%) abdominal pain, 3 (7.5%) cholangitis, 1 (2.5%) gastric ulcer. Only 2 pts (5%) had G3 late toxicity (gastric ulcer and stenotic fibrosis). Responses were evaluated in 39 pts (1 lost): 22 pts (56%) had PD (7 distant, 6 local, 9 local and distant). Median TTLP and TTDP from end of RT were 12.5 and 13.7 months, respectively. At a median follow up of 31 months (11.8- 110.6 m) 50% of pts were alive; 1 and 3 years OS were 72% and 36%, respectively.

Conclusions: Adjuvant Hypo-IGRT concomitant to capecitabine in pts with biliary tract carcinoma is feasible with a good toxicity profile and promising outcome.

**CO076**

## BONE-MARROW SPARING IMRT FOR ANAL CANCER PATIENTS: A PROSPETICVE PHASE II TRIAL

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Aims: This study was aimed at decreasing the acute hematologic toxicity (HT) profile in anal cancer patients treated with chemoradiation (CRT), employing a tailored IMRT approach in order to spare hematopoietic bone marrow (BM) identified with (18F)-FDG positron emission tomography (18FDG-PET)

Methods: A one-armed two-stage Simon's design was selected to test the hypothesis that BM sparing approach would improve by 20% the rate of G0–G1 (vs G2-G3) HT from 27% of RTOG 0529 historical data to 47% ($\alpha$=0.05 and the $\beta$=0.20). At the first stage, among 21 enrolled patients, at least 9 should have been scored as G0– G1 acute toxicity to further proceed with the trial. At the second stage, another 18 patients will be accrued for an overall sample size of 39 patients. The first step was conducted in 21 patients eligible for concurrent CRT following Nigro protocol, dose and constraints of RTOG 0529 trial. We employed 18FDG-PET to identify active BM within pelvic structures (active PBM) detached in 3 subsites: active iliac bone marrow (IBM), active lumbosacral bone marrow (LSBM), active lower pelvis bone marrow (LPBM). Active BM was defined according to the segmentation identifying regions within the pelvis with higher SUV than the mean SUV for that bony region, for each patient. Dose constraints were: V10< 90% and V20<75% for active PBM, V40< 41% and mean dose <32 Gy for active LSBM. Acute HT events and non-hematologic toxicity were recorded.

Results: From December 2017 to March 2019, 21 patients met the eligibility criteria and were enrolled onto the protocol. Six patients (28%) had stage II disease and 15 (72%) stage III. The median age was 64 years. Six out of 22 patients were male. Four patients experienced grade 3–4 HT,19% versus 58% of historical results; 17 patients had ≤G2 HT and 9 patients ≤G1 HT. None of the patients showed grade 4 thrombocytopenia. Figure 1 shows hematological values trends over the 8 weeks from the start of CRT. A total of 55% of patients had G0-G1 gastroenteric toxicity and 73% had urogenital toxicity <G2 (27% G2-G3), while G2-G3 acute skin toxicity was experienced by 75% of patients.

Conclusion: PET-guided BM sparing IMRT was able to reduce acute HT in anal cancer patients treated with CRT. These results prompted us to continue with the second part of this prospective phase II trial.

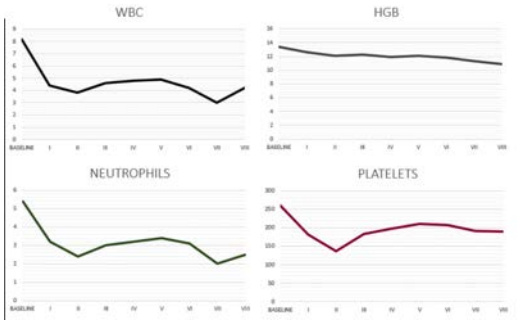


**Figure 1.**

## CO077

### DOSIMETRIC PREDICTORS OF ACUTE AND CHRONIC ALOPECIA IN BRAIN CANCER PATIENTS TREATED WITH VOLUMETRIC MODULATED ARC RADIOTHERAPY (VMAT)

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Aims: Radiation-induced hair loss is a side effect of relevant importance, given the huge psychological impact of alopecia and its negative effects on patient's quality of life. This work aims to define the dosimetric parameters that correlate with temporary and permanent hair loss following a radiation treatment for brain cancer in patients treated with conventionally fractionated VMAT for brain tumors. Analysis of time to recovery and definition of factors impacting on recover probability are described.

Methods: Patients treated for primary brain tumor at our Institute with a conventionally fractionated VMAT were included. Factors that may have an impact on alopecia such as age, smoking history, use of antiepileptic drugs (AEDs) and chemotherapy were registered. Dose received by 0.1 cc (D0.1cc), mean dose (Dmean), volumes receiving different doses (V16Gy, V20Gy, V25Gy, V30Gy, V35Gy, V40Gy and V43Gy) were registered for the scalp. Alopecia was assessed according to CTCAE version 4.0. Receiver operating characteristics (ROC) curve analysis was used to identify parameters associated with hair loss.

Results: A total of 101 patients were included. At the end of radiotherapy, 5 patients did not develop alopecia (Dmean to the scalp 3.1 Gy). The scalp of the patients with G1 (n=11) and G2 (n=85) alopecia received Dmean of 10.6 Gy and 11.8 Gy, respectively. At ROC curve analysis, V16Gy ≥16.7 cc and V20Gy ≥5.2 cc were the strongest predictors of risk of acute alopecia. Trichological follow-up was available for 74 patients: 65 patients (92.8%) completely recovered from alopecia. Median time to recovery was 5,9 months. The actuarial rate of hair regrowth was 98.1% at 18 months after the end of radiotherapy. At ROC curve analysis, V40Gy ≥5.4 cc and V43Gy ≥2.2 cc were the strongest predictors of risk of chronic alopecia. Kaplan Meier analysis and Cox regression showed that age, D0.1cc, Dmean, V30Gy, V35Gy, V40Gy and V43Gy are related to recovery probability.

Conclusions: Volumes that receive relatively low doses (V16Gy and V20Gy) and those that receive relatively high doses (V40Gy and V43Gy) are the strongest predictors for acute and chronic hair loss, respectively. By maintaining, during the inverse planning process, the doses to the scalp lower than the dosimetric thresholds that were identified, reduction of the risk of hair loss may occur. Furthermore, these data may assist radiation oncologists to predict the risk of alopecia during patient counselling.

## CO078

### FINAL RESULTS OF A PHASE I STUDY ON ACCELERATED RADIOTHERAPY WITH SIB VMAT TECHNIQUE AND CONCOMITANT TEMOZOLOMIDE IN GLIOBLASTOMA PATIENTS (ISIDE-BT-2)

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Aim. To determine the maximum tolerated dose (MTD) of Volumetric Modulated Arc Therapy (VMAT) with standard concurrent and sequential dose temozolomide (TMZ) in patients with resected glioblastoma multiforme.

Methods. A Phase I clinical trial was performed. Patients with histological proven glioblastoma underwent VMAT dose escalation. VMAT was delivered over 5 weeks with the simultaneous integrated boost (SIB) technique to the two planning target volumes (PTVs) defined by adding 5-mm margin to the respective clinical target volumes (CTVs). CTV1 was the tumor bed + MR enhancing residual lesion with a 10-mm margin; CTV2 was CTV1 plus 20-mm isotropic margin.

VMAT was delivered in 25 fractions. Only the dose for PTV1 was escalated while maintaining the same dose for PTV2 (45 Gy/1.8 Gy). Four PTV1 dose levels were planned: Level 1 (77.5/3.1 Gy), Level 2 (80/3.2 Gy), Level 3 (82.5/3.3 Gy) and Level 4 (85/3.4 Gy).

Patients were treated in cohorts of between three and six per group using a Phase I study design. The recommended dose was exceeded if one of the three patients in a cohort experienced dose-limiting toxicity within 3 months from treatment. Concurrent and sequential TMZ chemotherapy was administered accor-

ding to Stupp's protocol. Two arc techniques were used to cover at least 95% of the target volume with the 95% isodose line. Dose-limiting toxicity (DLT) were defined as any treatment-related non-haematological adverse effects rated as Grade > 3 or any haematological toxicity rated as > 4 by Radiation Therapy Oncology Group (RTOG) criteria.

Results. Twenty-one consecutive glioblastoma patients (male/female: 14/7; median age: 66 years) were treated. Dose to the PTV1: 10 patients 77.5 Gy; 9 patients, 80 Gy; 2 patients, 82.5 Gy,; 0 patients, 85 Gy. Median follow-up time was 10 months (range: 1-23.3 months). Grade 1-2 treatment-related neurological and cutaneous toxicities were registered (6 and 16 patients, respectively). Two patients experienced DLT to dose of 82.5 Gy (1 neurological toxicity grade 3, 1 haematological grade 4).

Conclusions. DMT was reached at the dose level of 82.5 Gy. Volumetric Modulated Arc Therapy in patients with resected glioblastoma multiforme to a dose of 80 Gy in 25 fractions is well tolerated with TMZ at a daily dose of 75 mg/mq.

## CO079

### A DOSIMETRIC COMPARISON OF LEFT-SIDED BREAST RADIOTHERAPY TECHNIQUES TO TREAT CHEST WALL AND REGIONAL NODES AND HEART SPARING

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Purpose: Radiation therapy is an essential component in the treatment of breast cancer, reducing the risk of local recurrences after surgery in the absence of relevant side effects. There is a potential risk of cardiotoxicity in patients undergoing radiation therapy on the left chest wall; this risk appears to be correlated with the dose received by the anterior descending artery (LAD). The aim of the study is to evaluate which radiation technique allows to obtain an adequate coverage of the PTV sparing as much as possible the organs at risk (OARs) with attention to the LAD. The techniques used are: conformal radiotherapy (3DCRT); IMRT; VMAT radiotherapy; Helical Tomotherapy.

Method: 10 treatment plans for patients with left breast cancer undergone to mastectomy and reconstruction with expansor and adjuvant radiotherapy are chosen and replanned retrospectively using 4 different treatment techniques. PTV includes left chest wall and regional lymph nodes. OARs include heart, LAD, lungs, right breast. LAD is delineated according to Lorenzei et al. For each treatment plan we evaluated: maximum dose and volume of PTV receiving at least 95%(V95%) of prescribed dose and average of V95%; average dose and maximum dose of LAD; average dose of the heart; volume of the left lung receiving 20Gy (V20); breast and right lung volume receiving 10Gy(V10).

Results: The coverage of the PTV is adequate with all techniques in study allowing the average value of V95% to be higher than 95% (V95% on PTV(%) 3D 94,1±1.9; IMRT 95.4±0.5; Tomotherapy 97.9±1.1;VMAT 95.2±0.7); however, Tomotherapy achieves the best results with an average of V95% higher and with a more homogeneous dose distribution. The LAD is spared in an equivalent way with IMRT, VMAT and Tomotherapy, which obtain maximum and avarage doses lower compared to 3DCRT (average and maximum doses(Gy): 3D 31.8±10.9, 51.4±1.8; IMRT 18.4±7.1, 39.7±6.5; Tomotherapy 23.5±10.4, 39.8±7.1; VMAT 20.4±9.1, 38±11). VMAT and Tomotherapy obtain a V10 Gy of breast and lung right higher compared to the other techniques (V10 breast and lung right (%): 3D 4.1±5.7, 0.4±0.4; IMRT 1.2±1.4, 0.09±0.10; Tomotherapy 24.2±22.2, 1.7±1.4; VMAT 17±8, 6.5±6.0).V20 of the ipsilateral lung is higher with 3DCRT (V20(%): 3D 26±8; IMRT 17.1±2.8; Tomotherapy 16.6±3.8; VMAT 21.8±4.9).

Conclusions: Tomotherapy and VMAT allow better sparing of LAD and PTV coverage, but at the price of a higher V10 of contralateral organs.

## CO080

### ABSTRACT WITHDRAWN

## CO081

### LONG TERM RESULTS OF IG-IMRT IN PROSTATE CANCER PATIENTS WITH HIGH-RISK OF RELAPSE

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Aims: To evaluate long-term results in patients (pts) with unfavourable intermediate-, high- and very high-risk prostate cancer (PCa) (NCCN 2019 classification), treated with image guided- intensity modulated radiotherapy (IG-IMRT).

Methods: From 12/2006 to 05/2011, 100 PCa pts were treated with radical moderately hypofractionated IG-IMRT in a phase I-II prospective study. All pts underwent prophylactic pelvic irradiation to 51.8 Gy in 28 fractions (EQD2 52.2 Gy, for α/β=1.5), with simultaneous integrated boost up to 65.5 Gy (EQD2 77.7 Gy) to seminal vesicles and 74.2 Gy (EQD2 88 Gy) to prostate. Neoadjuvant and/or adjuvant androgen deprivation therapy (ADT) was prescribed in 90/100 pts for a median of 28.9 months (3-120 months). All pts were treated with helical IMRT (Tomotherapy®, Accuray, Wisconsin) and daily IGRT (MVCT). Pts' characteristics are reported in Table 1.

Results: Median follow up was 94 (23-215) months. Cumulative late gastro-intestinal (GI) toxicity were: 13% G2 and 6% G3 (rectal bleeding), the latter

requiring Argon Plasma Coagulation (APC). At the last follow up none of the pts presented G3 GI toxicity. Cumulative late genito-urinary (GU) toxicities were 15% G2 and 13% G3-G4; 11 pts presented G3 urinary stenosis and in 7 the G3 toxicity was solved with urethrectomy, thus only 4% of pts presented G3 GU toxicity at the last follow up. Two patients presented G4 events (1 urethrostomy, due to repeated urethrectomies, and 1 cystectomy, due to hyperactive bladder). Thirty pts were dead at the last follow up, but only 5 due to PCa progression. Eleven pts experienced biochemical relapse, 1 of whom also with an intraprostatic relapse and 2 with bone metastases. Fifty-nine pts are alive and free from biochemical progression. Median biochemical relapse-free survival (bRFS) and distant progression-free survival from the last day of RT were 91.2 and 93.5 months, respectively.

Conclusions: IG-IMRT in PCa pts with high-risk of relapse allows dose escalation, with very good 8 year-outcomes: 89% bRFS, 1% local relapse, 2% distant relapse and 95% cancer specific survival. Rectal G3 toxicity was acceptable, and solved in all pts with APC. Genito-urinary G3 toxicity was fair, limited by the presence of the urethra in the field, and solved in 7 out of 11 pts.

**Table 1. Patients' characteristics.**

| Characteristics | tot=59 |
|---|---|
| Age at IBR, median (min-max) | 60.4 (37.4-88.2) |
| *Tumour side* | |
| Right, n (%) | 29 (49.2) |
| Left, n (%) | 30 (50.8) |
| CTV Re-Rtp / CTVm, median (min-max) § | 39.8 (31.6-73.6) |
| *Adjuvant therapy* | |
| Chemotherapy (alone or with hormonotherapy), n. (%) | 20 (33.9) |
| Hormonotherapy alone, n. (%) | 34 (57.6) |

## CO082

## TOXICITY ASSESSMENT AND CORRELATION WITH VOLUME EFFECTS AFTER RADIOTHERAPY FOR PROSTATE CANCER

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Aims: To identify dosimetric parameters derived from bladder and rectal dose distributions that correlate with acute genitourinary (GU) and late gastrointestinal (GI) toxicity in patients treated for prostate cancer who underwent daily IGRT with Cone Beam CT (CBCT).

Methods: A retrospective analysis to investigate dosimetric predictors for acute GU and late GI toxicity, scored with RTOG scale, has been performed on 28 patients at I.C.S. Maugeri (Pavia). 16 patients (toxicity group TGGU) presented G1-G2-G3 GU toxicity during treatment or within 3 months after RT, while 12 (control group CGGU) did not report any toxicity. 15 patients (toxicity group TGGI) presented G1-G2 GI toxicity from 6 months after RT, while 13 (control group CGGI) have not reported any disease. All the patients have been simulated with full bladder and empty rectum and irradiated with 6MV VMAT technique. Dose prescription was 2.7Gy/fr to prostate and 2.3Gy/fr to seminal vescicles for 26 fractions. Patients underwent a daily CBCT verification. Bladder and rectal volumes had been contoured on each CBCT and dose-volume histogram (DVH) for every single fraction had been generated. The variables derived from DVH were as follows: volume (VB), mean dose (DB) and % of volume receiving ≥ 65Gy (V65Gy) for the bladder [Pervez et al. IJROBP 76 (1) 57-64 2010], volume (VR), mean dose (DR) and % receiving ≥ 35-55-61Gy (V35Gy, V55Gy, V61Gy) for the rectum (from Pollack et al. IJROBP 64 (2) 518-526 2006, Peeters et al. IJROBP 64 (4) 1151-61 2006 and our constraints). Variables distributions are described by mean and standard deviation. The presence of statistically significant differences in term of mean variables doses between two groups was assessed by the Welch's two sample t-test.

**Table 1.**

| | | Tox = yes | | Tox = no | | | |
|---|---|---|---|---|---|---|---|
| Tox | | Mean | SD | Mean | SD | p-value | |
| Acute GU | Volume (cm3) | 276.08 | 96.83 | 334.58 | 100.23 | 0.13 | |
| | D mean (Gy) | 35.32 | 9.71 | 27.15 | 8.25 | 0.024 | * |
| | V65Gy (cm3) | 57.41 | 33.77 | 37.77 | 17.51 | 0.052 | |
| Late GI | Volume (cm3) | 77.15 | 15.08 | 63.45 | 13.65 | 0.018 | * |
| | D mean (Gy) | 41.27 | 6.05 | 41.92 | 3.65 | 0.727 | |
| | V35Gy (cm3) | 46.1 | 10.64 | 38.58 | 7.98 | 0.043 | * |
| | V55Gy (cm3) | 27.76 | 8.14 | 23.75 | 6.42 | 0.157 | |
| | V61Gy(cm3) | 19.95 | 6.25 | 15.27 | 5.56 | 0.046 | * |

Results: In the bladder DB was significantly higher in TGGU than in CGGU (35.3Gy vs 27.2Gy, p-value 0.024); VB and V65Gy did not show statistically significant differences between groups (p-value > 0.05) although VB was lower while V65Gy higher for TGGU than CGGU [Table 1]. In the rectum VR, V35Gy and V61Gy were significantly increased in TGGU compared to CGGU (p-value < 0.05), while no statistically significant difference was observed in terms of DR and V55Gy between the two groups (p-value > 0.05) Table 1.

Conclusions: different volume effects were found for various acute GU and late GI toxicity. These constraints can be used to evaluate and reduce the risk of toxicity in patient treated for prostate cancer, as reported in literature.

**CO083**

## THE ADDING VALUE OF IMAGE-GUIDED VMAT ON THE GASTROINTESTINAL AND GENITOURINARY TOLERANCE IN THE TREATMENT OF PROSTATE CANCER WITH A MODERATE HYPOFRACTIONATED SCHEDULE

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Aims: To compare the acute and 1-year post-RT GI and GU toxicity of men undergoing curative hypofractionated-RT (HFRT) and treated by three-dimensional conformal radiation therapy (3DCRT) or VMAT with daily IGRT.

Methods: A retrospective cohort of 101 men with low/intermediate risk prostate cancer (Pca) was selected according to the NCCN criteria. Patients were treated with a moderate HFRT schedule (60 Gy delivered in 20 daily fractions). A cone-beam based IGRT strategy was adopted in all treated patients according to the latest clinical indications (NCCN guidelines). Men were treated with VMAT (n=31) or with 3DCRT (n=70). Acute toxicity was assessed during treatment and at 2 and 4 weeks after the end of radiotherapy and every 12 weeks thereafter . Late toxicity, was analyzed 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 between the two groups were evaluated by the Fisher's exact test. A p-value lower than 0.05 was considered statistically significant.

Results: Two weeks after RT a lower rate of Grade 2 or higher acute toxicity was observed in the group of men treated by VMAT. Grade 2 or higher GI and GU toxicity was observed in 41.4 % vs. 9.7% (p=0.001) and in 40% vs. 6.5% (p=0.0007) of men treated by 3DCRT or VMAT, respectively. One month after RT, the reduced toxicity observed in the study group treated with VMAT was confirmed. The incidence of Grade 2 or higher GI and GU toxicity was 28.6% and 20% after 3DCRT and 9.7% and 3.2% after VMAT (GI toxicity: p=0.04; GU toxicity: p=0.03). At 12 months after RT, G2 or higher late GI toxicity was comparable between 3DCRT (4/70; 5,7%) and VMAT (2/31; 6,4%) (p=1.0) while a trend toward significant difference in the rate of late GU toxicity was observed between VMAT (29/2; 6,4%) and 3DCRT (54/16; 22,8%) (p=0.053).

Conclusions: Men undergoing HFRT with image-guided VMAT experienced a significantly lower acute GI and GU toxicity with respect to men treated by 3DCRT. VMAT did not provide advantages on 1-year GI toxicity while provided a trend toward significant difference in the rate of late GU toxicity. Longer follow-up and increased sample size will provide more definitive evidence concerning this important topic.

**Table 1.**

| | RTOG GI Acute Toxicity | | | | |
|---|---|---|---|---|---|
| | 3DCRT | | VMAT | | p value* |
| | No. | % | No. | % | |
| 1 week post RT | | | | | |
| Grade ≤ 1 | 41/70 | 58.6 | 28/31 | 90.3 | 0.001 |
| Grade ≥ 2 | 29/70 | 41.4 | 3/31 | 9.7 | |
| 4 weeks post RT | | | | | |
| Grade ≤ 1 | 50/70 | 71.4 | 28/31 | 90.3 | 0.04 |
| Grade ≥ 2 | 20/70 | 28.6 | 3/31 | 9.7 | |

| | RTOG GI Late Toxicity | | | | |
|---|---|---|---|---|---|
| | 3DCRT | | VMAT | | p value* |
| | No. | % | No. | % | |
| 12 months post RT | | | | | |
| Grade ≤ 1 | 66/70 | 94.3 | 29/31 | 93.6 | 1 |
| Grade ≥ 2 | 4/70 | 5.7 | 2/31 | 6.4 | |

| | RTOG GU Acute Toxicity | | | | |
|---|---|---|---|---|---|
| | 3DCRT | | VMAT | | p value* |
| | No. | % | No. | % | |
| 1 week post RT | | | | | |
| Grade ≤ 1 | 42/70 | 60 | 29/31 | 93.5 | 0.0007 |
| Grade ≥ 2 | 28/70 | 40 | 2/31 | 6.5 | |
| 4 weeks post RT | | | | | |
| Grade ≤ 1 | 56/70 | 80 | 30/31 | 96.8 | 0.03 |
| Grade ≥ 2 | 14/70 | 20 | 1/31 | 3.2 | |

| | RTOG GU Late Toxicity | | | | |
|---|---|---|---|---|---|
| | 3DCRT | | VMAT | | p value* |
| | No. | % | No. | % | |
| 12 months post RT | | | | | |
| Grade ≤ 1 | 54/70 | 77.2 | 29/31 | 93.6 | 0.05 |
| Grade ≥ 2 | 16/70 | 22.8 | 2/31 | 6.4 | |

CO084

## PRELIMINARY RESULTS OF HYPOFRACTIONATED POST-MASTECTOMY RADIOTHERAPY (PMRT-HF): DOSIMETRY, LOCO-REGIONAL CONTROL AND TOXICITY

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Aims: Post-mastectomy radiation therapy (PMRT) with conventional fractionation is typically delivered in 5 to 6 weeks. Data supporting hypofractionated PMRT is limited. This study aims to determine whether a short course of hypofractionated schedule in 15-16 fractions is safe and effective.

Methods and Materials: Eligible patients with stage IA to IIIB primary breast cancer received hypofractionated PMRT with fixed beam IMRT or VMAT technique to the chest wall (CW) with or without loco-regional lymph nodes. Prescription dose was 40.5 in 15 and 42.5Gy in 16 fractions daily, with an optional simultaneous integrated boost (SIB) of 3.2 Gy /fraction to 48Gy. The primary endpoint was loco-regional recurrence free survival (LRFS); secondary endpoints were acute and late skin toxicity, overall survival (OS) and disease free survival (DFS).

Results: Between 2012 and 2018, 83 patients with a median age of 51 years old were retrospectively analysed. All patients received adjuvant hypofractionated PMRT: 90,3% with 40,5Gy/15 frs /2.7Gy per fraction and 9,5% with 42,56Gy/16 frs /2,66Gy. SIB with 3.2Gy/fr was adopted in only 5 cases. Bolus 5 mm was used in 33 patients (40%). CTV- PTV volumes included CW in 8 patients (9,5%) and CW + regional LN in 75 patients (90,5%). At a median follow-up of 34 months, 2 patients developed loco-regional recurrence (locally, one in the scar and one in-field regional lymph node). 10 patients developed distant metastatic disease, including the 2 patients with loco-regional relapses. LRFS and distant metastasis free survival were 98.6% (95% CI 0.89 – 1.00) and 89.0% (95% CI 0.89 – 1.00), respectively. The hypofractionated regimen was well tolerated with 24.1% (20/83) G2 and 3.6% (3/83) acute skin toxicity. So far no cases of G3 late skin toxicity have been observed. The 3-year actuarial OS and DFS were 94.3% (95% CI 0.88 – 1.00) and 89.0 (95% CI 0.88 – 0.90), respectively.

Conclusions: Hypofractionated PMRT is well tolerated. Median follow-up in is still insufficient to assess long-term loco-regional control and late toxicity. Our experience suggests high local control rates and toxicity outcomes aligned with those already reported in literature with longer follow-up.

CO085

## HYPOFRACTIONATED WHOLE BREAST IRRADIATION AND SIMULTANEOUS INTEGRATED BOOST IN LARGE-BREASTED PATIENTS: LONG-TERM TOXICITY AND COSMESIS OF A PROSPECTIVE SERIES

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Purpose: To evaluate the impact of breast size on long-term toxicity and cosmesis in breast cancer patients treated with hypofractionation and simultaneous integrated boost using volumetric modulated arc therapy (VMAT).

Materials and Methods: Three cohorts were identified: small-breasted patients (<600 cc), medium-breasted patients (between 600 and 1000 cc) and large-breasted patients (>1000 cc), according to the 33^ percentile in our database. Two groups were analyzed: small-medium breasted patients (<1000 cc, 596 patients) and large breasted patients (>1000 cc, 256 patients). All patients undergoing breast-conserving surgery were treated with hypofractionated VMAT to the whole breast (40.5 Gy in 15 fractions) and concomitant boost dose to the tumor bed (48 Gy in 15 fractions). Skin toxicity and cosmetic data were analyzed as acute and late (at 2, 3, 4 and 5 years follow-up). Multivariate logistic regression analyzed, as covariates, the variables with $p<0.10$ on univariate analysis. P values <0.05 were considered significant.

Results: From August 2010 to March 2017, a total cohort of 1160 patients have been treated with VMAT and SIB in 3 weeks treatment. Of those, 852 patients had at least 2 year follow-up, and were included in the analysis. Breast size was highly significant predictor for acute grade 2 or greater skin toxicity (12.9% vs 20,7%; $p=0.004$). Late skin toxicity was significant for breast size from 2 to 5 year FU (4.7% had grade 1 or more late skin toxicity in the group <1000 cc at 5 years, respectively, to compare with 15.9% of the large breast group, $p=0.001$). No Grade 3 of late skin toxicity was recorded in both cohorts. Regarding breast pain, the breast size kept significance in multivariate analysis from 2 to 4 year FU. For cosmetic outcome, the multivariate analysis confirmed the significance only of the breast size at 2 years. No dosimetric or size related parameters were significant for cosmesis nor breast pain at 5 year FU.

Conclusions: Although increasing breast size leads to increased maximum skin dose, the incidence of overall skin toxicity, acute and late, was comparable to that reported in the literature. At 5 years of follow up we did not record significant differences in terms of cosmesis

or breast pain between large and small-medium breasted patients. These data suggest that hypofractionated radiation therapy using VMAT is a viable therapeutic modality in large-breasted patients.

## CO086

### PREDICTIVE PARAMETERS FOR LONG-TERM CARDIAC MORTALITY EXCESS RELATED TO LEFT-SIDED BREAST RADIOTHERAPY

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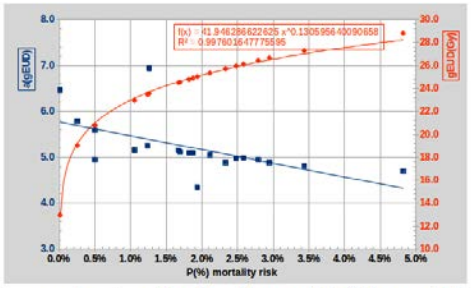
Aims: The risk of long-term secondary cardiac effects in left breast radiation cannot be considered negligible, mainly when it is may sum with those induced by chemotherapy schedules containing anthracyclines and/or trastuzumab. Although a risk of cardiac death <1% after breast RT is considered acceptable, QUANTEC constraint V25Gy<10% is not sufficient to limit the excess cardiac mortality risk for each patient and for every RT schedule of tangential beams left sided breast RT: evaluation of the heart-absorbed dose is necessary. Aim of this work is to analyze the heart dosimetric parameter of a group of patient for which QUANTEC constraint is respected but cardiac mortality probability results greater than 1%. Correlation with further derived "predictive" dosimetric parameters and cardiac mortality risk was then verified on a control group of patients.

Methods: About 300 women, from 2013 to 2019, underwent left sided breast tangential beams RT in our department. The analysis showed that heart constraint V25Gy<10% was respected in almost all patients. From a qualitative analysis of the differential heart DVHs, some high dose peaks emerged, then a direct calculation of long term cardiac mortality risk was performed applying the relative seriality model (α/β=3Gy, s=1, D50=52.4Gy, g=1.28). For each heart absorbed dose distribution the EQD2 was used and the gEUDs were also evaluated (a=5.2).

Results: In 25% of patients the probability of long-term cardiac mortality was found >1% despite V25Gy<10% for heart volumes. The dosimetric constraints V40Gy, D2%, and gEUD showed a good correlation (R=0.97, R=0.90 and R=1.00 respectively) with the risk of cardiac death. To keep the probability lower than 1%, the cut off levels were determined by the simultaneous occurrence of the conditions: V40Gy <2% and D2% < 38Gy or gEUD < 23 Gy. On a control group of 50 other patients (for whom V25Gy <10 was satisfied) these parameters were tested: if simultaneously V40Gy and D2% parameters or single gEUD were satisfied, the long term cardiac mortality probability resulted <1%. The parameter a in the gEUD was fixed at 5.1.

Conclusions: Our additional "predictive" parameters, are a calculation and not an observation of mortality and are closely connected to the irradiation technique used and aimed to specific end-points. Modern TPSs should promote, even more, the use of either radiobiological DVHs or algorithm optimization and gEUD metric, especially in the era of hypofractionation.




| parameters | relationship | Dose constraint | Volume constraint |
|---|---|---|---|
| $D_{2\%}$ | < | 35 Gy | |
| $V_{40Gy}$ | < | | 2% |
| gEUD | < | 23 Gy | |

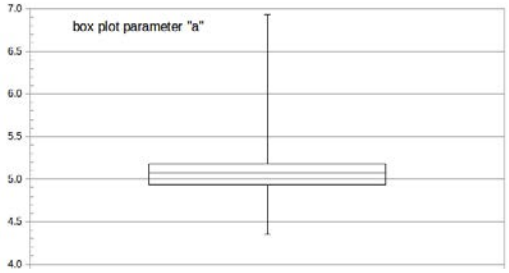



**Figure 1.**

## CO087

### RISK OF RADIATION-INDUCED SECONDARY LUNG CANCER AND ISCHEMIC HEART DISEASE AFTER THE INTERNAL MAMMARY CHAIN IRRADIATION IN LEFT BREAST CANCER: COMPARATIVE ANALYSIS BETWEEN IMRT AND 3DCRT

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Aims: To comparatively estimate the risks of radiation-induced secondary lung cancer and ischemic heart disease for different radiotherapy techniques (IMRT versus 3DCRT) in women with node-positive left-sided breast cancer, candidates for breast and regional node irradiation (RNI), including the internal mammary chain (IMC).

Methods: For this risk modelling study, computed tomography datasets of ten women with node-positive left-sided breast cancer were used for IMC contouring

and re-planning with a dose of 50Gy in 25 fractions. Four different treatment plans were generated for each patient: for both techniques (3D-CRT and IMRT) two treatment plans were created, based on the inclusion of IMC. We calculated estimates of excess relative risk (ERR) and excess absolute risk,(EAR) for lung cancer and major coronary events, as following: ERRlung= δGrantzau·OEDlinear (δGrantzau=0.085Gy-1, Grantzau *et al.*[1] with an excess relative risk of 8.5% per Gy of radiation-induced secondary lung cancer; OEDlinear=mean lung dose, MLD) and ERRheart= δDarby· OEDlinear (OEDlinear=mean cardiac dose, MCD; δDarby=0.074Gy-1 derived from dose-response relationship reported by Darby *et al.*[2]). Statistical analyses were conducted using Wilcoxon signed-rank tests to estimate statistical significance.

Results: The IMC irradiation increased significantly the MCD and the ipsilateral MLD in both, 3DCRT and IMRT plans (p=0.002), with a consequently significant increase of the relative risk of secondary lung cancer (64% vs 38%) and ischemic heart disease (41% vs 27%). As compared to 3DCRT, the use of IMRT significantly reduced the MCD in IMC plans (p= 0.002) and in plans not including the IMC (p=0.02). Similarly, the MLD was significantly reduced in IMC plans (p=0.004) and non-IMC plans (p=0.04), resulting in significant reduction of ERRlung in IMC plans (75% vs 58%, p=0.002) and no-IMC plans (51% vs 44%, p=0.02). Higher ERR and 10-year EAR for major coronary events were showed for 3D-CRT as compared to IMRT plans in boths, IMC-plans(64% vs 41%, p=0.002) and no-IMC plans(38% vs 27%, p=0.02, Figure 1).

Conclusions: Despite IMC irradiation has been shown to increase survival rates in women with nodal positive breast cancer, Budach *et al.*[3], the addition of IMC to RNI also increases heart and lung doses, resulting in a significant increase in 10-year secondary lung cancer and ischemic heart disease risk. In this setting, the adoption of IMRT is advantageous when compared to 3DCRT.

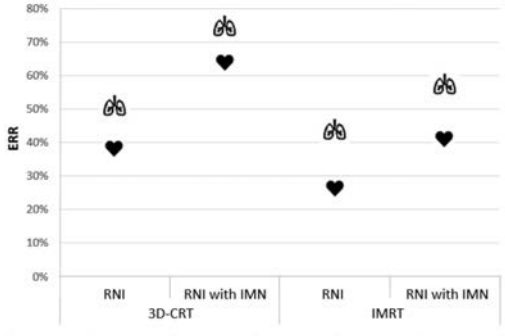


**Figure 1.**

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## CO088

## LEFT SIDED BREAST CANCER PATIENTS AND ADVANCED RADIATION THERAPY TECHNIQUES. A CARDIAC SPARING APPROACH

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Aims: To improve target coverage and reduce dose to heart and left anterior descending artery (LAD) in left breast cancer patients (pts) with comorbidities and unfavorable anatomy using volumetric modulated arc therapy (VMAT) with or without deep inspiration breath hold (DIBH).

Methods: Between July 2015 and April 2019 52 consecutive patients affected by left breast cancer with comorbidities and unfavorable anatomy underwent radiotherapy (RT) with VMAT techniques. 29 pts received RT to whole breast in 15 fractions (total dose 40.05 Gy) and 23 pts to whole breast or chest wall plus regional lymph nodes in 25 fractions (total dose 50 Gy). A sequential boost to the tumor bed of 10-16 Gy was performed, if indicated. In 6 cases DIBH technique was performed. VMAT plans in free breathing (FB) were generated using 3 arcs (180-220°), in order to reduce the interplay effect due to dynamic delivery and briefing motion, while VMAT plans in DIBH were obtained using 6 partial arcs with a width of 12-15 degrees to limit the time of delivery per arc; a virtual 10 mm bolus helped extending the dose fluency outside the body to compensate for small changes in shape and volume due to respiration or edema. Most pts received anthracycline and taxanes regimen before RT, followed by trastuzumab. In all patients, echocardiography was performed before starting RT and after 1- and 6-months. Dose constraints to heart were: Dmean ≤ 5 Gy, V5Gy ≤ 40%, V25Gy ≤ 8% in FB and conventional fractionation (CF); Dmean ≤ 4 Gy, V8Gy < 30%, D5% < 16 Gy in FB and hypofractionation (HF); Dmean ≤ 3Gy, V25 ≤ 5% in DIBH. Dose constraints to the LAD were Dmean ≤ 20-25 Gy in FB, Dmean ≤ 15 Gy in DIBH.

Results: The treatment was well tolerated in all patients. Median V95% to breast/chest wall CTV was 96% and median V95% to lymph nodes CTV was 98%,

both in FB and in DIBH. In FB we obtained a heart Dmean= 3 Gy in HF treatment and Dmean= 5 Gy in CF. LAD Dmean was 10.5 Gy and 16 Gy, respectively. In DIBH treatment we reported a heart V25=2% and a mean LAD dose of 7 Gy. The 1- and 6-months echocardiographic control after RT completion showed unchanged cardiac functioning parameters.

Conclusions: The VMAT technique +/- DIBH is useful in the treatment of left breast cancer pts (especially with cardiac comorbidities and unfavorable anatomy) by ensuring an excellent target coverage and sparing heart and LAD. Long-term follow-up data are needed to assess late toxicity and clinical outcomes for this subset of patients.

## CO089

### ASSOCIATION OF MRI-BASED RADIOMIC FEATURES WITH PROGNOSTIC FACTORS IN PROSTATE CANCER

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Aims: To decode tumor phenotype in prostate cancer (PCa) using a radiomic approach based on multiparametric magnetic resonance imaging (MRI).

Methods: Give-me-five trial is a prospective phase II study designed for the treatment of PCa patients with ultra-hypofractionated radiotherapy scheduled in 5 fractions with 36.25 Gy delivered to the whole prostate and a concomitant boost of 37.5 Gy to the dominant intraprostatic lesion (DIL) identified by multiparametric MRI. T2-weighted (T2W) MRI sequences acquired with homogenous characteristics (0.59x0.59x3 mm3 voxel size, XX Te, YY Tr) on a 1.5T Magnetom Avantofit scanner (Siemens) were selected and the prostate gland contours were analyzed. The extraction of radiomic features (shape, first-order statistics and textural features) was performed using the IBEX software. We tested association of each radiomic features with Gleason score (GS, 3+3 vs 3+4 vs 4+3), extracapsular extension (ECE, 1/2 vs 2 vs 3) score, Prostate Imaging – Reporting and Data System (PIRADS, 2/3 vs 4 vs 5) score and risk class (intermediate vs low), and selected the feature with the lowest p-value in each cluster as representative. Statistical analysis was performed with SAS/STAT® software.

Results: Of the 65 prospectively enrolled patients, 49 T2W-MRI sequences fulfilled the inclusion criteria. For each patient, 1058 radiomic features were identified and then grouped in 30 clusters to reduce dimensionality. A logistic regression (machine learning) classifier was trained to predict clinical outcomes. Results are shown in Table 1. Radiomic signature for prediction of high Gleason score included only GLCM3 texture features. Radiomic signature for prediction of cT2 stage as well as for 3/4 ECE score included first-order statistics intensity features. A GLCM3 texture feature was the most predictive feature for 4/5 PIRADAS score, with excellent predictive accuracy. Finally, radiomic signature for prediction of intermediate risk class included both GLCM3 texture and first-order statistics intensity features, with good predictive accuracy.

Conclusions: MRI-based radiomics in PCa for the prediction of tumour phenotype is a feasible and promising approach. It might lead to a semi-automated definition of tumour characteristics and thus reduce the intra/inter-operator variability in the radiologic image interpretation. We plan to increase the dataset dimensionality in order to strengthen the statistical power and to validate results.

**Table 1. Predictive accuracy of radiomic signature.***

| Outcome | Predictive features | p-value | AUC (95%CI)^ | Cross-validated AUC (95%CI)^ |
|---|---|---|---|---|
| Gleason Score 3+4/4+3 | • GLCM3_2-4AutoCorrelation<br>• GLCM3_10-4InverseVariance | 0.004<br>0.01 | 0.80 (0.68-0.93) | 0.75 (0.61-0.89) |
| T stage cT2 | • ID_ 15Percentile | 0.004 | 0.81 (0.61-1.00) | 0.74 (0.51-0.98) |
| ECE score 3/4 | • ID_ 80Percentile | 0.003 | 0.84 (0.69-0.99) | 0.81 (0.65-0.97) |
| PIRADS score 4/5 | • GLCM3_ 12-7ClusterProminence° | 0.008 | 0.94 (0.86-1.00) | 0.90 (0.79-1.00) |
| Risk class Intermediate | • GLCM3_6-4Correlation<br>• ID_60Percentile | 0.02<br>0.01 | 0.86 (0.74-0.98) | 0.82 (0.68-0.97) |

*AUC=Area Under the receiving operator characteristic Curve;*
*CI=Confidence Intervals;*
*GLCM=GrayLevelCooccurenceMatrix;*
*GLRLM=GrayLevelRunLengthMatrix;*
*GOH=GradientOrientHistogram;*
*ID=Intensity Direct.*
**obtained by unconditional logistic regression models with stepwise selection of the cluster representative radiomic features for each outcome. ^95% CI obtained by the De Long method (ref). ° per 1000 unit increase.*

## CO090

### INTRODUCING INFORMATION ON SALIVA MICROBIOTA INTO TOXICITY MODELING: PRELIMINARY RESULTS FROM A TRIAL

N.A. Iacovelli[1], A. Cavallo [2], T. Rancati [3], L. De Cecco[4], E. Mancinelli [4], M.S. Serafini[4], A. De Vecchi[4], N. Facchinetti[1], T. Di Florio[3], E. Ivaldi[1], D.A. Romanello[1], S. Alfieri[5], L. Licitra[6], C. Fallai[1], R. Valdagni[7], E. Orlandi[1]

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Aims: A mono-institutional trial was set up to investigate the role of saliva/gut microbiota (MB) in toxicity (tox) after RT for head & neck (HNC) and prostate cancers. We here focus on introducing information on saliva MB into a normal tissue complication probability (NTCP) model for acute oral mucositis (OM) in HNC.

Methods: 130 consecutive HNC patients (pts) receiving either postoperative (60-66Gy @2Gy/fr) or radical IMRT (70Gy @2-2.12Gy/fr) with/o chemotherapy were enrolled. A detailed evaluation was done pre, during and at RT end, including saliva MB measurement. Saliva samples were collected using OMNIgene oral devices (DNA genotek). DNA extraction was carried out using the QIAamp-DNA-Stool-Mini-Kit (Qiagen). The bacterial 16S ribosomal-RNA reads were analyzed with the QIIME software and pooled in Operational Taxonomic Units (OTUs) with Uclust software. Grade≥3 CTCAE acute OM (OM3) was the primary endpoint. Among 24 pts selected for this preliminary analysis, 13 scored OM3. Unsupervised clustering (fuzzy c-means) was used to separate pts into 2 MB clusters, based on relative abundance of OTUs at bacterial class level before RT start. Information on MB clustering was introduced as a dose-modifying factor into a logistic NTCP model. Dosimetric variables were derived from a previous model for OM3: dose to oral cavity (Equivalent Uniform Dose, OCEUD, with n=0.05) and mean dose to parotid glands (PGmD).

Results: Unsupervised clustering identified 12 pts included in a first (A) and 12 in a second MB cluster (B). 4/12 (33.3%) and 9/12 (75%) pts with OM3 were found in clusters A and B, respectively (p=0.05). MB clustering resulted in AUC=0.71 (95%CI=0.50-0.87) for OM3 discrimination. The following bacterial classes presented with significantly different abundances (p<0.01) in MB clusters A and B: Proteobacteria_ Gammaproteobacteria and Acidobacteria-6 were more abundant in cluster A, while Bacteroidetes_Bacteroidia, Firmicutes_Clostridia and Actinobacteria_ Corio-bacteriia were more abundant in cluster B. NTCP model including only dosimetry had OR=1.19 (for 1 Gy increase) for PGmD and 1.03 for OCEUD (AUC=0.80, 95%CI=0.59-0.94). When MB clustering was introduced resulted in OR=4.1 and AUC=0.85 (95%CI=0.64-0.96), with 10% decrease of both high and low residual pts.

Conclusions: This preliminary study demonstrates the possibility of introducing pts-specific MB data into NTCP model, through use of unsupervised clustering to exploit the whole MB information (292 classes) without dramatically increasing the number of features to be included in the model. Results in a small sample of HNC pts seem promising, indicating that pts with/o acute OM3 have different constitutional saliva MB profiles. If confirmed in the whole population, this could represent an important finding for tox prediction and design of possible interventional trials to reduce tox by modifying saliva MB before RT start.

**CO091**

## GLI.F.A. PROJECT: GLIOBLASTOMA MULTIFOME RADIOMICS FEATURES ANALYSIS FOR THE PREDICTION OF PATIENTS OUTCOMES

S. Chiesa[1], I. Palumbo[2,3], F. Beghella Bartoli[1], C. Mazzarella[1], M. Iacco[2], C. Masciocchi[1], M. Lupattelli[3], A. Rongoni[4], R. Russo[5], G. Sabatino[6], P. Floridi[4], N. Dinapoli[1], S. Longo[8], L. Boldrini[1,8], R. Tarducci[4], M. Balducci[1,8], C. Aristei[2,3], V. Valentini[1,8]

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Aims: A comprehensive analysis of Glioblastoma multiforme (GBM) heterogeneity could be useful to personalize treatment strategies. Radiomic provides a tool for quantification and visualization of intra-tumor heterogeneity and converts images into mineable data. The multi-centric study, the GLI.F.A. (Glioblastoma: advanced Imaging Features Analysis) Project, aims to investigate whether radiomic feature-based MRI signature allow to predict clinical outcomes in GBM.

Methods: Patients affected by GBM, who were treated with surgery and standard chemo-radiotherapy, were considered. Two radiomic analysis were performed: one on pre-operative magnetic resonance images (MRI) and the other as a delta-radiomic evaluation using MRIs after radiotherapy, during adjuvant chemotherapy and follow-up. The Gross Tumor Volume (GTV) (i.e. the macroscopic lesion at the baseline) and Clinical target Volume (CTV) (i.e. the tumor bed +/- residual mass + 1.5cm of margin) were contoured in the contrast-enhanced T1 and T2 and T2-FLAIR weighted images as region of interest (ROI). The MODDICOM software was used for the extraction of MRI features. The Mann Whitney or t-test were used to assess the difference in radiomic features between different responses and the Log-rank test for Kaplan-Meier curves was used to evaluate the significance of the features, using their median value to categorize the continue variables.

The overall survival (OS), the progression fee survival (PFS) and the response to radio-chemotherapy (RTCT) were considered.

Results: Forthy-three patients, treated from 2014, with a median age of 63 years (range 45-80) were enrolled. The first analysis on pre-operative MRI extracted 92 features from each ROI. The textural features correlated with PFS, LC and response to RTCT on T1 images and one features, describing the homogeneity, impacted on all three clinical outcomes (Table1). For delta-radiomic analysis, the pre-RTCT MRI and the MRI after the 6th cycle of chemotherapy resulted useful for significant features: the textural features for both MRI, the first order and morphological features for pre-RTCT MRI (Table 2).

Conclusions: This radiomic analysis suggests that is possible to stratify patients according MR based quantitative imaging. A prospective enrollment is ongoing in order to confirm the role of imaging features in identifying, according to other known prognostic factors, high risk patients that could benefit of dose-dense strategies.

**Tables 1 and 2.**

Table 1 Radiomic features analysis on MRI at diagnosis

| MRI sequence | Outcome | Feature (categorized according to median value) | Median | Feature order | adjusted p-value (Log-Rank test) | Median survival (days) |
|---|---|---|---|---|---|---|
| contrast-enhanced T1 weighted | PFS | Inverse difference moment normalized | 0.998 | II | 0.019 | <median: 348 |
| | | | | | | ≥median: 135 |
| | LC | Inverse difference moment normalized | 0.998 | II | 0.016 | < median: 459 |
| | | | | | | ≥ median: 93.5 |
| | | First measure of information correlation | -0.611 | II | 0.027 | < median: 317 |
| | | | | | | ≥ median: 121 |
| | | Run percentage | -0.986 | II | 0.038 | < median: 168 |
| | | | | | | ≥ median: 464 |
| | | Feature (continuous) | | | p-value (Wilcoxon Mann Whitney test) | |
| | Response to RTCT | Inverse difference moment normalized | | II | 0.025 | |

Table 2 Delta Radiomic features analysis: univariate imaging features for PFS and LC on contrast enhanced T1 weighted

| MRI sequence | Outcome | Timing MRI | Features (categorized according to median value) | Feature order | adjusted p-value (Log-Rank test) |
|---|---|---|---|---|---|
| contrast-enhanced T1 weighted | PFS | Pre-RT | F_stat.10percentile | I | 0.007 |
| | | | f_stat.energy | I | 0.007 |
| | | | f_morph.surface | III | 0.019 |
| | | | f_morph.volume | III | 0.019 |
| | | | f_morph.av.a | III | 0.007 |
| | | | F_morph.comp.1.x | III | 0.007 |
| | | | f_morph.sph.discr. | III | 0.007 |
| | | | f_morph.sph | III | 0.007 |
| | | | f_morph.pca.flatness | III | 0.002 |
| | | | f_cm.joint.var | II | 0.002 |
| | | | f_cm.sum.entr | II | 0.002 |
| | | | f_cm.dvar.asym | II | 0.021 |
| | | | f_rlm.glnu.norm | II | 0.019 |
| | | | f_szm.glnu.norm | II | 0.021 |
| | | | f_cm.idmn.x | II | 0.021 |
| | | After 6° CT cycle | f_rlm.glnu.norm.x | II | 0.019 |
| | LC | Pre-RT | F_stat.10percentile | I | 0.020 |
| | | | f_stat.energy | I | 0.020 |
| | | | f_morph.volume.x | III | 0.035 |
| | | | f_morph.av.a | III | 0.015 |
| | | | F_morph.comp.1.x | III | 0.015 |
| | | | f_morph.sph.discr. | III | 0.015 |
| | | | f_morph.sph | III | 0.015 |
| | | | f_morph.pca.flatness | III | 0.009 |
| | | | f_cm.sum.entr | II | 0.009 |
| | | After 6° CT cycle | f_dvar.dvar.asym.x | II | 0.043 |
| | | | f_cm.idmn.x | II | 0.043 |
| | | | f_rlm.glnu.norm | II | 0.035 |
| | | | f_szm.glnu.norm | II | 0.035 |

## CO092

## ABSTRACT WITHDRAWN

## CO093

## RADIOMIC ANALYSIS IN LOCALLY ADVANCED PANCREATIC CANCER TREATED WITH STEREOTACTIC BODY RADIATION THERAPY

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Aim: Aim of this study was to evaluate the relationship between radiomic analysis based on contrast-enhanced computed tomography (CT) images and the local control (LC) to treatment and progression free-survival (PFS) in a retrospective cohort of 37 patients affected by locally advanced pancreatic cancer (LAPC) treated with stereotactic body radiation therapy (SBRT).

Methods: Gross tumor volume of the primary disease (GTVp) for each patient was contoured by two expert Radiation Oncologists. A total of 30 features were derived and selected from the CT images and grouped by intensity, shape and second or higher order features, according to significant results by literature. Radiomic analysis were performed using an imaging biomarker explorer software that runs in MatLab platform. Based on median value of each variables, the continuous quantitative variables were converted to dichotomous variables. The univariate and multivariate logistic regression was performed to investigate the predictive value of each radiomic features relatively to LC. The prognostic value of radiomic analysis relative to PFS was evaluated with univariate Cox regression. The statistical analysis was carried out in R platform.

Results: The main clinical and treatment characteristics of the study cohort were reported in a previous published paper [https://doi.org/10.1007/s00066-018-1306-2]. The 30 radiomic features were divided in 12 intensity (IntensityHistogram) features, 6 shape (S) features and 12 second or higher order (GrayLevelCooccurence Matrix25-GLCM25/ Neigh borIntensityDifference25 -NID25) features. The main summary indicators of the radiomic variables were reported in Table 1. From the analysis of textural data, 4 predictors resulted significant at univariate test for LC: IH_Energy(p=0.05), S_Compactness(p=0.05), S_Mass(p=0.05) and GLCM25_Correlation(p=0.05). The multivariate analysis showed statistical significance for 2 variables: IH_Energy(p=0.05) and GLCM25_Correlation(p=0.05). The Area Under the Curve for the multivariate logistic regressive model was 0.783 (95% CI 0.571-0.905). Between all radiomic features, only the GLCM25_Correlation was significantly correlated with PFS (hazard ratio 2.5;95%CI 1-6.3,p=0.04).

Conclusion: Radiomic analysis based on contrast-enhanced CT images in LAPC treated with SBRT iden-

tifies predictive and prognostic imaging biomarkers for LC and PFS, respectively, representing a promising field of research.

**Table 1. Main summary indicators of the radiomic variables with symmetric (A) and asymmetric (B) distribution.**

(A)

| | Min | I qrt | Median | Mean | III qrt | Max |
|---|---|---|---|---|---|---|
| GLCM25_Dissimilarity | 0.4687 | 0.7430 | 0.9449 | 0.9249 | 1.1017 | 1.4467 |
| GLCM25_Entropy | 3.189 | 4.555 | 5.121 | 5.007 | 5.633 | 6.118 |
| GLCM25_InverseDiffNorm | 0.9863 | 0.9892 | 0.9907 | 0.9910 | 0.9927 | 0.9954 |
| IH_Entropy | 2.063 | 2.910 | 3.327 | 3.262 | 3.616 | 4.012 |
| IH_MedianValue | 1019 | 1048 | 1066 | 1061 | 1074 | 1107 |
| IH_StdValue | 17.45 | 30.31 | 42.33 | 44.08 | 52.69 | 94.90 |
| IH_IQR | 19 | 37 | 49 | 48.61 | 59 | 86 |
| NID25_Contrast | 19.29 | 60.84 | 79.49 | 87.36 | 106.47 | 219.72 |
| S_Compactness | 0.2017 | 0.8804 | 1.0835 | 1.1796 | 1.5161 | 2.0469 |
| S_Roundness | 0.1924 | 0.2921 | 0.3496 | 0.3696 | 0.4355 | 0.6293 |
| S_Sphericity | 0.5657 | 0.7221 | 0.7780 | 0.7679 | 0.8366 | 0.9242 |
| S_SurfaceArea | 6.578 | 41.241 | 64.853 | 70.978 | 98.386 | 146.441 |

(B)

| | Min | I qrt | Median | Mean | III qrt | Max |
|---|---|---|---|---|---|---|
| GLCM25_Contrast | 0.5276 | 1.3055 | 1.7381 | 2.1255 | 2.2323 | 10.7163 |
| GLCM25_Correlation | 0.3972 | 0.7000 | 0.7984 | 0.7526 | 0.8189 | 0.8782 |
| GLCM25_Energy | 0.02093 | 0.03279 | 0.04398 | 0.05595 | 0.06697 | 0.16313 |
| GLCM25_Homogeneity | 0.5723 | 0.5952 | 0.6242 | 0.6418 | 0.6873 | 0.7752 |
| GLCM25_Variance | 2.334 | 7.354 | 13.917 | 16.757 | 20.796 | 54.943 |
| IH_Energy | 548525585 | 7510236909 | 14287493106 | 17039133133 | 25006640450 | 65555777985 |
| IH_MaxValue | 1079 | 1203 | 1267 | 1488 | 1456 | 3093 |
| IH_MinValue | 576.0 | 869.0 | 885.0 | 883.1 | 910.0 | 1001.0 |
| IH_Uniformity | 0.07358 | 0.10370 | 0.12204 | 0.13775 | 0.17030 | 0.29948 |
| IH_Kurtosis | 2.854 | 3.622 | 4.409 | 19.812 | 10.007 | 157.412 |
| IH_Range | 140.0 | 290.0 | 383.0 | 604.5 | 585.0 | 2220.0 |
| IH_Skewness | -1.7876 | -0.6782 | -0.3754 | 0.4906 | 0.3076 | 8.8446 |
| IH_Variance | 304.3 | 918.4 | 1792.0 | 2222.9 | 2776.2 | 9006.5 |
| NID25_Busyness | 0.0001495 | 0.0003557 | 0.0004530 | 0.0004659 | 0.0005566 | 0.0018290 |
| NID25_Coarseness | 0.04914 | 0.06149 | 0.06812 | 0.07763 | 0.09643 | 0.14098 |
| NID25_Complexity | 5047 | 31686 | 54226 | 129425 | 84379 | 1293439 |
| S_Convex | 0.8198 | 0.9254 | 0.9570 | 0.9443 | 0.9709 | 0.9844 |
| S_Mass | 1.521 | 19.815 | 36.046 | 42.632 | 61.733 | 97.638 |

## CO094

## DELTA RADIOMICS TO ASSESS RECTAL CANCER BEHAVIOR AND PREDICT DISTANT METASTASIS

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Aims: To assess the role of the variation of radiomics parameters between staging and post- neoadjuvant chemoradiation (nCRT) re-staging Magnetic Resonance Imaging (MRI) for the prediction of 2 years Distant Metastasis rate (2yDM) in a single institution cohort of patients (pts) affected by locally advanced rectal cancer (LARC).

Methods: Data regarding 217 LARC pts treated with nCRT in a single institution from November 2007 to January 2016 were retrospectively collected. Only pts with available pre- and post-nCRT diagnostic MRI and with at least 3 years of follow-up were selected. A radiation oncologist (RO) and a radiologist defined the Gross Tumour Volume (GTV), with the validation of another RO. Pts were randomly assigned to a training group (90% of the dataset) and a testing group (10%), the same outcome proportion was maintained between the two groups. The features selection process was performed on the training set with a 5-fold cross-validation and only features significative ($p<0.05$ at Wilcoxon Mann-Withney test) for at least 3 times after 5 iterations and with a Pearson correlation coefficient less than 30% were selected. The model performance was then assessed on the testing data.

Results: From the initial database of 217 LARC pts, 4 pts were discarded for missing data regarding the endpoint. 2606 features were extracted and tested from the pre- and post- nCRT GTV. Four features were identified after the selection process: i) medianFD30,60.delta (the variation between pre- and post- MRI median fractal dimension); ii) F_szm.lzlge1.1.delta (the variation between pre- and post- MRI of the value of a radiomic feature using Laplacian of Gaussian (LoG) filter; F_morph.pca.flatness.pre (the ratio between the minor axis and the major axis of the ellipsoid calculated on the volume of the GTV of the pre-MRI) and iv) F_cm.clust.prom0.6.pre (a radiomic feature extracted from the co-occurrence matrix of the pre-MRI using (LoG) filter). A logistic regression based model was provided with a testing set balance accuracy of 79%, a sensitivity of 0.71% and a specificity of 0.86%.

Conclusions: In this single center study, Delta Radiomics appears to have a predictive role in characterizing tumor behavior in rectal cancer after nCRT. The early prediction of biological aggressiveness could help in treatment personalization and follow-up intensification in high risk pts. Further studies are needed to confirm these results on an independent validation dataset.

**Table 1. Patient characteristics.**

| | |
|---|---|
| Age: Median (range), years | 64 (26-83) |
| Sex | Female 79 (36.4%)<br>Male 138 (63.6%) |
| Stage (cT) | cT2 15 (6.9%)<br>cT3 134 (61.8%)<br>cT4 68 (31.3%) |
| Stage (cN) | cN0 13 (6.0%)<br>cN1 71 (32.7%)<br>cN2 133 (61.3%) |
| TRG (according to Mandard) | TRG 1: 55 (25.4%)<br>TRG 2: 44 (20.3%)<br>TRG 3: 89 (41.0%)<br>TRG 4: 17 (7.8%)<br>n.a.: 12 (5.5%) |
| Distant Metastasis at 2 years | No: 177 (81.6%)<br>Yes: 36 (16.6%)<br>n.a.: 4 (1.8%) |

## CO095

### LOCAL RESPONSE BASED ON RADIOMIC ANALYSIS IN EARLY-STAGE NON-SMALL CELL LUNG CANCER TREATED WITH STEREOTACTIC ABLATIVE RADIATION THERAPY

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Purpose: Stereotactic ablative radiation therapy (SABR) is a treatment option for early-stage non-small cell lung cancer (NSCLC). This study investigates the performance of radiomic features for disease recurrence after stereotactic ablative radiation therapy (SABR).

Methods and Materials: Patients with early stage NSCLC, treated with SABR were considered. The lung lesions received a total dose of 42 Gy in 3 or 50 Gy in 5 fractions according to the site. A 4D-CT were performed to delineated the internal target volume (ITV) and the radiomic features were extracted from the ITV reported on average intensity projection (AIP), through the use of MODDICOM software. The Wilcoxon Mann Whitney test was applied to evaluate the significance of the features; afterwards a Logistic Regression model was built for each significant feature. The response to SABR according to RECIST Criteria was considered.

Results: Overall 42 early stage NSCLC patients and 47 lesions, receiving SABR, were considered for this analysis. Thirteen lesions presented a local recurrence. Ninety-four features were extracted using MODDICOM software and the correlation between the radiomic features and the local recurrence at 12-24 and 36 months was investigated. Seventeen features showed a significant correlation ($p<0.01$) with local recurrence at 12 and 24 months at Wilcoxon Mann Whitney test: 3 intensity based statistical features; 2 Grey level co-occurrence based features-Texture features (GLCM); 6 Grey level run length based features-Texture features (GLRLM); 6 Grey level size zone based features-Texture features (GLDZM), according to Image biomarker standardization initiative v.7 (https://arxiv.org/abs/1612.07003). No correlation was found between radiomic features and local recurrence at 36 months. At the kernel density estimation of Skewness ($p<0.01$ at the Mann Whitney test) is shown on the picture on the left for both, the positive (blue) and negative (red) lesions, on Figure 1. In the middle the distribution of positive and negative outcomes (same colors) depending on the value of Skewness and on the right the ROC curve of the associated Logistic Regression model (AUC = 0.847).

Conclusions: These results suggest that radiomic can help in detecting, under specific circumstances (e.g. Skewness greater or equal than 0.5), local recurrence at 12 months after SABR and that this decision support system could potentially allow a personalized treatment strategy for early salvage therapy.

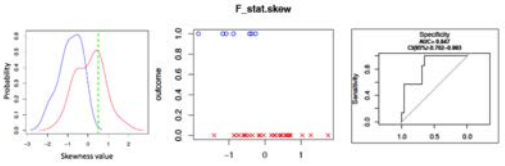


**Figure 1.**

## CO096

### RADIATION-INDUCED GENE EXPRESSION PROFILING OF DIFFERENT BREAST CANCER SUBTYPES

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Aims: The aim of this study was to assess the gene expression changes induced by high doses of ionizing radiation (IR) on immortalized and primary BC cell lines grouped according to human epidermal growth factor receptor (HER2), estrogen and progesterone receptors status (ER, PR), in order to study how HR status influences the radiation response, affecting clinical outcomes. Radiation therapy (RT) is a crucial treatment for BC, either alone or in combination with other treatment modalities, however, RT treatment planning take in account physic metrics, nonetheless it emerges the necessity to include biological biomarkers of tumor radiosensitivity, to optimize therapeutic efficacy.

Methods: A genomic approach using cDNA microarray was utilized to analyze gene expression profiles induced by two doses (9 and 23 Gy) of IR, 24 h post-treatment, on in vitro and ex-vivo models (e.g., primary cells). For this purpose, three human immortalized cell lines (MCF10A, MCF7, and MDA-MB-231) and three primary cell cultures (HMEC, BCpc7, and BCpcEMT), obtained from both tumor and healthy specimens, were classified into three BC groups: 1) the triple negative group (ER−/PR−/HER2−), including MDA-MB-231 and BCpcEMT cells; 2) the HR positive group (ER+/PR+/HER2−), including MCF7 and BCpc7 cells; 3) a group originating from healthy tissue, including MCF10A and HMEC cells.

Results: Overall, the IR-induced gene expression

profiles and pathways appear to be cell-line dependent and linked to HR status. Precisely, few genes (11) and one pathway were commonly deregulated in the healthy samples. Instead, BC cells shared well defined responses to RT according the HR status. Indeed, while the HR positive cells activate cellular process involved in cell cycle regulation, repairing DNA strand breaks, and cell survival/death balance through the activation of apoptosis signaling, particularly driven by the activation of p53 signaling pathway, the triple negative cells response in strongly characterized by chromatin remodeling mechanisms, through the activation of cell cycle regulation, nucleosomes, chromosome, and telomere maintenance.

Conclusions: Genomic biomarkers and gene-signatures of specific tumor subtypes, selected according to their HR status and molecular features, could be used to achieve personalized biological-driven RT treatments planning alone or in combination with targeted therapies.

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## *Discussed Poster*

**DP01**

### MULTIMODAL APPROACH WITH 18-F-FDG PET-CT AND MPMRI AS PREDICTOR FOR PCR IN LOCAL ADVANCED ESOPHAGEAL CANCER TREATED WITH CROSS REGIMEN. IS ORGAN-SPARING POSSIBLE?

F. De Renzi[1], S. Bissoli[2], P. Bullian[3], C. Furlan[1], R. Malaguti[1], C. De Toffol[4], F. Martinelli[2], T. Iannone[1]

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Purpose: In locally advanced esophageal cancer, neoadjuvant chemoradiotherapy (nCRT) followed by surgery improved survival over surgery alone. nCRT according to the CROSS[1] regimen followed by surgery may be considered as standard of care. In our Center, from 2010 to date, 75 patients with a diagnosis of carcinoma of thoracic tract or lower third of esophagus were evaluated for a radiation treatment. In 2019 we have treated locally advanced gastroesophageal junction carcinoma according CROSS for a preoperative approach: carboplatin/paclitaxel-based chemoradiotherapy with radiation doses of 41.4 Gy (1.8 Gy/fr).18-F-FDG PET-CT prior to nCRT was always requested and used to identify GTV and Nodal Volume during contouring.In GI multidisciplinary group, we have discussed about PRIDE trial.[2] Here we describe that protocol of study, because an organ-sparing approach in local advanced gastroesophageal junction tumor could be evaluated by GI AIRO board for a future investigation.

Methods: PRIDE (2) is a multicenter observational trial with the aim to obtain a prediction model of a pathologic complete response(pCR) after nCRT delivered according to CROSS in potentially resectable, locally advanced (cT1b-4aN0-3 M0) esophageal or gastroesophageal junction tumor, squamous cell carcinoma or adenocarcinoma. 200 patients should be included. Diagnostic work-up and staging for esophageal cancer includes DW MRI, DCE MRI and 18-F-FDG PET-CT prior to, during (after 10-15 fractions of radiotherapy) and after nCRT with an optional endoscopic assessment. MRI post performed 6–8 weeks after the completion of nCRT, and no sooner than 2 weeks before surgery. Blood samples at 3 time points and 1 postchemoradiation endoscopic and endosonographic assessment. Primary endpoint: pCR prediction. Secondary: PFS e OS.

Results and Conclusions: PRIDE is a clinical oncologic ongoing trial, based on an interesting protocol. Endoscopic biopsy after chemoradiotherapy for esophageal cancer is a very specific but not a sensitive method.[3] A model based on mpMRI, FDG PET-CT and circulating tumor DNA biomarkers could lead to an active surveillance after nCRT in patients with a clinical complete response, obtaining a prediction of pCR without surgical resection, improving quality of life and reducing costs.

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## DP02

### PHASE II STUDY OF FOLFIRINOX-BASED INDUCTION CHEMOTHERAPY FOLLOWED BY RADIOCHEMOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER: PRELIMINARY RESULTS

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Purpose: To evaluate the safety and efficacy of FOLFIRINOX-based induction chemotherapy followed by a high weekly dose of gemcitabine-based radiochemotherapy in patients with borderline resectable or unresectable locally advanced pancreatic cancer.

Materials and Methods: From October 2015 twenty-six patients with pancreatic cancer have been included in the study. In all cases an accurate pre-treatment staging including laparoscopy and 18F-FDG PET/CT has been performed. Patients received chemotherapy with FOLFIRINOX regimen for four doses. Patients without disease progression after restaging received conformal radiation therapy and concurrent gemcitabine at the dose of 600 mg/mq weekly.

Results: Further to the results of the pre-treatment workup, twelve patients (46%) were excluded from the protocol because of the evidence of metastatic disease, and thus a total of 14 patients were consequently enrolled. Grade 3-4 toxicity was observed in two patients (grade 3 elevated levels of alkaline phosphatase in one case; grade 4 febrile neutropenia in another one). Three patients (21.4%) experienced disease progression after induction chemotherapy. One patient has not yet completed the induction phase at the time of evaluation. Ten patients completed the radiochemotherapy protocol. Only haematological grade 3-4 toxicities were observed. Seven patients were evaluated through surgical exploration and six patients underwent surgical radical resection. With a median follow-up of 13 months, the median PFS was 14.2 months. One-year PFS was 62.3%. One-year and two-year LC were 92% and 61%, respectively. One-year MFS was 72% (median, 14.2 months). Median OS was 12.8 months. One-year OS, two-year OS were 66% and 35%, respectively.

Conclusions: Our preliminary results suggest that this protocol treatment is feasible with an acceptable toxicity profile for patients with borderline resectable and unresectable pancreatic cancer. An accurate staging is crucial for the appropriate treatment of patients.

## DP03

### STRAIT-LUC TRIAL: STEREOTACTIC RADIOTHERAPY AND IMMUNOTHERAPY FOR BRAIN METASTASES FROM NON SMALL CELL LUNG CANCER (NSCLC): A PROSPECTIVE OBSERVATIONAL MULTICENTER TRIAL ON BEHALF OF BRAIN AND THORACIC ONCOLOGY NATIONAL GROUP OF AIRO

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Aims: The STRAIT- LUC trial is the result of the collaboration between AIRO Brain group and AIRO Thoracic Oncology group to investigate the association between Stereotactic Radiotherapy (SRT) and Immunotherapy (IT) for the treatment of brain metastases (BM) from NSCLC. Many retrospective trials, with

a small number of patients and with several bias, suggest that concomitant treatment may improve the outcomes of these patients. Primary endpoints of the study are safety, feasibility and intracranial control assessment; secondary endpoint is the evaluation of Quality of Life (QoL).

Methods: Data about patients with brain metastases from NSCLC treated with concomitant IT and SRT will be prospectively collected in different Italian Radiotherapy Centers. Eligibility criteria are: patients with a maximum of 10 brain lesions to be treated with single fraction SRT or hypo-fractionated SRT (3-5 fractions); concurrent SRT and IT, defined as IT and SRS being administered within one month of one another; SRT performed during a first line, a second line or a further line of IT with or without the association of chemotherapy. Toxicity such as the development of brain radionecrosis will be evaluated according to the CTCAE v.4.1. MRI scanning will be performed every 3 months during follow-up and radiological response will be evaluated according to the i-RANO criteria. Local-PFS and Distant-PFS, defined as the time from SRT to local progression of the treated lesions and to the appearance of new BM, respectively, will be analyzed. EORTC QL 30 BN module will be used to assess patients QoL. Survival analysis will be performed using Kaplan-Meyer survival curves and log-Rank test.

Results: Fifty patients are expected to be enrolled during a period of two years. An interim analysis will be performed after the enrollment of the first 30 patients. A pre-planned subgroup analysis will be performed according to the number of BM (1 vs 2-4 vs 5-10), the number of SRT fractions (1 vs 3 vs 5), PDL-1 level. Use of corticosteroids (dose and duration) will be registered.

Conclusions: To our knowledge this is the first multicenter prospective trial evaluating the association of IT and SRT for BM from NSCLC. This trial will contribute to provide evidence to confirm the encouraging results that were reported by retrospective studies.

## DP04

### A MODIFIED THREE-ISOCENTER JAGGED-JUNCTION (TIJJ) INTENSITY-MODULATED RADIATION THERAPY (IMRT) APPROACH FOR THE TREATMENT OF MEDULLOBLASTOMA

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Aims: Craniospinal irradiation (CSI) is one of the most difficult treatments. The aim of this study was to show the efficiency of a modified three-isocenter jagged-junction (TIJJ) Intensity-Modulated Radiation Therapy (IMRT) in terms of Conformity Index (CI) and Homogeneity Index (HI).

Methods: Image data of 4 patients with histologically diagnosed medulloblastoma who underwent CSI were used. The prescription dose was 25.5 Gy in 15 fx for whole brain and spinal cord, with a sequential boost of 10.8 Gy in 6 fx on the whole brain and 20Gy in 10 fx on the posterior cranial fossa. The TIJJ IMRT technique was used to create the delivered plan. The Oncentra MasterPlan treatment planning system was employed to delineate the planning target volume (PTV) and organs at risk (OARs) on CT images with the patients in prone position using a personalized immobilization device. The PTVcns included the PTVbrain and the PTVspinal1/2. The PTVbrain included the whole brain with a 3 mm isotropic expansion. The PTVspinal1/2 included C1 through S3 with a 5 mm isotropic expansion. The PTVbrain and PTVspinal1/2 have been used to create three different IMRT plans, each with a proper isocenter. The three isocenters were collinear and placed near the patient's midline. The PTVbrain and PTVspinal1/2 were modified every 5 fx in order to stagger the field edges, keeping the three isocenters fixed, thus shifting the junctions (PTVbrain-PTVspinal1 and PTVspinal1-PTVspinal2). The field set of IMRTbrain contained seven fields with gantry angles of 0°, 50°, 75°, 110°, 245°, 280° and 315°, respectively. The field sets of IMRTspinal1/2 had five radiation fields with gantry angles of 295°, 325°, 0°, 35° and 65° respectively.

Results: The modified TIJJ IMRT technique reached the goal of the 95% isodose curve covering at least 99% of the PTV and respected all OARs constraints. The CI and HI were 0.79+-0.04 and 0.18+-0.04 respectively (mean+-sd). In addition, neither cold nor hot dosing spots were found in the radiation beams overlapping regions between the PTVs.

Conclusions: Modifying the extension of the PTV every 5 fx in order to change the topography of the junctions overcomes problems associated with field junctions and beam edge matching and improves planning and treatment setup efficiencies with homogenous target dose distribution. This technique is a valid option for the treatment of medulloblastoma as it is comparable to the helical tomotherapy in terms of CI and HI.

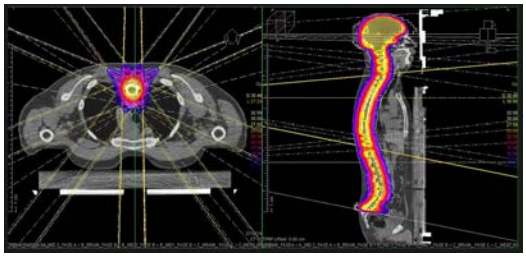

**Figure 1.**

## DP05

### ONLINE ADAPTIVE MRI GUIDED RADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER: FIRST APPLICATION IN ITALY

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Aims: Magnetic Resonance-guided Radiation Therapy (MRgRT) allows more precise identification of therapy volumes and reliable online monitoring of treatment delivery, using high-temporal resolution MR cine imaging. MRgRT allows to online adapt the treatment plan (i.e. Online Adaptive RT) optimizing the dose distribution on patient's anatomy of the day, just before fraction delivery. Aim of this study is to evaluate the OA workflow implemented in our institution for locally advanced pancreatic cancer (LAPC) patients in terms of target coverage and organs at risk (OARs) sparing, comparing the adapted treatment plan with both the baseline plan and the "predicted" one, that is the baseline plan evaluated on the patient's daily anatomy.

Methods: We retrospectively analyzed LAPC patients treated with MRgRT using the OA workflow from January to August 2018. MRgRT was delivered using video-assisted inspiratory breath-hold for a total of 38 fractions with a dose ranging from 30 Gy to 40 Gy in 5 fractions. Plan quality was assessed using institutional OARs constraints and PTV coverage (V95%), GTV (V98%) coverage as secondary quality index. Prior to each fraction, alignment daily volumetric MR-imaging was performed. The dose distribution of the baseline plan was firstly calculated on the anatomy of the day, obtaining the "predicted" plan and, if the dose distribution did not meet the constraints set in the planning phase, PTV and OARs were re-contoured within a distance of 3 cm from the PTV external edge and a new online "adaptive" plan was generated.

**Table 1. Targets and OARs metrics in terms of mean values before and after the online adaptation of the plan.**

| | Predicted plan | | | | | | | Adaptive plan | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PTV | GTV | Duodenum | | Stomach | | Bowel | PTV | GTV | Duodenum | | Stomach | | Bowel |
| | V95% mean | V98% mean | V33 (cc) mean | V25 (cc) mean | V33 (cc) mean | V25 (cc) mean | V33 (cc) mean | V95% mean | V98% mean | V33 (cc) mean | V25 (cc) mean | V33 (cc) mean | V25 (cc) mean | V33 (cc) mean |
| PT 1 | 67,71 | 79,99 | 0,37 | 8,61 | 0,04 | 3,18 | 0,25 | 75,50 | 91,93 | 0,68 | 5,67 | 0,06 | 4,39 | 0,27 |
| PT 2 | 83,02 | 85,93 | 10 | 16,19 | 0,02 | 0,93 | 0,81 | 92,06 | 96,72 | 0,74 | 6,15 | 0,08 | 3,66 | 0,59 |
| PT 3 | 74,81 | 80,19 | 2,70 | 11,81 | 0 | 3,77 | 0 | 95,63 | 97,90 | 0,69 | 9,50 | 0,13 | 3,06 | 0 |
| PT 4 | 66,8 | 76,93 | 0 | 0,01 | 2,47 | 8,67 | 0 | 78,96 | 90,39 | 0,05 | 0,65 | 0,04 | 1,71 | 0,47 |
| PT 5 | 54,65 | 65,67 | 1,77 | 4,62 | 0 | 0,61 | 0 | 60,39 | 73,02 | 0,04 | 0,56 | 0,12 | 2,58 | 0 |
| PT 6 | 66,39 | 78,49 | 0,07 | 1,92 | 0,15 | 4,01 | 0,15 | 72,94 | 88,34 | 0,03 | 1,99 | 0,15 | 4,61 | 0,02 |
| PT 7 | 74,14 | 81,61 | 0 | 0 | 2,85 | 16,86 | 0,14 | 87,85 | 99,09 | 0 | 0 | 0,73 | 13,29 | 0,22 |
| PTS | All fractions treated with Original Plan | | | | | | | | | | | | | |

Results: Eight patients affected by LAPC were enrolled in this study. Median age was 64 years. Out of 38 total fractions, 26 (68.4%) were adapted and 12 (31.6%) were delivered using the baseline plan. The use of the adaptive workflow resulted to be advantageous in all the patients: mean PTV V95% increased by 10.8% (5.7-20.8) while mean GTV V98% of 12.6% (7.3-17.7). Also OARs V33 and V25 showed a positive trend in avoiding unnecessary irradiation. Dosimetric results are summarized in Table 1. Acute G1 diarrhea was observed in one patient (CTCAE v.4). At median follow-up of 14 months all patients were alive with 75% local control rate.

Conclusion: Online adaptive MRgRT is associated with acceptable toxicity and promising local control rates in LAPC. Daily re-optimization prevents the occurrence of high-doses to OARs, increasing the safety of stereotactic treatment for LAPC.

## DP06

### RADIOMICS ANALYSIS OF MRI IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER, CORRELATION WITH TRG (TUMOR REGRESSION GRADE)

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Aims: To evaluate the correlation between MRI texture analysis before and after preoperative radiochemotherapy (RCT) and Tumour Regression Grade (TRG) in locally advanced rectal cancer.

Methods: This is a retrospective study with 53 patients, median age of 65 years, diagnosis of locally advanced rectal cancer hystologically confirmed. All patients were treated with neoadjuvant radiochemotherapy followed by Total Mesorectal Excission surgery. For the RT were planned 50.4 Gy in 28 fractions; concomitant chemotherapy consisted in continuos intervenous infusion of 5-Fluorouracil (225 mg/m$^2$/die) for 11 patients or capecitabine (825 mg/m$^2$/BID) for the others; all patients completed the planned treatment and underwent surgery 6 - 8 weeks after. All the patients were studied with a MRI before and after RCT. On the MRIs the tumour was identified as Region of Interest (ROI) in the T2-weighted images, contouring was performed by two radiation oncologist with the supervision of a dedicated radiologist. On the MRI were analyzed 27 radiomics features.

Results: 73% of the study population had a downstaging after RCT. In particular 11% had TRG1, 45% had TRG2, 26% had TRG3 and 17% had complete anatomopathological tumor regression (TRG 4). As showed in table 1, before RCT all 27 radiomics features analyzed don't show a significant relationship with TRG. After RCT, the Cluster Prominence Value resulted the best variable to predict TRG. The post-CRT tumor volume is also related to TRG. Cluster Prominence is a measure of the skewness and asymmetry of the Gray Level Co-occurrence Matrix, a low cluster prominence (and cluster shade) value describe

many patterns of narrowly represented gray-scale levels. Post-RCT Cluster Prominence Values, divided into the 4 classes of TRG, showed that the values are higher in patients who have better response to preoperative RCT.

Conclusion: Our results indicate post-CRT Cluster Prominence as the most significative texture analysis features for the correlation with response to treatment : a lower value is correlated with poor tumour regression (TRG 1-2), a higher Cluster Prominence is significantly correlated to pathological complete response (TRG 4). Imaging biomarkers might early identify patients who will have a complete or non-complete tumor response to treatment, allowing individualization of medical and surgery therapy. Further studies are desirable in order to identify these biomarkers.

**Table 1.**

| Explanatory variable before RCT | p-value | Explanatory variable after RCT | p-value |
|---|---|---|---|
| Autocorrelation | >0.05 | Autocorrelation | >0.05 |
| Cluster Prominence | >0.05 | Cluster Prominence | 0.037* |
| Cluster Shade | >0.05 | Cluster Shade | >0.05 |
| Contrast | >0.05 | Contrast | >0.05 |
| Correlation | >0.05 | Correlation | >0.05 |
| Difference Entropy | >0.05 | Difference Entropy | >0.05 |
| Difference Variance | >0.05 | Difference Variance | >0.05 |
| Dissimilarity | >0.05 | Dissimilarity | >0.05 |
| Energy | >0.05 | Energy | >0.05 |
| Entropy | >0.05 | Entropy | >0.05 |
| Homogeneity | >0.05 | Homogeneity | >0.05 |
| Information Measure of Correlation 1 | >0.05 | Information Measure of Correlation 1 | >0.05 |
| Information Measure of Correlation 2 | >0.05 | Information Measure of Correlation 2 | >0.05 |
| Inverse Difference | >0.05 | Inverse Difference | >0.05 |
| Maximum Probability | >0.05 | Maximum Probability | >0.05 |
| Sum Average | >0.05 | Sum Average | >0.05 |
| Sum Entropy | >0.05 | Sum Entropy | >0.05 |
| Sum of Square Variance | >0.05 | Sum of Square Variance | >0.05 |
| Sum Variance | >0.05 | Sum Variance | >0.05 |
| kurtosis | >0.05 | kurtosis | >0.05 |
| Skewness | >0.05 | Skewness | >0.05 |
| Pixel Intensity Mean | >0.05 | Pixel Intensity Mean | >0.05 |
| Pixel Intensity Standard Deviation | >0.05 | Pixel Intensity Standard Deviation | >0.05 |
| Pixel Intensity Median | >0.05 | Pixel Intensity Median | >0.05 |
| Pixel Intensity P25 | >0.05 | Pixel Intensity P25 | >0.05 |
| Pixel Intensity P75 | >0.05 | Pixel Intensity P75 | >0.05 |
| D2D | >0.05 | D2D | >0.05 |
| Volume | >0.05 | Volume | 0.047** |

*Notes:* * $r = 0.291$; ** $r = -0.277$

**DP07**

## OPEN SOURCE PLATFORM FOR SEGMENTATION, DEFORMABLE IMAGE REGISTRATION, AND FEATURES EXTRACTION OF LUNG CANCER LESIONS

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Aims: to show an effective, reliable and free-of-charge method that allow any institution to conduct radiomics studies applied to lung cancer.

Methods: The process has been tested on 21 NSCLC (Non Small Cell Lung Cancer): lung lesions (GTVs) have been identified and segmented with the Fast GrowCut tool, allowing an advanced semi-automatic segmentation that significantly reduced the inter-operator variability. Only non-contrast enhanced CT images were used for features extraction, the corresponding enhanced studies were used for a better definition of GTVs in all doubtful cases.The deformable 3D-Slicer registration tool, Plastimatch, allowed to distinguish GTV from atelectasis or mediastinic borders on the contrast-enhanced study. The 3D Slicer Radiomics tool extracts radiomic features from the non-processed raw images. Using Radiomics, 94 features were determined for each volume: 19 first order, 16 shape, 27 Gray Level Co-occurrence Matrix (GLCM), 16 Gray Level Run Length Matrix (GLRLM) and 16 Gray Level Size Zone Matrix (GLSZM). The free software R has been used for statistical analysis and graphical results.

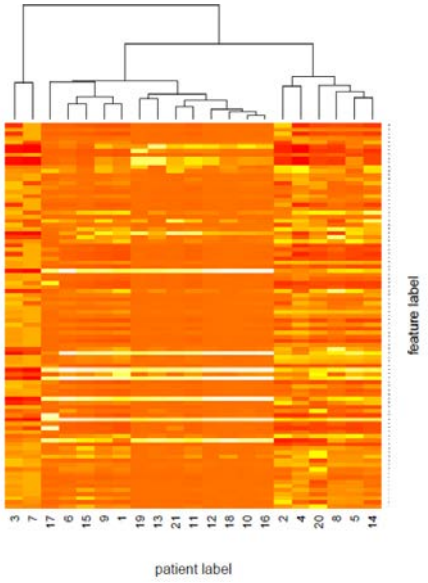


**Figure 1.**

Results: The study of the statistical distribution of the 94 features among the 21 patients GTVs has been useful for their comprehension. In particular, some features appear to be inherently influenced by the volume data, and the normalized features densities could delete this volume influence with a good approximation: the direct consequence of this is that features values and ranges are more easily comparable. The R heatmap function tool allowed a cluster analysis of the normalized features densities (Figure 1), suggesting a natural clustering behavior, beside any clinical data, that could exhibit some interesting properties of two or more features in highlighting some intrinsic characteristics of the tumour. For example, patient 3 and 7 are clustered and it can be hypothesised that their lesions have similar traits.

Conclusions: In this work a complete radiomic process has been described by means of 3D Slicer and R platforms. 3D Slicer coregistration, contouring and features calculation modules have proved to be accurate and fast. Finally, it is equally important to note that 3D Slicer and R platforms offer the opportunity for small radiological departments to carry out radiomic analysis where advanced radiomics commercial softwares are not commonly available.

**DP08**

## RADIOCHEMOTHERAPY OF ANAL CANAL CANCER: FROM CONFORMAL THERAPY TO INTENSITY MODULATED RADIOTHERAPY (IMRT)

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Aims: To evaluate the toxicity and the efficacy of Intesity Modulated Radiotherapy (IMRT) in the treatment of squamous cell anal canal cancer.

Methods: A retrospective analysis has been performed on 12 patients treated with IMRT since 2015 comparing toxicity and outcome against 34 pts treated from 2004 to 2014 with 3D conformal radiotherapy (3DCRT). In most cases radiotherapy was associated with concomitant chemotherapy with Mitomycin C and 5-Fluorouracil (Nigro scheme), 3 patients were treated with radiotherapy alone for older age (> 80 years). IMRT treatments were performed with SIB (Simultaneous Integrated Boost) technique according to RTOG protocol 0529 with 54 Gy in 27 fractions (2 Gy/fr) to the primary tumor and lymphnodes > 3 cm, 49.95 Gy (1.85 Gy/fr) to the intermediate risk areas (lymphnodes < 3 cm) and 45,9 Gy (1,7 Gy/fr) to the low risk areas. 3DCRT was delivered with sequential boost: a dose of 45 Gy was delivered to the pelvis and a median dose boost of 14.4 Gy to the primary tumor (range 5.4-21.6 Gy).

Results: Median age of patients was 60 years (range 46-77) in the IMRT group and 65 years (range 47-85) in the 3D conformal radiotherapy group. In the IMRT group 7 pts were female and 5 male; in the 3DCRT group 23 were female and 11 male. Five patients (2 in the IMRT group and 3 in the 3DCRT group) had HIV positive status. In the IMRT group T stage was T2 in 9 pts and T3 in 3 pts; in the 3DCRT group was T2 in 20 pts, T3 in 8 pts, T1 in 5 pts e T4 in 1 pts. In the IMRT group N stage was N0 in 5 pts and N1a in 7 pts; in the 3DCRT group was N0 in 22 pts and N1a in 12 pts (AJCC, 8th edition). 4/12 pts (33%) in the IMRT group and 20/34 pts (58%) in the 3DCRT group interrupted the treatment more than 5 consecutive days due to acute toxicity. IMRT treatments lead to lower incidence of acute toxicity events (according to RTOG scale): grade 2-3 toxicity, compared to 3DCRT, reduced from 100% to 75% for skin, and from 35% to 25% for gastrointestinal toxicity. No differences were observed concerning complete response (RC): 8/12 pts (66.7%) in IMRT group and 22/34 (64,7%). At the last follow up 23/34 pts (67%) in the 3DCRT were alive with a median follow up of 96 months (range 54-178); all of the patients of the IMRT group were alive at the last follow up with a median follow up of 16 months (range 7-49).

Conclusions: In our experience, in anal canal carcinoma, IMRT treatment has revealed equally effective than 3DCRT but it was associated to a reduction of toxicity.

**DP09**

## IMPACT OF ACCELERATED FRACTIONATION ON ACUTE TOXICITY IN PATIENTS TREATED WITH TOMOTHERAPY FOR SQUAMOUS CELL ANAL CANCER (SCAC): A FREQUENCY-MATCHED COHORT ANALYSIS

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Aims: It is known from randomized studies that a prolonged overall treatment time (OTT) has a detrimental effect on outcome for non-metastatic SCAC. From a radiobiological point of view, a shorter OTT may be beneficial to offset accelerated repopulation typical of epithelial cancers, at the cost of increased morbidity. Tomotherapy is among the most accurate RT techniques to achieve differential dose distributions with high conformity. The aim of our work was to evaluate the impact of an accelerated regimen (AF) on non-hematologic acute toxicity in comparison with conventional fractionation (CF).

Methods: Between May 2014 and August 2018, patients affected by SCAC treated with Tomotherapy in

two different institutions were considered for our study. A frequency-matched cohort analysis was performed to balance patients' characteristics between the two groups (AF and CF): median age, disease stage and administration of concurrent chemotherapy were the considered variables. The chosen dose/fractionation were 55 Gy/2.2 Gy fx and 59.4 Gy/1.8 Gy fx to high-risk CTV, 45 Gy/1.8 Gy fx to low risk CTV in 25 and 33 fractions in the AF and CF cohorts, respectively. Acute toxicity was scored according to NCI – CTCAE v.4.

Results: Overall, 94 subjects were included. Patients' characteristics were well matched between the two groups: the median age and incidence of stage II/III were 66 and 67 years, and 40% and 49% (TNM AJCC 7th ed.) in CF and AF groups, respectively. In addition, concurrent chemotherapy was prescribed to 84% and 71% of patients, with mytomicin C-5FU as the most common regimen. The rate of > G2 radiation dermatitis, diarrhea and cystitis were 73% vs. 63% (p=0.41), 18% vs. 31% (p=0.22), and 11% vs. 2% (p=0.17) in CF and AF cohorts, respectively. In terms of overall non-hematologic acute toxicity, the >G2 rate was 80% and 69% (p=0.32), respectively. In particular, no statistically significant difference could be found between the two groups. The median length of RT interruptions was 0 days (0-38 days).

Conclusions: Our dual-institution experience showed that the tolerability profile of a 5-week accelerated regimen was proved to be non-significantly worse than a more prolonged regimen. Further analysis is ongoing to assess the impact of an AR on treatment outcome, and to investigate the predictivity of metabolic parameters at the baseline FDG-PET.

## DP10

### REIRRADIATION IN DIFFUSE INTRINSIC PONTINE: SALERNO' S EXPERIENCE

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Introduction: Diffuse intrinsic pontine glioma (DIPG) are very aggressive neoplasm that typically involve the pediatric age with a high recurrence rate at short term and poor survival. Since January 2013 to January 2019 at "SS Radioterapia Pediatrica - AOU San Giovanni di Dio e Ruggi d'Aragona of Salerno" received irradiation ten patients, age between 4 and 15, with progressive DIPG . In this retrospective study we report data relating to three cases of re-irradiation (Re-RT).

Materials and Methods: Diagnosis of DIPG was achieve by biopsy in one case (A) and by imaging in the others (B+C). All patients had performed magnetic resonance imaging pre-treatment. Progression after initial chemoradiation had been confirmed clinically and by magnetic resonance imaging. All three patients, with PS between 1-2 and age from 5 to 10 years old, underwent concomitant chemotherapy (nimotuzumab and vinorelbine) and RT (VMAT technique) on Elekta VersaHD (TPS Monaco Montecarlo).

Results: Two patients (A e B) had previously receveid initial radiation to a dose of 54 Gy in 30 fractions of 1.8 Gy no reported G1-G4 toxicity; the third patient (C) stopped at dose of 43.2Gy, (herpetic intestizial pneumonia), then he receveid first re-RT (without progression) at dose 19.8 in 11 fraction of 1,8 Gy, reaching the total dose of 63 Gy. After RT all patients had an improvement of the initial symptoms and performed sequential chemotherapy. At progression disease (PD), all of them receveid re-irradiation at doses di 19.8 Gy in 11 fractions of 1.8 Gy with concomitant chemotherapy (nimotuzumab and vinorelbine). Interval between the initial radiation therapy and Re-RT was at 6 months in A , 11 months in B and 31 months in C. The PS was 0-1, age from 5 to 13 years old. The Re-RT was well tolerated, without toxicity reported; all three patients showed neurological improvement. The patient A died after 4 months the RE-RT, with an overall survival (OS) of 12 months, calculated from the initial radiation therapy. Two other patients are still alive with good performance status. The OS, from the initial radiotherapy, of 9 months and 45 months, respectively in B and C patient. The OS from the re-irradiation was 4 months in patient B and 14 months in patient C.

Conclusion: Based on our experience, the re-irradiation proved to be safe in the absence of acute and/or chronic toxicity and with improvement in symptoms, associated with a response rate, although partial, in two of three patients.

## DP11

### ABSTRACT WITHDRAWN

## DP12

### STEREOTACTIC RADIOTHERAPY FOR PROSTATE BED RECURRENCE AFTER PROSTATECTOMY, A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aims: This work reports the impact of Salvage Stereotactic Radiotherapy (SSRT) in naïve patients (pts) with Macroscopic Prostate Bed Recurrence (MPBR) and compares, in terms of outcome, two definitions of Biochemical Relapse Free Survival (BRFS).

Methods: We retrospectively reviewed the experience of AOU Careggi Radiation Oncology Unit– Florence between January 2014 and December 2018. In order to better express outcome and help clinicians to choose the correct timing of restaging after treatment, two BRFS were used: BRFS1 (PSA>10% respect to PSA pre-SRST) and BRFS2 (PSA increase>0.2ng/mL in pts with PSA nadir<0.2ng/mL or 2 consecutive PSA increases >25% if compared to nadir in pts with a PSA nadir>0.2ng/mL). Kaplan-Meier survival analysis cur-

ves (Figure 1) were performed to explore the association between BRFS and pre-defined prognostic factors.

Results: 46 cases were collected, pts were treated with SSRT for a total dose of 30-40Gy in 5 fractions. Median follow up was 21 months (IQR 9-39 months), pts had a mean age of 70.78 years (63.84-77.73). Gleason Score (GS) at diagnosis was >7 in 29 cases (63.04%). 54.35% (25pts) were pT3 and 95.65% (45pts) were N0/Nx. Risk group was high in 56.52% (26pts). Median pre-SSRT PSA was 9.09 ng/mL (IQR 7-13). Concomitant Androgen Deprivation Therapy (ADT) was prescribed in 18 pts (39.13%) with a median duration of 24 months (IQR 6-69.75). No acute or late toxicity ≥ G2 related to SRST was observed. ADT free survival rate at 1 year was 65.22% (30pts). Considering BRFS1 definition, 15 pts (32.61%) had biochemical recurrence, with a median BRFS1 time of 17 months (IQR 5-25). BRFS2 definition was applicable in 20 pts (43,48%) with a median BRFS2 time of 16 months (IQR 5-23). There were any local recurrences and 10 sites of distant/pelvic recurrence. Complete biochemical response, defined as PSA nadir<0.2ng/mL, was obtained in 23 (50%) pts. BRFS1 and BFRS2 were statistically related to GS≤7 and PSA nadir<0.2ng/mL. Furthermore, BRFS2 were also statistically related to pre-SRST PSA<1ng/mL and time to MPBR>36 months.

Conclusions: SSRT significantly improved biochemical control of disease and allowed ADT delay despite adverse features. Ablative SSRT of small recurrence might increase the efficacy of salvage therapy and reduce toxicity when compared to conventionally fractionated salvage irradiation to the entire prostate bed. BFRS2 it proved to be a reliable tool to improve outcome and further diagnostic-therapeutic procedures.

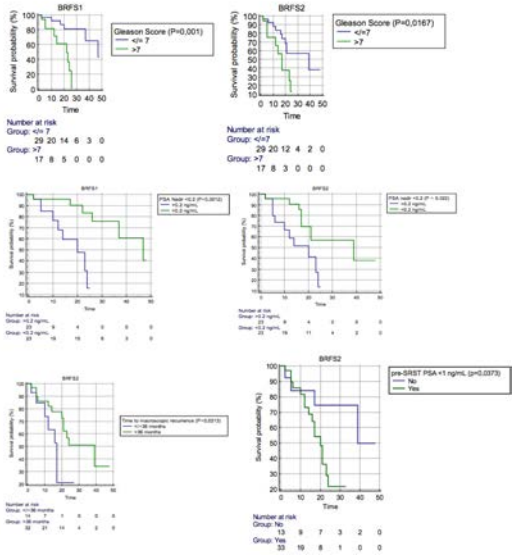


**Figure 1.**

**DP13**

## DOSIMETRIC INFLUENCE OF ROTATIONAL SETUP ERRORS IN VMAT RADIATION THERAPY OF PROSTATE CANCER

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Aims: To evaluate the setup errors and the dosimetric impact of rotations in prostate cancer radiotherapy treatment with VMAT-SIB technique.

Methods: A total of 26 patients with prostate cancer (5 low, 8 intermediate and 13 high risk) were included in this study. For high risk patients CTVs included the pelvic lymph nodes. The patients underwent a moderate hypofractionated radiotherapy (70,2 Gy/27 fr.) with daily Image Guidance. The treatments were planned with VMAT technique and performed with an Elekta Synergy® accelerator equipped with HexaPOD™ a robotic couch with six degree of freedom. The patient positioning was assessed before each fraction, through the matching between the reference CT and the daily online acquired CBCT. The rototranslational correction were applied through the robotic couch and positional errors were recorded for the principal axes, left-right, supero-inferior, antero-posterior, and for the rotational angles pitch, roll and yaw. The dosimetric analysis of the consequences of rotations was performed on a subgroup of 11 patients by manually rotating the simulation CT and the contoured structures. Using MIM Maestro®, the simulation CT was rotated around the isocenter by ±3° for each axis, obtaining six rotated CT for each patient. The reference treatment plan was recalculated on the new CTs and the DVHs statistics were compared.

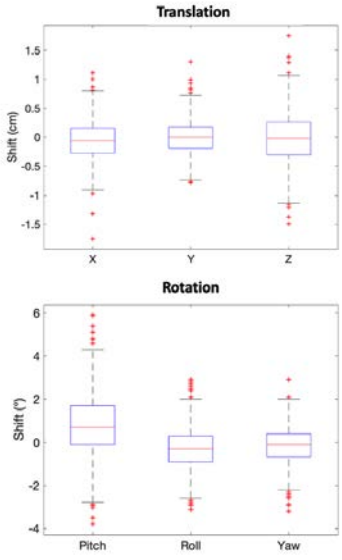


**Figure 1.**

Results: A total of 675 CBCT were retrospectively evaluated for this analysis. The largest magnitude for systematic and random error was for the translation in the antero-posterior direction and for the pitch rotation (Figure 1). The major dosimetric changes for organs at risk, compared to the planned doses, were observed for pitch rotation and especially for structures distant from the isocenter. In high risk patients the average differences for V40 and V65 of rectum were ±5% and ±4% with a maximum variation of +10%. For the bladder the maximum difference was +4%. Femurs were more sensitive to yaw rotation with a maximum variation of the D2%=4 Gy. With the currently used PTV margins (1 cm isotropic margin, 6 mm to the rectum) the CTV coverage was not affected by rotations.

Conclusions: In prostate cancer treatment the rotational errors could cause dosimetric changes in organs at risk especially when the pelvic lymph nodes are treated, due to the major distance of the structures from the isocenter. Robotic couch corrections become more important in SBRT with high dose gradients and when reduced margins are used.

## DP14

### UTILITY OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING (MPMRI) IN SALVAGE RADIOTHERAPY PLANNING IN PATIENTS WITH BIOCHEMICAL RELAPSE AFTER RADICAL PROSTATECTOMY

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Introduction: Patients (pts) with biochemical relapse (BR) after radical prostatectomy may still be cured with salvage radiotherapy (SRT). To maximize chance for cure, irradiated volumes should completely encompass the extent of disease. Current imaging technique has limited sensitivity for detection of macroscopic disease in prostate bed at BR. Recently, MPMRI has become more widely used and integration into routine evaluation of prostate bed in pts with BR may improve accuracy of SRT planning.

Methods: Between 2017 and 2018, 35 men with BR after radical prostatectomy underwent MRI with T2-weighted imaging, diffusion weighted imaging and dynamic contrast-enhanced imaging, before SRT at Papa Giovanni XXIII Hospital, Bergamo. We performed dose escalation to the T2/DCE-MRI defined as high risk region by dose painting at 2.25 Gy/frx to 72 Gy, while the rest of CTV received 2 Gy/frx to 64 Gy. In pts with negative MPMRI dose prescription was 70 Gy/35 frx and CTV include prostatic bed. We used Chi-Square test to identify possible relationship between clinical, pathological and MPMRI results.

Results: Local recurrence was identified in 31% of pts. The median interval between radical prostatectomy and MPMRI was 31 mo (range, 8.3-143.7 mo). Median PSA value at time of BR was 0.25 ng/mL (range 0.15-3.04 ng/mL in pts with positive MPMRI and range 0.10-0.54 ng/mL in pts with negative MPMRI). Median PSA doubling time was 7.8 mo (1.8-20.7 mo) and 7.5 mo (1.5-31.1 mo) in pts with and without macroscopic recurrence at MPMRI, respectively. The perianastomotic site was the most common location of local recurrence. The median follow-up was 13 mo (0-32.3 mo); 12.5% of pts with negative MPMRI had BR, none of pts with positive MPMRI had BR after SRT. We didn't find statistically significant differences in clinical and pathological variables between two groups of pts.

Conclusions: Our findings suggest that MPMRI can identify a significant minority of patients with macroscopic local recurrence. Macroscopic recurrence in prostate bed was identified even at low PSA levels with 33% incidence in pts with PSA <0.2 ng/mL, although numbers were limited in this subgroup. It is possible that pts with low PSA levels and macroscopic recurrence could have a better prognosis after SRT given that a source of PSA production is identified locally. However, longer follow-up is necessary to better understand how macroscopic recurrence in prostate bed might affect biochemical control after SRT.

## DP15

### SALVAGE RADIOTHERAPY GUIDED BY 68GA PSMA 11 PET/CT IN PATIENTS WITH BIOCHEMICAL PERSISTENCE (BCP) AFTER RADICAL PROSTATECTOMY FOR PROSTATE CANCER

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Aims: Prostate cancer (PCa) patients with persistent high PSA levels (BCP) after radical prostatectomy (RP) showed less favourable survival rates. Thus, localizing residual disease after surgery is crucial to define the planned target volume (PTV) of salvage radiotherapy (SRT). We evaluated the impact of 68Ga PSMA 11 PET/CT on SRT planning in BCP patients.

Methods: 68Ga PSMA 11 PET/CT is performed in our institution through a prospective, single center, open label study in hormone naïve PCa. We performed a retrospective analysis in BCP patients matching these inclusion criteria: 1) RP as primary therapy; 2) PSA nadir >0.1 ng/mL at 8 weeks after RP; 3) No adjuvant/salvage therapy or hormonal therapy performed after RP; 4) all patients eligible for SRT in prostate bed; 5) PET scan performed within 12 months from RP.

Changes in clinical management and SRT planning were defined by a multidisciplinary tumour board.

Results: Twentyeight (n=28) patients matched all inclusion criteria and were analysed. ISUP grade <=3 (n=11/28), >=4 (n=17/28); stage >=pT3a (n=17/28); pN1 (n=7/28); R1 (n=16/28). Median/mean PSA-nadir=0.34/0.48 ng/mL (0.1 3.3); median/mean PSAdt=2.8/7.1 months (0.6 44.6); median/mean PSAvel=0.8/3.1 ng/mL/year (range 0.1 24.7). 68Ga PSMA 11 PET/CT detection rate was 57.1% (CI95% 37.4% 75.0%). Median/mean PSA at time of imaging=0.53/1.06 ng/mL (range 0.22 8.9). Prostate bed relapse was detected in 3.6% of cases, intra pelvic relapse (pelvic lymph nodes with/without prostate bed) in 21.4% and extra pelvic relapse (extra pelvic nodes and/or bone) in 32.1%. Oligometastatic disease was detected in 53.6% of cases, in this patients SRT planning was changed: 7/28 patients performed SRT in prostate bed and additional stereotactic radiotherapy (SBRT) on PET positive findings. In 2/28 cases PTV was modified including only PET positive pelvic nodes without standard radiotherapy in prostate bed. SRT was aborted in 5/28 patients and ADT was administrated instead. In 1/28 case SRT was aborted and pelvic lymph node dissection was performed. In 46.4% of patients (13/28), SRT was confirmed as intended before PET scan.

Conclusions: 68Ga PSMA 11 PET/CT proved its role in BCP setting detecting disease outside prostate bed in 53.5% of cases and SRT planning was modified due to the integration of 68Ga PSMA 11 PET/CT results. These data highlight the importance of PET imaging in BCP setting being able to detect the presence of disease not identified by conventional imaging.

## DP16

### THE ROLE OF MORPHOLOGIC AND FUNCTIONAL 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 180 PATIENTS

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Aims: From 15 to 40% of patients undergoing radical prostatectomy have a biochemical relapse at five years. Salvage radiotherapy (SRT) is the standard treatment for biochemical relapse with at least 66 Gy delivered to prostatic fossa. Dynamic 18F-Choline PET/CT and mpMRI could identify site of recurrence, allowing dose escalation to a biological target volume (BTV).

Methods: From January 2009 to December 2017 were reviewed data of over 200 patients with biochemical progression after radical prostatectomy. One-hundred eighty patients at time of diagnosis of biochemical recurrence underwent to dynamic 18F-Choline PET/CT and mpMRI, which revealed in all cases a local recurrence without distant metastasis. Patients received a total dose of 80 Gy fractionated into 2Gy/die to the BTV. Acute and late toxicity were collected using the CTC scale (vers. 4.3).

Results: The treatment was mostly well tolerated: 168 patients (93%) completed treatment without any interruption. Acute toxicity was: Gastro-intestinal (GI) in 53 patients (29%); Genito-urinary (GU) in 35 patients (19%). No grade > 3 acute toxicity was recorded. Late toxicity was: 41 events (23%) of grade 1 GU toxicity and 24 patients (13%) with grade 1 GI. Nineteen patients (10%) experienced grade 2 toxicity (nine gastro-intestinal and ten genito-urinary toxicity) and only one patient experience a grade >3 late toxicity. With a median follow-up of 67 months 53/180 patients (29%) experienced a biochemical recurrence.

Conclusions: The new imaging techniques (dynamic 18F-Choline PET/CT and mpMRI) allow a better definition of disease recurrence in these patients. With a median follow-up greater than 5 years, high-dose SRT appears feasible and well tolerated, with low rate of late toxicity and promising activity.

## DP17

### MODERATE VERSUS EXTREME HYPOFRACTIONATED RADIOTHERAPY: A COMPARATIVE ANALYSIS IN LOW AND FAVORABLE INTERMEDIATE RISK PROSTATE CANCER PATIENTS

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Purpose: External beam radiotherapy (EBRT) is an effective treatment option for low and intermediate risk prostate cancer (PCa) and it is usually delivered in conventional fractionation or with moderate hypofrationation (hRT), with comparable results. In the last years, a new treatment approach with stereotactic body radiotherapy (SBRT) has shown promising results. The aim of the present study was to directly compare the outcome and toxicity between hRT and SBRT in low-to-intermediate PCa patients.

Material and Methods: The hRT schedules were: 71.4 Gy or 74.2 Gy in 28 fraction for low or intermediate risk PCa, respectively, while the SBRT schedules were: 35 Gy or 37.5 Gy in 5 fractions, for low or intermediate risk, respectively. Toxicity assessment was performed according to CTCAE v5.0 grading. The International Prostatic Symptoms Score (IPSS) was also recorded.

Results: One hundred-forty nine patients were

analyzed, overall 81 (54.36%) patients were low risk and 68 (45.64%) were intermediate risk. Sixty-nine (46.3%) patients were treated with hypo-RT and 80 (53.7%) with SBRT. Median follow-up was 33 months (range 11-58 months). The actuarial survival rate was 98.66%. The 3-years BFS rates were 95.5% and 100% for hRT and SBRT, respectively (p= 0.051). One case (0.6%) of acute grade 3 urinary toxicity occurred in a patient with intermediate risk treated with hRT. No differences in acute, late or severe toxicity were detected.

Conclusion: SBRT reported a good clinical outcome and safe toxicity profile. Results are comparable to hRT, but a longer follow-up is needed to assess the late effectiveness and toxicity.

**DP18**

## STEREOTACTIC BODY RADIOTHERAPY +/- CHEMOTHERAPY VS EXTERNAL BEAM RADIOTHERAPY +/- CHEMOTHERAPY: AN ITALIAN MULTICENTRIC CASE-CONTROL STUDY ABOUT LOCALLY ADVANCED PANCREATIC CANCER (PAULA-2)

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Aims: Chemoradiotherapy and chemotherapy (CT) are both well-established options for locally advanced pancreatic cancer (LAPC). Stereotactic body radiotherapy (SBRT) is an emerging option for LAPC. Aim of this multicentric case-control study is to compare two cohorts of LAPC patients treated with EBRT +/- CT or SBRT +/- CT in terms of overall survival (OS), local control (LC), distant metastases-free survival (DMFS), and toxicity.

Methods: Eighty patients were included. Patients in the two cohorts were matched according to: age </≥ 65years; tumor diameter < 3.0 cm, ≥ 3.0 cm and ≤ 3.9 cm, > 3.9 cm; cT; cN; neoadjuvant or adjuvant CT. Median prescribed total dose was 30.0 Gy (range: 18.0-37.5) and 54.0 Gy (18.0-63.0) for patients treated with SBRT +/- CT and EBRT +/- CT, respectively. Toxicity was evaluated by CTCAE v4.0 scale. Survival curves were assessed by Kaplan-Meier method. For hypothesis testing, an equivalence and a non-inferiority test was calculated.

Results: Descriptive analysis is reported in Table 1. At univariate analysis no statistically significant differences based on the matching criteria and acute and late toxicities, were recorded. Median, 1-, and 2-year OS were: 21.0 and 16 months, 73.8% and 79.8%, 40.1% and 14.7% (p= 0.470), for EBRT +/- CT and SBRT +/- CT, respectively. Median, 1-, and 2-year LC were: 16.0 and 22 months, 53.1% and 80.4%, 40.5% and 49.8% (p= 0.017), for EBRT +/- CT and SBRT +/- CT, respectively. Median, 1-, and 2-year DMFS were: 12.0 and 16.0 months, 49.3% and 64.5%, 41.7% and 20.3% (p= 0.610), for EBRT +/- CT and SBRT +/- CT, respectively. A statistically non inferiority significance in terms of OS between EBRT +/- CT and SBRT +/- CT was recorded (95% CI: 2.24, p= 0.031).

Conclusions: Our analysis demonstrated that SBRT is comparable to EBRT in terms of clinical outcomes and yet convenient for the patients due to its short duration. Therefore, our study seems to justify randomized studies to compare SBRT +/- CT and EBRT +/- CT.

**Table 1.**

| Variable | Value | SBRT | EBRT | p |
|---|---|---|---|---|
| Age (years) | Median (range) | 67 (36-89) | 67 (36-83) | |
| | ≤ 65 | 17 (42.5) | 17 (42.5) | 0.589 |
| | > 65 | 23 (57.5) | 23 (57.5) | |
| Gender | M | 24 (60.0) | 27 (67.5) | 0.321 |
| | F | 16 (40.0) | 13(32.5) | |
| ECOG | 0 | 22 (55.0) | 20 (50.0) | 0.493 |
| | 1 | 16 (40.0) | 15 (37.5) | |
| | 2 | 2 (5.0) | 5 (12.5) | |
| Tumor site | Head | 28 (70.0) | 24 (60.0) | 0.638 |
| | Body | 10 (25.0) | 13 (32.5) | |
| | Tail | 2 (5.0) | 3 (7.5) | |
| Tumor diameter (cm) | Median (range) | 4.0 (1.2-8.7) | 4.0 (2.0-7.0) | |
| | <3.0 | 5 (12.5) | 5 (12.5) | |
| | ≥ 3.0 and< 3.9 | 13 (32.5) | 18 (32.5) | 0.631 |
| | ≥ 3.9 | 22 (55.0) | 22 (55.0) | |
| cT | 3 | 11 (27.5) | 11 (27.5) | 0.599 |
| | 4 | 29 (72.5) | 29 (72.5) | |
| cN | 0 | 22 (55.0) | 22 (55.0) | 0.589 |
| | 1 | 18 (45.0) | 18 (45.0) | |
| Biliary stent | No | 15 (37.5) | 19 (47.5) | 0.078 |
| | Yes | 23 (57.5) | 13 (32.5) | |
| | Unknown | 2 (5.0) | 8 (20.0) | |
| Acute GI toxicity | 0 | 24 (60.0) | 31 (77.5) | 0.175 |
| | 1 | 12 (30.0) | 8 (20.0) | |
| | 2 | 4 (10.0) | 1 (2.5) | |
| Late GI toxicity | 0 | 35 (92.1) | 39 (97.5) | 0.244 |
| | 1 | 1 (2.6) | 0 (0.0) | |
| | 2 | 2 (5.3) | 0 (0.0) | |
| | 3 | 0 (0.0) | 1 (2.5) | |
| Neoadjuvant CT | No | 16 (40.0) | 16 (40.0) | 0.590 |
| | Yes | 24 (60.0) | 24 (60.0) | |
| Neoadjuvant CT drugs | Gemcitabine | 8(33.3) | 3 (12.5) | ***0.002*** |
| | Folfox | 1 (4.2) | 1 (4.2) | |
| | Folfirinox | 2 (8.3) | 6 (25.0) | |
| | Gemcitabine + Nab-placlitaxel | 0 (0.0) | 9 (37.5) | |
| | Gemcitabine + Oxaliplatinum | 13 (54.2) | 5 (20.8) | |
| Adjuvant CT | No | 31 (77.5) | 31 (77.5) | 0.605 |
| | Yes | 9 (22.5) | 9 (22.5) | |
| Adjuvant CT drugs | Gemcitabine | 7 (77.8) | 2 (22.2) | ***0.073*** |
| | 5-Fluorouracil | 0 (0.0) | 1 (11.1) | |
| | Folfirinox | 1 (11.1) | 4 (44.4) | |
| | Gemcitabine + Nab-placlitaxel | 0 (0.0) | 2 (22.2) | |
| | Gemcitabine + Oxaliplatinum | 1 (11.1) | 0 (0.0) | |

DP19

## POST-OPERATIVE INTENSITY MODULATED RADIOTHERAPY (IMRT) IN PROSTATE CANCER: A SINGLE INSTITUTE RETROSPECTIVE ANALYSIS

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Aims: The aim of this study was to retrospectively analyse genitourinary (GU) and gastrointestinal (GI) toxicities in a single institute cohort of patients (pts) treated with moderate hypofractionated or conventionally fractionated post-prostatectomy radiotherapy.

Methods: From September 2011 to May 2016, 63 post-operative pts with localized prostate cancer underwent adjuvant (n=49) and salvage (n=14) IMRT. Of the 63 pts, 16 pts (25,4%) received prophylactic lymph-nodal irradiation . IMRT was delivered at conventional (CF: 1,8-2 Gy/fr, n=27) or moderate hypofractionated (HYPO: 2,3 Gy/fr, n=36) fractionation scheme. The total dose ranges to the prostatic bed were 64-70 Gy and 59.8-68.2 Gy for CF and HYPO group of pts, respectively. Pelvic lymph-nodes were always treated with conventional fractionation (50.4 Gy, daily dose: 1.8 Gy/fr). A two-tailed t-test was performed to assess statistical difference between CF and HYPO groups. Toxicities was graded according to Common Terminology Criteria for Adverse Events (CTCAE), version 4.0.

Results: Median overall follow-up (FU) was 35 months (range 16-74). At the end of radiotherapy, 13/63 (20.6%) pts showed acute Grade ≥2 urinary toxicity, 5/27 (18.5%) and 8/36 (22.2%) in conventionally fractionated RT and hypofractionated RT, respectively. Eight pts (8/27; 29.6%) and 9 pts (9/36 ; 25%) reported acute Grade ≥2 GI for CF and HYPO cohort, respectively. Six pts (6/27; 22.2%) and three pts (3/36; 8.3%) showed late Grade ≥2 GU in the CF and HYPO group. Late Grade ≥2 GI were reported in 2/27 pts (7.4%) in the CF group and 2/36 (5,6%) in the hypofractionated group. Only 1 late Grade 4 urinary toxicity was reported in the CF group of pts. No Grade 4 acute or late GI/GU in the hypofractionated group was observed. No significant correlation between toxicity and fractionation scheme was found.

Conclusions: In the post- operative setting, a moderate hypofractionated radiotherapy resulted well tolerated in our cohort of patients. Rate of grade ≥2 late toxicity in the hypofractionated group was lower than in CF group, but this difference was not statistically significative.

DP20

## CLINICAL RESULTS AND TOXICITIES OBSERVED AFTER PROTON PENCIL-BEAM SCANNING OF PEDIATRIC CNS TUMORS

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Aims: we report the clinical results and toxicities in 16 children with various CNS tumors treated with proton pencil-beam scanning.

Methods: between 2015 and 2019, 16 patients (M/F: 10/6; median age 6 years [13 mo-17 yrs]) with CNS tumors received proton therapy (PT), 12 of whom with daily anesthesia: 8 medulloblastomas (MB; 3 standard, 5 high risk), 2 pilocytic astrocytomas, 3 Atypical Teratoid/Rhabdoid Tumors (AT/RTs), 1 pure germinoma, 1 choroid plexus carcinoma (CPC) and 1 invasive meningioma. All patients received surgery (3 total, 10 partial resections or near total resection, 3 biopsies) and 15/16 received chemotherapy: 9 before PT with 5 hematopoietic stem cell transplantations (HSCT), 2 both before and after PT and 4 after PT. Toxicity was graded using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Median total dose was 54 CGE (1.8 daily fractions).

Results: at a median follow-up of 20 months [5-43 mo] all patients are alive, 8 with a complete response (CR) and 6 with stable disease (SD). Two patients experienced progression (PD): one with a diencephalic AT/RT showed 10 months after a 1st PT to the primary site a distant relapse, that was treated with chemotherapy, HSCT and proton craniospinal irradiation (CSI) with CR; one with PA had an increase of both cystic and solid residual tumor 10 months after PT. Hematological toxicity was mild, no transfusions were necessary; only 4 cases of G3 neutropenia were seen in patients who received CSI at 36.0 CGE (3 of them received HSCT before PT). The other >G2 acute/subacute toxicities were: 1 G3 PRES, 1 G3 perilesional brain edema, 1 G3 fatigue and 1 G3 headache; 3/4 recovered completely, 1/4 partially. Late toxicities were as follows: 1 MB patient had a self-limiting intracranial bleeding (G2) 24 months after PT (on that site, the total dose was 54.0 CGE); the AT/RT patient who received PT twice developed 15 months after the 1st PT an asymptomatic Moya-Moya-like arteriopathy (G1; local dose of 54.0 CGE) and 2 patients (1 CPC, 1 MB) developed asymptomatic cavernomas (G1; both had received 36.0 CGE CSI) 21 and 9 months after PT, respectively.

Conclusions: our experience shows that PT can be a viable option for radiotherapy of pediatric CNS tumors, showing good disease control and only limited toxicity. However, longer follow-ups and higher patient numbers are needed to draw conclusions on long term results and toxicities.

**DP21**

## THE ROLE OF FDG PET/CT TO PREDICT RESPONSE TO INDUCTION CHEMOTHERAPY IN EWING SARCOMA

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Aims: Histological response to induction chemotherapy is an important prognostic factor in patients with Ewing sarcoma (EWS). The role of FDG PET/CT in predicting response remains unclear. The aim of our study was to assess the prognostic value of quantitative indices derived from FDG PET/TC performed at baseline and after induction chemotherapy.

Methods: We retrospectively collected data from EWS patients treated at our Institution between 2008 and 2017 who performed FDG PET/CT at diagnosis and after induction chemotherapy +/- neoadjuvant radiotherapy, before surgery. All patients underwent surgery of the primary tumor after induction chemotherapy. We evaluated the primary tumor SUVmax at baseline (SUV1), the SUVmax after induction chemotherapy (SUV2) and the metabolic response calculated as [(SUV1-SUV2)/SUV1]x100. The correlation of metabolic response with Histologic response according to Picci grading system was also assessed.

Results: Twenty-seven patients were included. Median age was 13 years (range: 4-67). Primary EWS was bone-located in 23 patients (85,2%) and derived from soft tissue in 4 patients (14,8%). Median SUV1 was 6.2 (range 2.1-13.5). In 21 (77,8%) patients SUV1≥4 and in 6 (22,2%) was <4. 14 (51,8%) patients received preoperative radiotherapy. After surgery a II/III Picci grade necrosis was achieved in 16 patients (59,3%). At univariate statistical analysis stage of disease correlated with progression free survival (PFS, p=0,025). In patients with SUV1≥4, SUV1 had a trend of correlation with Picci grade (p=0,072), even without statistical significance. 26 (96,3%) patients had FDG PET/CT after induction chemotherapy before surgery. Median SUV2 was 0 (range 0-7.1). Median metabolic response was 100% (range 31,11%-100%). At statistical analysis SUV2 is related with PFS (P<0,0001). Considering SUV distribution, at Wilcoxon test for paired samples all SUV values decrease with treatment. Only in one patient SUV2 was not inferior to SUV1; in this case SUV1 at diagnosis was low.

Conclusions: FDG PET/CT is an effective and noninvasive approach to assess response to induction chemotherapy in EWS patients. SUV1, SUV2 and metabolic response values could be useful in predicting chemotherapy resistance and in selecting patients with a more aggressive disease to risk adapted treatments before surgery but the role of FDG PET/CT needs to be further investigated in future trials.

**DP22**

## ANALYSIS OF 6D COUCH COMPENSATIONS IN VOLUMETRIC MODULATED ARC THERAPY (VMAT): OUR EXPERIENCE IN 248 PATIENTS

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Aim: To evaluate the compensations of a positioning system with six degrees of freedom (lateral, longitudinal, vertical, pitch, roll and yaw) in the radiation treatment of various diseases.

Methods: We progressively analyzed 248 patients treated with Volumetric Modulated Arc Therapy (VMAT) at our Radiation Therapy Unit from September 2018 till April 2019, for a total of 2810 fractions. During the set-up of each fraction, patient anatomy from planning CT was aligned through cone beam CT (CBCT) by a Clinician and 6D movements were executed, so that we collected the couch compensations. Among these patients 68 were treated for prostate, 58 for head and neck, 48 for brain, 28 for lung, 20 for gynecological district, 18 for rectum, 8 for breast tumours. Mean values and standard deviations were calculated for all sites. We considered as statistically significant a couch compensation >0.5 cm (lateral, longitudinal and vertical) and >1° (pitch, roll and yaw).

Results: Considering all the patients, mean absolute values are as follows: 0.253 cm lateral, 0.231 cm longitudinal, 0.31 cm vertical, 0.76° pitch, 1.072° roll, 0.924° yaw. According to the different disease, the mean values differ significantly, with the head and neck tumor showing the lower compensations (respectively <2% and <28% showing compensations >0.5 cm and >1°) and the lung cancer showing the higher compensations (respectively <37% and <60% showing compensations >0.5 cm and >1°).

Conclusion: Adjustments in six dimensions, inclu-

ding unconventional pitch, roll and yaw rotations, improve the patient set-up in all treatment sites, but seems to be especially important in the treatment of lung cancer patients.

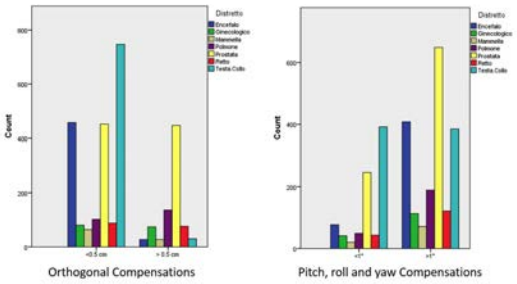


**Figure 1.**

## DP23

### SEMI-QUANTITATIVE METABOLIC PARAMETERS IN OROPHARYNGEAL CANCER UNDERWENT RADICAL TREATMENT: PREDICTIVE ROLE FACTORS OF RESPONSE? A MONO-INSTITUTIONAL RETROSPECTIVE STUDY

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Aim. The role of pre-treatment semi-quantitative metabolic parameters was herein analyzed, as potential predictors of Local Control (LC) and distant progression free-survival (DPFS) in Oropharyngeal cancers (OPC).

Methods. Inclusion criteria of the present retrospective study were: 1) age >18 years old; 2) histologically proven HPV positive or negative OPC; 3) patients underwent definitive Intensity Modulated RT+/- Chemotherapy; 4) pre-treatment FDG PET/TC performed in the Medicine Nuclear Medicine of our Institution; 5) patients affected by early or locally advanced disease by means of FDG PET/TC. The following semi-quantitative metabolic parameters on primary tumor and nodal disease were retrospectively analyzed: (1) standardized uptake value or SUV-max; (2) SUV-mean; (3) metabolic tumor volume (MTV), tumor volume with a SUV ≥3, threshold 40%; (4) total lesion glycolysis (TLG), i.e. the product of SUV-mean and MTV. LC was defined as absence of local failure (primary tumor and nodal disease). DPFS was defined as the interval between the end of RT and the diagnosis of distant metastases.

Results. According to the inclusion criteria, thirty-one OPC patients were included for the analysis. The median follow up was 16 months (range, 6-90 months). Patients median age was 65 years old (range, 39-80). Regarding the HPV status, 16/31 (51%) were HPV/p16 positive. Globally, 8/31 (26%) patients had smoked for more than ten pack-years. All patients were treated with RT +/- Cht according to guidelines. At the univariate analysis the median local progression-free survival (LPFS) was 75 months (range 22-85 months). The median LPFS according to HPV-status was 22 and 75 months for HPV- and HPV+ patients, and the 2-year LPFS was 42.8% and 83.9% for HPV- and HPV+ patients, respectively (p=0.01; HR 3,5725, i.c. 0,91-13,94). The median distant progression-free survival (DPFS) was 75 months (range 27-85 months). The median DPFS stratified for HPV-status was 22 and 85 months, and the 2-year DPFS was 48.5% and 92.3% for HPV- and HPV+ patients, respectively (p=0.01; HR 4.0028, i.c. 0.86-18.56). The ROC analysis showed that no semi-quantitative tumor and nodal metabolic parameters before irradiation was correlated to LPFS and DPFS.

Conclusion. In our experience HPV status remains the only predictive factor of local response and distant progression in OPC.

## DP24

### THE PREDICTIVE POWER OF MAGNETIC RESONANCE IMAGING IN IDENTIFYING THE PATHOLOGICAL GRADING OF MENINGIOMAS

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Aims: To assess whether Magnetic Resonance Imaging (MRI) is able to predict the histological WHO grading of meningiomas and in particular if it is able to differentiate WHO I from WHO II and WHO III

Methods: 76 histologically proven meningioma patients with 77 lesions undergoing particle-therapy were enrolled in the study (43 WHO I, 27 WHO II, 7 WHO III). MRI data were acquired before treatment (Siemens Verio 3T) based on T1 and T2- weighted MRI and diffusion (DWI) MRI. T1 were used to delineate tumor, whereas DWI to derive multi-parametric imaging features based on conventional ADC and Intra-Voxel-Incoherent-Motion (IVIM) model (i.e. ADC, D, D*, f). Median ADC, D, D* and f values were compu-

ted within tumor volume. Morphological variables of the meningiomas were also considered: tumor localization, T1- and T2- signal intensity relative to grey matter, shape, tumor-brain interface, peritumoral edema, capsular enhancement and tumor enhancement after intravenous injection of gadolinium.

Results: Regarding the DWI parameters, median values of ADC, D, D* resulted higher for WHO I than WHO II and WHO III and, by grouping together WHO II and WHO III, statistically significant differences were observed with respect to WHO I in D and D* ($p<0.05$). Also, statistically significant differences ($p<0.05$) were found between WHO I and WHO II/III in terms of morphological features such as tumor localization, T1- and T2- signal intensity relative to grey matter, tumor shape, peritumoral edema, capsular enhancement, tumor enhancement, while the presence of tumor-brain interface did not demonstrate a statistically significant difference between the two groups.

Conclusion: Preliminary results show that both image-derived and morphological features could be potential predictors of meningioma histological grade. In future these features may be useful to characterize lesions with no histological diagnosis and for application in tailored particle therapy treatments.

## DP25

**ABSTRACT WITHDRAWN**

## DP26

### MR-BASED RADIOMICS MODEL FOR TREATMENT RESPONSE PREDICTION AFTER NEOADJUVANT CHEMORADIOTHERAPY IN PATIENTS AFFECTED BY LOCALLY ADVANCED CERVICAL CANCER

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Aim: To investigate the potential role of MRI radiomics to predict pCR following neoadjuvant chemoradiotherapy (NACRT) in patients (pts) with locally advanced cervical cancer (LACC) before therapy starts.

Methods: Patients with LACC (FIGO IB2-IVA) with a 1.5 T staging MRI were considered for this multicentric analysis. All patients underwent NACRT with concomitant weekly cisplatin, followed by radical surgery. Pathological response to treatment was assessed on surgical specimen and defined as absence of any residual tumour after treatment in any site. Patients' images were divided into a training (site A) and an independent external validation set (site B) and underwent radiomics analysis. A total of 1889 features were extracted and selected for the predictive model definition following an iterative method ad-hoc developed for this study. Fifteen different classifiers were trained on this dataset: the training set was then partitioned in five folds and the training process was repeated in cross-validation for three times. Model selection was carried out using the Area Under the Curve (AUC) of the Receiving Operator Characteristic (ROC) curve as target metric.

Results: A total of 183 pts were analysed and divided in a 156 pts training set from site A and a 27 pts external validation set from site B. The model showing the highest performance was the random forest (RF_DEF) initialized with the default parameters, with an AUC of 0.76 on the training set and 0.82 on the external validation set, as reported in Figure 1.

Conclusions: Radiomics appeared to be a reliable tool in the prediction of pCR for LACC pts undergoing NACRT, supporting the identification of patient's risk group and allowing to tailor treatments according to the predicted outcome. The technical robustness of the model and its encouraging AUC values offer clinicians an innovative tool of clinical decision support, omics based treatment guidance and personalization.

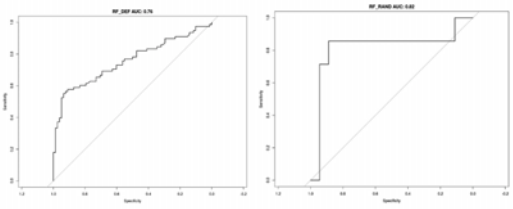

**Figure 1. ROC curve for internal and external validation.**

## DP27

### VULCAN STUDY 1.0 - THE ROLE OF ADJUVANT RADIATION THERAPY IN THE MANAGEMENT OF VULVAR CANCER

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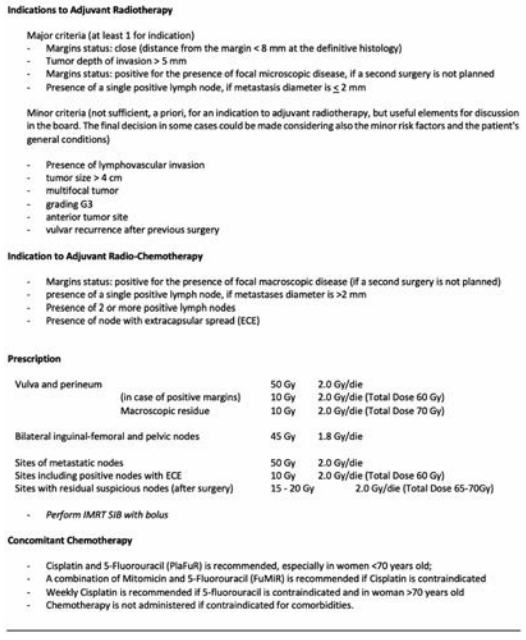
Aims: Multidisciplinary clinical approach should be evaluated to offer personalized treatment strategy in patients with vulvar cancer, a rare disease accounting 0.6% of women malignancies. Adjuvant External Beam Radiotherapy (EBRT) +/- Chemotherapy (CT) can be

administered in presence of high-risk factors. VULvar CANcer Multi-Disciplinary Team (Vul.Can MDT) was settled in 2013 in Policlinico Universitario A.Gemelli IRCCS, in order to propose tailored treatment strategies for vulvar cancer patients. The aim of this work is to update the Vul.Can MDT experience in the management of adjuvant EBRT.

**Table 1. Vul.Can MDT internal recommendation for adjuvant radiotherapy in Vulvar Cancer and schedules for dose delivery.**



**Indications to Adjuvant Radiotherapy**

Major criteria (at least 1 for indication)
- Margins status: close (distance from the margin < 8 mm at the definitive histology)
- Tumor depth of invasion > 5 mm
- Margins status: positive for the presence of focal microscopic disease, if a second surgery is not planned
- Presence of a single positive lymph node, if metastasis diameter is ≤ 2 mm

Minor criteria (not sufficient, a priori, for an indication to adjuvant radiotherapy, but useful elements for discussion in the board. The final decision in some cases could be made considering also the minor risk factors and the patient's general conditions)

- Presence of lymphovascular invasion
- tumor size > 4 cm
- multifocal tumor
- grading G3
- anterior tumor site
- vulvar recurrence after previous surgery

**Indication to Adjuvant Radio-Chemotherapy**

- Margins status: positive for the presence of focal macroscopic disease (if a second surgery is not planned)
- presence of a single positive lymph node, if metastases diameter is >2 mm
- Presence of 2 or more positive lymph nodes
- Presence of node with extracapsular spread (ECE)

**Prescription**

| | | |
|---|---|---|
| Vulva and perineum | 50 Gy | 2.0 Gy/die |
| (in case of positive margins) | 10 Gy | 2.0 Gy/die (Total Dose 60 Gy) |
| Macroscopic residue | 10 Gy | 2.0 Gy/die (Total Dose 70 Gy) |
| Bilateral inguinal-femoral and pelvic nodes | 45 Gy | 1.8 Gy/die |
| Sites of metastatic nodes | 50 Gy | 2.0 Gy/die |
| Sites including positive nodes with ECE | 10 Gy | 2.0 Gy/die (Total Dose 60 Gy) |
| Sites with residual suspicious nodes (after surgery) | 15 - 20 Gy | 2.0 Gy/die (Total Dose 65-70Gy) |

- *Perform IMRT SIB with bolus*

**Concomitant Chemotherapy**

- Cisplatin and 5-Fluorouracil (PlaFuR) is recommended, especially in women <70 years old;
- A combination of Mitomicin and 5-Fluorouracil (FuMiR) is recommended if Cisplatin is contraindicated
- Weekly Cisplatin is recommended if 5-fluorouracil is contraindicated and in woman >70 years old
- Chemotherapy is not administered if contraindicated for comorbidities.

Methods: Retrospective analysis of data vulva cancer patients treated in adjuvant setting from April 2013 to September 2017 was conducted. Adjuvant EBRT+/-CT was performed according to the internal protocol and recommendations proposed by Vul.Can MDT in high risk patients defined by margin status, tumor invasion and nodal involvement. EBRT was administered with doses between 50 Gy-60 Gy to perineum and 45 Gy to negative nodal regions; patients with pathological positive nodes received EBRT doses between 45 Gy-60 Gy. Patients after 2015 were treated using IMRT (Simultaneous Integrated Boost) and EBRT was performed with bolus. Concomitant CT schemes were Cisplatin and 5-Fluorouracil (PlaFuR) or weekly Cisplatin. Toxicity was revealed in regular follow-up using CTCAEv4.

Results: Data of 35 patients were analyzed, with a median FUP time of 32 months (6-72 months). Concomitant CT was performed in 15 patients, 20 patients underwent exclusive EBRT. At 12- and 24 months overall survival (OS) was respectively 96.9%, and 94%, while the Disease-Free Survival (DFS) was 90% and 77%. In patients with positive nodes at 12- and 24 months the OS was respectively 100% and 95.8% while DFS was respectively 87.5%, 83.3%. For patients without positive nodes at 12- and 24 months OS was 100% and 90.9%. No grade 4 toxicity was reported, 4 patients (13%) experienced G3 acute cutaneous toxicity while 1 patient (3%) showed G3 late cutaneous toxicity; no other G3 toxicity occurred.

Conclusions: Our experience show as multidisciplinary approach can help in personalizing the management of adjuvant treatment of vulvar cancer. Data of our experience confirms that in patients with high-risk Vulvar Cancer adjuvant EBRT+/-CT is safe and has an effective impact in preventing local relapse and improving OS.

## DP28

## ANALYSIS OF ACUTE AND LATE TOXICITY IN LOCALLY ADVANCED HEAD AND NECK CANCER PATIENTS TREATED WITH HYPOFRACTIONATED SIB-IMRT

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*Radioterapia Oncologica Ospedale San Francesco, Nuoro, Italy*

Aims: To report the acute and late toxicity in a cohort of patients (pts) treated with a moderate hypofractionated Simultaneous Integrated Boost Intensity Modulated Radiation Therapy (SIB-IMRT) for locally advanced Head and neck squamous cell carcinoma (HNSCC).

**Table 1.**

| Incidence of G3-G4 toxicity (CTCAE V 4.0) expressed in percentage values (cases with toxicity/cases evaluable) | | | |
|---|---|---|---|
| | G3 | G4 | G5 |
| Acute toxicity | | | |
| - Skin | 17% | | |
| - Mucositis | 17% | | |
| - Dysphagia | 3% | 6% | |
| - Hematological | 16% | | |
| - Bleeding | | | 1% |
| Late toxicity | | | |
| - Xerostomia | 3% | | |
| - Dysphagia | 3% | 7% | |

Methods: From 2011 to 2017 at Radiation Oncology of San Francesco Hospital, 70 pts affected by locally advanced HNSCC were treated with SIB-IMRT with or without concomitant chemotherapy. Median age

was 60 years (range 43-86), 83% males, 17% female and 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; 98% (69 pts) squamous cells cancer; PET-staged 67% IV a-b, 19% III, 10% II, 4% I (AJCC-7 th edition). 52 pts received SIB-IMRT with concurrent CDDP-based chemotherapy or cetuximab (51 and 1 respectively) and the remaining pts underwent SIB-IMRT alone. The prescribed 3 level of doses were 67.5Gy (2.25Gy/fr), 60 Gy (2Gy/fr), 54 Gy (1.8Gy/fr) for the high risk PTV, intermediate risk PTV and low risk PTV respectively in 30 fractions (one fraction daily) in 40 days. Pts were examined once a week during radiation treatment, after 1, 3, 6 and 9 months, then every 6 months up to 5 years. Toxicity was graded using Common Terminology for Adverse Events (CTCAE) Version 4.0. The median follow-up of patients still alive was 21 months (range 4-96).

Results: 96% of patients completed the treatment. The following severe acute toxicities were observed: 17% G3 skin reactions, 17% G3 mucositis, 9% G3 and 6% G4 dysphagia, 16% G3 hematological toxicity (all with concurrent chemotherapy). One patient died because of fatal bleeding during radiotherapy. The following late severe toxicities were observed: 1% G3 xerostomia, 3% G3 and 7% G4 dysphagia. No chondronecrosis of the larynx was observed (Table 1). Patients who experienced any severe acute toxicity were 3 G3 and 1 G4 in RT alone and 22 G3 and 4 G4 in CRT group respectively. Patients who experienced any severe late toxicity were 1 G3 and 2 G4 in RT alone and 7 G3 and 3 G4 in CRT group respectively.

Conclusions: Moderate hypofractionation for locally advanced HNCC has substantial benefits for patient-centric care, including shorter treatment duration, and reduced travel time. Moderately accelerated chemo-IMRT is safe and feasible with good compliance and acceptable acute and late reactions.

## DP29

### LATE TOXICITY IN IMRT-IGRT TREATMENT OF NASOPHARYNX IN THE PEDIATRIC AGE: EXPERIENCE OF A SINGLE CENTER

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*Università degli studi di Palermo, Italy*

Aims: Nasopharyngeal carcinoma is a rare tumor in children with an incidence of 1/100000. It originates from epithelial cells of the nasopharynx. Risk factors include: EBV infection, environmental factors such as nitrosamines and genetic factors. Diagnosis occurs in 10% of cases when the disease is locally advanced and metastases are present. Current care protocols manage excellent prognosis with overall survival above 85%.

Methods: Form 2015 to 2017, three children aged 11-15 years with locally advanced (stage III) nasopharyngeal disease were treated in our institution and received three cycles of induction chemotherapy with cisplatin-5Fluorouracil followed by concomitant radiochemotherapy treatment like TREP protocol. Treatments were performed with Tomotherapy on the primary tumor and bilateral laterocervical lymphonodes with a total dose of 63 Gy in 35 fractions.

Results: Late toxicity was assessed according to CTCAE 5.0 scale. Reported late effects were: G1 photosensitivity skin, G1 xerostomia, G1 hearing impaired, G1 skin fibrosis and periodontitis with loss of dental elements despite recommendations for oral hygiene and supportive therapy with fluoride. At 19 months follow-up, 35 months and 37 months respectively all patients are alve with complete response.

Conclusions: Multimodal therapy of children with nasopharyngeal carcinoma is associated with long-term survival. It is expected that further advances in the management of these patients, with improved radiotherapy and chemotherapy, will achieve better quality of life for treated children. IMRT-IGRT treatments in tumors have allowed a dose saving in organs at risk and a consequent reduction in late toxicity.

## DP30

### REPEATED COURSES OF STEREOTACTIC RADIOSURGERY (SRS) FOR INTRACRANIAL OLIGO-PROGRESSIVE METASTASES USING A NON-COPLANAR MONO-ISOCENTER LINAC-BASED DELIVERY TECHNIQUE (HYPERARC™) VERSUS UPFRONT WHOLE-BRAIN RADIOTHERAPY (WBRT): A MATCHED-PAIR ANALYSIS

L. Nicosia[1], V. Figlia[1], G. Napoli[1], M. Rigo[1], R. Mazzola[1], F. Ricchetti[1], N. Giaj-Levra[1], R. Ruggieri[1], F. Alongi[1,2]

*[1]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center; [2]Radiation Oncology Department, University of Brescia, Brescia, Italy*

Introduction: Brain metastases (BMs) are a major cause of cancer death from many solid tumor and are associated to a poor survival. SRS or stereotactic fractionated radiotherapy (SFRT) is an effective treatment option in multiple BMs management. Modern techniques allow the delivery of multiple SRS courses in case of subsequent intracranial progression, nevertheless little is known regarding the effectiveness and the toxicity when compared to WBRT. Through a retrospective matched-pair analysis, we compared a series of patients affected by limited BMs (≤10) from solid tumors treated with multiple SRS/SFRT courses using a mono-isocenter non-coplanar technique (HyperArc™ Varian Medical System) or WBRT.

Material and Methods: Between July 2017 and January 2019, 44 total multiple treatment courses accounting for 201 metastases treated with HyperArc™, were evaluated in 19 patients and matched with 38 patients treated with WBRT. This latter technique was the standard of choice before the implementa-

tion of HyperArc™ at our Institution in July 2017. Matching criteria were life expectancy >3 months, performance status, primary tumor histology and BMs number. Median BMs number was 4 (range 2-10) for HyperArc™ and 5 (range 2-10) for WBRT. The Median RT dose in the Hyperarc™ population was 25 Gy (range 20-25 Gy) for SRS and 25 Gy in 3-6 fractions (range 18-30 Gy) for SFRT. RT dose in the WBRT population was 30 Gy in 10 fractions. Overall survival (OS) and toxicity were evaluated.

Results: Median follow-up was 9 months (range 1-18 months). Median OS was 10 months for HyperArc™ patients and 7 months for WBRT patients, the 12 month OS was 77% and 34.6% for HyperArc™ and WBRT, respectively (p=0.001; HR4.77, I.C.: 1.62-14). One case of radionecrosis occurred in a patient 12 months after the first SRS course.

Conclusion: HyperArc™ is an effective and safe technique for the treatment of multiple BMs. Further subsequent courses can be safely delivered in selected cases of intracranial oligoprogression. SRS showed improved survival when compared to WBRT, in patients with a limited number of BMs.

## DP31

## THE ASSISI THINK TANK MEETING BREAST LARGE DATABASE FOR STANDARDIZED DATA COLLECTION IN BREAST CANCER TUMOR – ATTM.BLADE

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Background: In clinical practice and multicentre research purposes, a shared large database and data privacy control are mandatory. In Assisi Think Tank Meeting (ATTM) 2016 a team of radiation oncologists, expert in breast cancer care, elaborates a statement in which necessity of a Standardized Data Collection (SDC) for generating evidences was highlighted. For this reason, a project focusing on breast cancer was developed.

**Table 1. Timeline framework for ATTM.BLADE project.**

| Number of Phase | Description of Phase |
|---|---|
| 1 | Multidisciplinary Team Creation |
| 2 | Literature and Guidelines review |
| 3 | Ontology development |
| 4 | Ontology validation |
| 5 | Organization of Ontology according to Open Clinica's Criteria |
| 6 | Ontology uploading into BOA system |
| 7 | Interface validation |

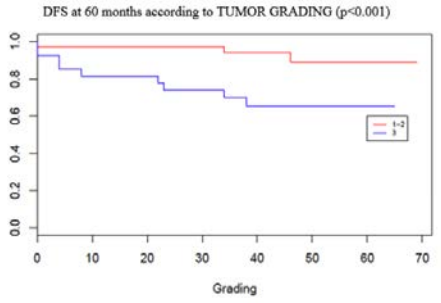


**Figure 1. Extract of sample analysis after uploading of BC post-mastectomy radiotherapy patients uploading for usage test.**

Material and Methods: The BLADE project consisted in a multiphase workflow for development of SDC system for breast cancer research. Standardized language ontology, platform for sharing data, inferential and machine learning statistic were elaborated for supporting creation of Decision Supporting Systems (DSSs) in breast cancer treatment (Table 1). The study methodology protocol was approved by Ethical Committee of Fondazione Policlinico Gemelli IRCCS with Prot N. 0043996/18 on October 2018. A data entry and an engeneer performed a usage test with a database of patients treated with post-mastectomy radiotherapy.

Results: BLADE project developed a system in which a validated semi-formal ontology with 630 relevant variables was defined from a consensus between a panel of experts. Variables were organized in 6 Case Report Forms (CRFs) according to OpenClinica's Criteria. Privacy protection was guaranteed thanks to distributed learning technology. The usage test on 72 pts confirmed the potentials of the system in terms of privacy protection, coherence of data collection and possibility to analyzed them. In Figure 1 is reported a frame of statistical analysis on these database test. The system allow inferential statistics for testing large number of variables (even from PACS or treatment plan DVHs).

Conclusion: A validated SDC system, promoted by

ATTM, has been created for supporting breast cancer care. Further multicentre use can implement the system itself and promote creation of DSSs from big data with the aim of personalizing treatments.

## DP32

### VOLUMETRIC MODULATED ARC THERAPY (VMAT) WITH FLATTENING FILTER FREE (FFF) IN DEEP INSPIRATION BREATH-HOLD (DIBH) VERSUS FREE BREATH (FB) FOR ADJUVANT LEFT-SIDED WHOLE BREAST RADIOTHERAPY (RT): A PLAN COMPARISON STUDY

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Aims: To evaluate the potential dosimetric benefits of DIBH in terms heart sparing and to compare the performances of different techniques for left-sided whole breast RT.

Methods: Ten patients (pts) planned for post-operative RT (50Gy/25fractions) were included. Two CT-scans were acquired for each pt, one in FB and one in voluntary DIBH. All pts were instructed to deeply inspire and hold the breath for 15 seconds with audio coaching, tracking the breathing signal with the Varian RPM (real-time position management) system to assess the reproducibility. The clinical target volumes were contoured both on FB and DIBH scans. Three different techniques were carried out and compared both on FB and DIBH CT scans: a plan based on tangential parallel opposed fields modulated with step and shoot intensity modulated radiotherapy (IMRT), the same technique with sliding window IMRT, a VMAT approach with two opposed mini-tangential arcs. VMAT-DIBH plans were calculated using both flattening filter free (FFF) and Flattering filter (FF) 6 MV beams. Planning was performed using the treatment planning system (TPS) Raystation with robust optimization. A phantom was used to verify the dosimetric equivalence of the different techniques in terms of dose delivered to the skin.

Results: Regarding the reproducibility of contours on FB and DIBH scans, not significant differences were found in terms of planning target volumes (PTVs) (p=0.25) and heart (p=0.26). Left lung volumes increased in DIBH (p<0.,001). No significant differences were shown in the PTVs coverage with the different techniques in terms of D95 (p=0.97), dose homogeneity (p=0.95) and conformity (p=0.35). A slightly increase in hotspots (D2) for the VMAT FFF (p=0.02) were found. A significant reduction of maximum dose D2 (p=0.0003) to the heart, maximum (p=0.0002) and mean dose (p=0.0006) to the left anterior descending coronary (LAD) were found. LAD dose reduction is related to heart to lung volumes ratio on FB SCAN. The planning technique had no impact on dose distribution to the PTVs and OARs. For VMAT treatments dose distribution is shifted 0.5 mm toward the surface; no dosimetric difference were detected between FF and FFF. The estimated dose delivery time with VMAT-FFF approach is 7 seconds for each of the two arcs.

Conclusions: DIBH improves heart and LAD sparing significantly minimizing the high doses. VMAT FFF is an attractive option considering the reduction of delivery time in DIBH.

## DP33

### CLINICAL IMPLEMENTATION OF DIBH WITH OPTICAL SYSTEMS FOR LEFT-SIDED BREAST CANCER: PRELIMINARY RESULTS

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Aims: Adjuvant radiotherapy (RT) is a crucial part of multimodal management of breast cancer patients (pts). In this setting, late cardiac toxicities that can be induced by breast RT are now recognized as rare but relevant sequelae. Deep inspiration breath hold (DIBH) technique can reduce cardiac dose in whole breast irradiation (WBRT). In the present study, the implementation of DIBH using surface monitoring systems is described.

Methods: Patient selection included women undergoing WBRT for breast cancer with at least 1 of the following characteristics: age ≤50 years (ys), cardiac diseases, previous cardio-toxic chemotherapy regimens. The respiratory gating systems used were optical surface scanning devices: Sentinel for simulations and Catalyst HD for treatments (C-Rad). Simulations were performed with pts positioned supine on wing or breast boards with both arms raised above the head. The patient training was carried out by providing women with electronic eyeglasses (video coaching) where they can see their breathing signal. Only pts able to follow the training to find their individual deep inspiration level and to retain breathing for almost 20s have been selected. Finally, a DIBH CT scan was taken. All pts were also studied in free breathing (FB) in order to compare the dose distribution for PTV and OARs. Thus contouring and 3D conformal treatment planning were realized and evaluated on both CT studies. The prescribed dose was 40Gy (15 fx) to the whole breast +/- 10Gy boost to the tumour bed.

Results: Of 55 evaluated pts, 14 pts were screened according to the selection criteria, 2 pts withdrew, 2 pts were excluded due to their inconstant breathing, 10 pts were selected (age:46-69ys) and 9 pts successfully completed the DIBH treatment. Comparison of FB and DIBH treatment plans in all pts confirmed the DIBH able to reduce heart mean dose by ~50% and heart D2cc by 15-85%. The analysis of the entire process of DIBH

shows a certain increase of time for some procedures: patient training, doubled contouring and treatment planning and longer delivery.

Conclusions: The DIBH technique was successfully implemented and resulted a safe and feasible treatment strategy. Despite the small sample size and the preliminary analysis, DIBH provides better treatment quality due to the cardiac dose sparing. Considering workforce requirements and time commitments, clinical correlations of the DIBH dosimetric benefits with the reduction in cardiac mortality are expected.

## DP34

### IRREGULAR SURFACE COMPENSATOR TECHNIQUE FOR POSTOPERATIVE BREAST RADIOTHERAPY: EVALUATION OF ACUTE SKIN TOXICITY

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Background: The irregular surface compensator (ISC) is an electronic compensator and a kind of forward planning IMRT (FP-IMRT) that allows significant improvements in dose distribution in whole breast radiotherapy (WBRT) compared with the traditional field-in-field (FIF) technique. The aim of this study is to evaluate acute toxicity of patients treated with ISC WBRT technique.

Material and Methods: The prevalence of moist desquamation among patients treated with 3D radiotherapy in the current literature is about 25%. To achieve 80% power to reduce the rate of moist desquamation to 15% or less a minimum of 132 patients were needed. Prescribed dose to the breast was 50 Gy in 25 fractions. Patients with negative prognostic factors received a tumor bed boost of 10 Gy in 5 fractions. Toxicity was assessed using the Common Terminology Criteria for Adverse Events.

Results: 185 consecutive patients received ISC WBRT technique. Ninety-nine (53.5%) patients were left sided, 86 (46.5%) right sided. One hundred eleven (60%) patients received tumor bed boost. Median age was 64 (range=33-95). Median PTV cc was 643.6 (range=112.29- 1984.4). Grade 1 dermatitis occurred in 48.6%. The incidence of moist desquamation was 15.1%. Only in three patients, all with breast CTV cc greater than 1500 cc, the moist desquamation area was greater than 2 cm. Eight patients (4.32%) suspended radiotherapy course (median days= 6 ; range=4-8).

Conclusions: ISC WBRT technique was associated with a lower rate of moist desquamation compared with literature reported rate of 3D-WBRT. Therefore, this technique seems to confirm in a clinical setting the dose distribution advantages showed in planning studies.

## DP35

### EVALUATION OF LONG-TERM CARDIAC MORTALITY EXCESS RISK IN LEFT-SIDED BREAST RADIOTHERAPY: A COMPARISON BETWEEN VMAT AND FIELD-IN-FIELD (FIF) TECHNIQUE

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Aims: In left breast radiotherapy, late cardiac damage is the most important side effect to be kept under strict control. The purpose of this paper was to compare the risk of long-term cardiac mortality between a standard FIF technique and VMAT.

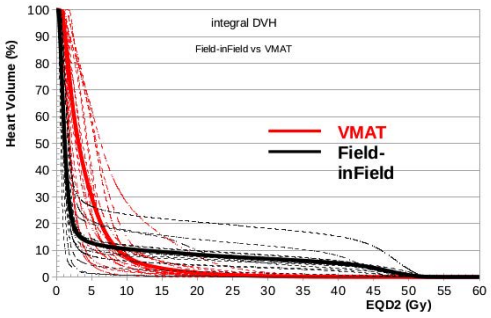


**Figure** *As it can be seen from the graphs, the low absorbed doses to the heart increase using VMAT technique while the high absorbed doses peaks, responsible of the cardiac mortality, decrease.*

| | P(%) 3D | P(%) VMAT | $P_{VMAT}/P_{FIF}$ |
|---|---|---|---|
| PZ 1 | 0.499% | 0.001% | 0.002 |
| PZ 2 | 2.585% | 0.026% | 0.010 |
| PZ 3 | 2.338% | 0.113% | 0.048 |
| PZ 4 | 2.483% | 0.150% | 0.060 |
| PZ 5 | 2.792% | 0.018% | 0.006 |
| PZ 6 | 2.951% | 0.040% | 0.013 |
| PZ 7 | 2.572% | 0.343% | 0.133 |
| PZ 8 | 0.011% | 0.000% | 0.015 |
| PZ 9 | 1.237% | 0.024% | 0.019 |
| PZ 10 | 1.875% | 0.053% | 0.028 |
| PZ 11 | 3.437% | 0.085% | 0.025 |
| PZ 12 | 8.813% | 0.009% | 0.001 |
| PZ 13 | 3.539% | 0.233% | 0.066 |
| PZ 14 | 0.867% | 0.000% | 0.000 |
| PZ 15 | 3.406% | 0.015% | 0.004 |
| PZ 16 | 3.967% | 0.028% | 0.007 |
| PZ 17 | 2.145% | 0.025% | 0.012 |
| PZ 18 | 2.566% | 0.033% | 0.013 |
| | | **average=** | **0.026** |

**Table** *Using the Relative Seriality model, the risk of late cardiac mortality was assessed for several patients, for whom two plans were optimized.*

Materials: Data from 18 female patients undergoing left breast radiotherapy were evaluated, for which the estimate of long-term cardiac mortality, with the relative serial model, had a range from 0.5% to 9% with the FIF technique. Two treatment plans were optimized for every patient, one with FIF technique (2Gy/fr x 25fr, boost 2Gy/fr x 5fr) and one with VMAT (1.8Gy/fr x 28 fr, SIB 2.1Gy/fr x 28 fr).The schedules were chosen to keep, as possible, the same BED values both on the target and on the heart tissues. EQD2 was calculated for each heart absorbed dose distribution and the Relative Seriality model ($\alpha/\beta$=3Gy, s=1, D50=52.4Gy and g=1.28) was used as method to evaluate the probability

of late cardiac mortality.

Results: The use of VMAT technique leads to an increase in low doses to the heart but a significant reduction in high dose peaks which, according to the relative serial model, are responsible for the increase in the value of long-term cardiac mortality. Moreover, VMAT technique allows a better dose distribution to the PTV and the Conformity Index (COIN) is greater than 30%. LADCA (Left Anterior Descending Coronary Artery) absorbed dose is less than 60% if VMAT technique is adopted. The average of the ratios between the probability of long-term cardiac mortality with VMAT technique vs FIF in the 18 patients was 0.027 (min 0.001; max 0.133). Paired data t-Student test showed a statistical significant differences between the two sets of data ($p<0.001$)

Conclusions: VMAT technique seems to be safer than FIF in terms of probabilities of risk of late heart damage. The probabilities evaluated in this work are the result of a calculation and are closely related to the irradiation technique used and targeted at specific endpoints. During the optimization of the treatment plan, attention is needed to check for the hot-spots dose, especially when a hypofractionated scheme is adopted. Every dose distribution should be evaluated in terms of EQD2 and the radiobiological DVHs should be evaluated alongside physical ones. For this reason, modern TPSs should promote, even more, the use of either radiobiological DVHs or algorithm optimization.

## DP36

### HYPOFRACTIONATED RADIOTHERAPY WITH PD1 AND ANTI PDL-1 IN OLIGOMETASTATIC NSCLC: SAFETY AND FEASIBILITY

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Aims: Five-year survival rates for metastatic non small cell lung cancer (NSCLC) is < 5%. Radiotherapy is an option of treatment in these setting of patients and is often given concurrently or sequentially with chemotherapy. Related chemotherapy toxicity often worsens adherence to radiation treatment, hence the need to perform less toxic systemic therapies such as immunotherapy. Radiationtherapy (RT) might modify the cancer immune enviroment to enhance the antitumor effect of immune checkpoint inhibitors. We analyzed NSCLC metastatic pts treated with hypofractionated radiotherapy and PD1 and PD-L1 inhibitors. The primary endpoint was safety and feasibility, secondary was local control and progression free survival.

Methods: From December 2016 to February 2019 we have retrospectively examined 30 pts with lung (n.10 pts) and bones metastases (n.20 pts) from NSCLC, chemotherapy pretreated. The inclusion criteria were oligometastatic pts, after chemotherapy-failure. All pts were treated with anti PD1/PDL-1 and hypofractionated RT to the disease sites. The prescription doses was for lung metastases 48 Gy/4 fx, for bones metastases was 20 Gy/4 fx. Ten pts receveid immunotherapy concurrent at RT, 14 pts within 2 weeks after the end of RT; 6 pts performed before immunotherapy and after RT. All pts continued immunotherapy every 2 weeks thereafter until progression disease or unacceptable toxicities. The primary endpoint was the occurrence pneumonitis or other non-hematological toxicity; the secundary endpoint was local control and progression-free survival. The toxicities was evaluated according RTOG scale.

Results: Grade 3 pneumonitis occurred in 1 patient, for which hospitalization has been requested. Fatigue in 15 pts and fever in 3 pts, no endocrinological toxicities has been reported. Follow-up time was 26 months and were recorded: 4 complete response and 7 partial responses after 6 months after the end radiotherapy, 7 progression disease outside the radiation field after 5 months of immunotherapy, 10 pts continued immunotherapy. In 2 pts recorded worsening of PS-ECOG after 8 months of immunotherapy.

Conclusions: PD1 and PDL-1 inhibitors with hypofractionated radiation therapy is a treatment safe and feasibility. There is still no gold standard in treatment sequencing. In all schedules the treatment was well tolerated and we had a good local control.

## DP37

### EFFECT OF POLY(ADP-RIBOSE) POLYMERASE-1 INHIBITION ON HUMAN SOFT TISSUE SARCOMA CELLS RADIOSENSITIVITY: *IN VIVO* STUDY

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Aims: Soft-tissue sarcomas (STS) are malignant tumors with a poor prognosis and limited therapeutic options. Poly-ADP ribose polymerase (PARP)-1 is a DNA-binding protein, activated by nicks in the DNA molecule, who play a role in DNA strand repair. Some STS have defects in DNA repair, so PARPi may be used to kill these cells selectively. Previous studies demonstrated that PARPi can inhibit DNA damage repair when used in combination with irradiation, reducing cell survival. The aim of this study was to investigate the effect of PARP inhibition in a xenograft model of rhabdomyosarcoma in mice after tumor cells irradiation.

Methods: Rhabdomyosarcoma cells were irradiated with 3 Gy, with or without a pre-treatment with 24 hours olaparib (1 μM) . The control was made with non-irradiated cells. Four group of mice were compared:1) control; 2) olaparib; 3) irradiation; 4) irradiation+olaparib. Rhabdomyosarcoma xenograft was obtained by s.c. injection of $6\times10^6$ cells in the flank of CD1 nude mice.

Twice a week tumor volume was measured, for a period of 30 days, by the formula [lenght x(width x width)]/2. Immunofluorescence and western blotting analysis have been performed.

Results: In comparison to control group olaparib alone reduced tumor growth, but without reaching a statistical significance. Moreover, a significant reduction of tumor volume was shown with irradiation alone relative to control. The association of olaparib and irradiation showed an even higher decrease in tumor volume compared to irradiation alone, reaching the statistical significance vs. irradiation or olaparib alone after 8 days. The mean immunofluorescence of gamma H2AX on rhabdomyosarcoma cells was significantly increased after treatment with olaparib and with radiation alone; a higher intensity of fluorescence was obtained with combined treatment. Tumor growth was inversely proportional to the mean immunofluorescence of gamma H2AX. With western blotting analysis we observed that irradiation increased the level of phosphorylated-active ERK1/2 (p44/42 MAPK) compared to the control. The add of olaparib to irradiation significantly reduced the irradiation-induced phosphorylation of ERK1/2. PCNA, involved in DNA repair pathway.

Conclusions: In this study we showed that olaparib have a synergic therapeutic effect with irradiation on rhabdomyosarcoma xenograft, with significant reduction of tumorigenesis, confirming previous studies in vitro. This results encourages future research about this association.

## DP38

### COMBINED IMMUNE CHECKPOINT INHIBITORS AND ENCEPHALIC RADIOTHERAPY: ACUTE AND LATE TOXICITY EVALUATION

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*Università Campus Biomedico, Roma, Italy*

Aims: Immune checkpoint inhibitors (ICIs) have shown highly promising responses in solid tumors. Intracranial metastases are frequently managed with radiation therapy (RT). The safety of cranial RT in the setting of treatment ICIs has not been established. We aimed to assess acute and late toxicity in patients treated with cranial RT and anti programmed cell death-1(PD-1).

Methods: We identified patients with brain metastases from different primaries, who received cranial RT and were concurrently treated with anti PD-1. RT-related AEs were evaluated and analyzed according to ICI treatment status, cranial RT type, and timing of RT with respect to ICI.

Results: Between July 2017 and May 2019 20 patients with advanced solid tumors were treated: 15 (75%) Non Small Cell Lung Cancer (NSCLC), 3 (15%) melanoma, 1 (5%) Sarcomatoid tumor of the lung and 1 (5%) renal cell carcinoma. Fifteen (75%), 2 (10%), and 3 (15%) patients received stereotactic RT, whole brain RT or both, respectively. We observed seizures in one patient during whole brain RT who was symptomatic before radiotherapy and successfully treated with Levitaceram and mannitol. We observed two radionecrosis (10%) occurring at 2 months and 4 months after the end of stereotactic RT. One of these two latter patients was treated with WBRT followed to several stereotactic radiotherapy treatments at different timepoints, while the other was treated to 6 lesions with stereotactic radiotherapy at the same time. We observed no significant difference in acute neurological toxicity between patients who received whole brain RT or stereotactic RT. Additionally, there was no difference in AE rates on the basis of timing of ICI administration with respect to RT. With a median follow up was 6 months (range 1-16 months), 16 patients (80%) were evaluable for response: 5 (31.25%) had brain progression after stereotactic RT, 5 (31.25%) had stable disease after stereotactic RT, 3(18.75%)complete response after stereotactic RT and 3 (18.75%) partial response after whole brain RT. 6 patients (30%) died during follow up for extracranial disease progression and 1 patient (5%) will have MRI in the next few months.

Conclusions: Treatment with an ICI and cranial RT seems feasible. However dose escalation in these patients may be at risk of increased radionecrosis. Additional studies on larger series are needed.

## DP39

### HYPOFRACTIONATED IRRADIATION IN ELDERLY BREAST CANCER PATIENTS: AN OBSERVATIONAL STUDY

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Aims: To assess efficacy, acute and late toxicity of hypofractionated radiotherapy (Hypo-RT) and impact of age and comorbidities in elderly breast cancer (BC) patients (pts).

Methods: From June 2009 to December 2017 we analyzed 808 pts receiving 42.4 Gy in 16 daily fractions. A boost was administered in cases of grade 3 primary tumor and close/positive margins. Acute and late toxicity was prospectively assessed, based on the

RTOG scale. Baseline comorbidities included in the hypertension-augmented Charlson Comorbidity Index (hCCI) were retrospectively retrieved. Five-year disease-free survival (DFS) and overall survival (OS) were assessed by Kaplan-Meier method and log-rank test was used to compare groups of age and comorbidity. Hazard ratios (HRs) were estimated by Cox proportional hazards models adjusting for tumor size, lymph node status, molecular subtype, grading, chemotherapy. Odds ratios (ORs) of acute and late toxicity by of age, comorbidity and boost administration were estimated by ordinal or multinomial logistic models.

Results: The median age was 74 years (range 65-91 years), and 76.1% of the pts were over 70. The median follow-up was 46.8 months (range 4-115 months). At baseline, 70.4% of pts were affected by at least one comorbidity. Invasive ductal carcinoma was the most common histological type (81.2%), and the most common subtype was luminal A (46.5%). 21.5% of the pts underwent chemotherapy. At the latest follow-up date, 90.4% pts were still alive, 5.8% experienced disease progression (relapses, contralateral BC, metastases), 18 died of BC and 60 died of other causes. DFS was 92.6, 87.2, 83.5 and 71.3% for 65-69, 70-74, 75-79 and ≥80 years, respectively ($p<0.001$). OS for increasing age-class was 94.7, 93.0, 86.7 and 80.9% ($p=0.002$). Five-year DFS and OS were 91.9% and 94.3% for pts without comorbidity and 74.3% and 84.5% for pts with hCCI≥2 (DFS $p<0.001$, OS $p=0.017$).Elderly pts had significantly higher odds of increasing score in acute asthenia. Pts with hCCI≥2 had significantly increased odds of late edema and fibrosis. Boost administration was significantly related to acute skin toxicity and late fibrosis and edema.

Conclusions: Hypo-RT in elderly BC pts is effective and well-tolerated. This study shows that age and comorbidities negatively impact DFS and OS. Further studies focusing on a better selection of elderly BC pts based on genomic and biological features and with tailored treatment approaches are warranted.

**DP40**

## STEREOTACTIC BODY RADIOTHERAPY AS DOSE INTENSIFICATION FOR BONE AND SPINAL METASTASES: A RETROSPECTIVE MONOISTITUTIONAL ANALISYS

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*[1]Department of Radiotherapy, San Raffaele Scientific Institute, Milano; [2]Department of Radiotherapy, University Milano Bicocca; [3]Medical Physics, San Raffaele Scientific Institute, Milano, Italy*

Aim: The treatment of spine and bone metastases with standard external beam radiotherapy ensures a six months symptomatic and local control, which could be insufficient for long term survival oligometastatic patients (pts). Recent studies demonstrated long term pain and local control by dose intensification delivered with stereotactic body radiotherapy (SBRT). The aim of this study is to evaluate clinical effectiveness and safety of SBRT using Cyberknife in spinal and bone metastases.

Material and Methods: From October 2017 to May 2019, 71 pts with 94 oligometastatic/oligoprogressive spinal and bone metastases were treated with Cyberknife in our Institution: 78.7% were spinal lesions, while 21.3% was non-spine. The most common histology was prostate cancer 62.8%, followed by breast 11.7%, kidney 7.4%, lung 6.4%, bladder 4.3%, rectal 3.2%, pancreatic 2.1%, ovarian 1.0%, and uterine cervix cancer 1.1%. Pain was present before SBRT in 32% of pts with a median value of 5 (3-8), according to Visual Analogue Scale (VAS). Two mg of dexamethasone were prescribed in 51% of pts for 1 week. In 80% of pts with spinal lesions, to maximize tumor coverage and minimize spinal cord exposure, a simulation CT a T1 and T2 MRI were fused and used to outline the gross tumor volume (GTV). GTV to planning target volume (PTV) expansion was 2 mm. Median dose prescription was 18 (16-35) Gy, delivered in a median of one fraction (1-7).

Results: Median follow-up was 5 (1-17) months. Early pain relief was observed in all symptomatic pts. Local progression occurred in 5.3% of pts with a median time to local failure of 2.42 (1-3) months. Median total dose of pts presenting progression at follow up CT/MRI was 27 (18-27) Gy, delivered in a median of 3 (1-3) fractions. The histology of progressive tumors were colon cancer, bladder cancer and uterine cervix cancer. One patient developed G2 acute pain flare toxicity (according to CTCAEv4.03), after one day of dexamethasone suspension. The pain was controlled prolonging dexamethasone for two additional days. In 66 lesions with a follow up longer than 3 (3-17) months, no late toxicities and SBRT-related fractures were observed.

Conclusions: Our experience with dose intensification in spinal or bone metastases matches with the published studies, which demonstrated that vertebral and bone SBRT is a safe treatment providing a low acute and late toxicity and early pain relief in all pts. A longer follow up is necessary to confirm the very good local control.


# *Poster*

**PO001**

## EVALUATION OF ACUTE GENITOURINARY AND GASTROINTESTINAL TOXICITY IN PATIENTS TREATED WITH VOLUMETRIC INTENSITY MODULATED / IMAGE-GUIDED RADIOTHERAPY (VMAT/IGRT) FOR PROSTATE CANCER

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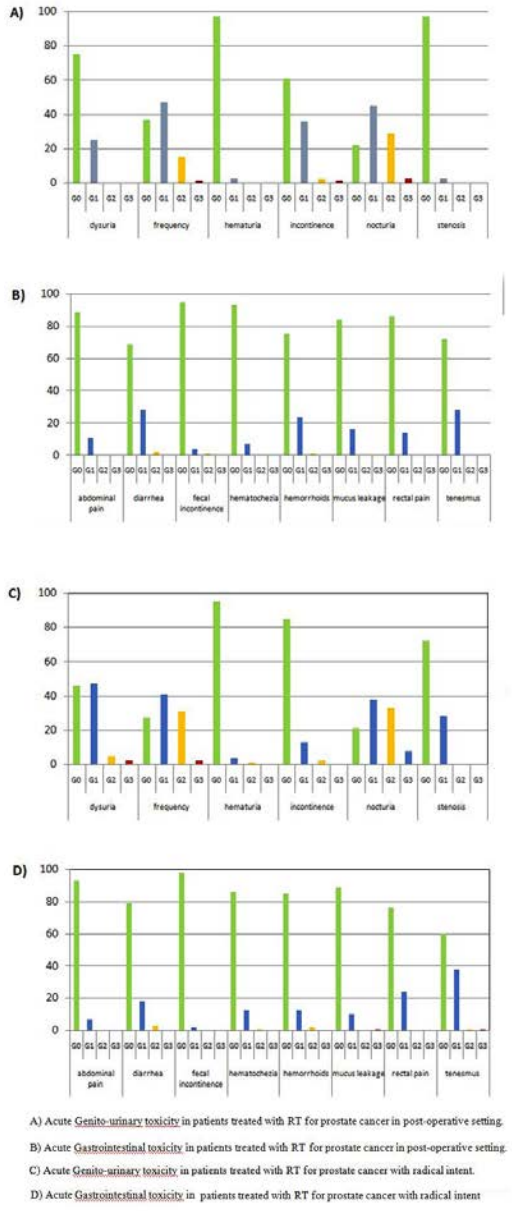
Aims: The introduction IGRT-IMRT allows an improvement of precision and accuracy in the treatment of patients (pts) with prostate cancer. To reduce prostate displacemnts during the dose-delivery we introduce a written protocol for reproducible filling bladder and empty rectum. The study aims to evaluate the compliance to this protocol and the acute genito-urinary (GU) and gastrointestinal (GI) toxicity.

Methods: We analyzed 193 consecutive pts (98 with radical intent and 95 in the post-operative setting) treated for prostate cancer from 2017. Patients were treated with moderate hypofractionated VMAT/IGRT (28-30 fractions) on prostate and seminal vesicles (2.5 Gy/fx) or prostate bed (2.2-2.25 Gy/fx), +/- pelvis nodes (1.8 Gy/fx) and +/- ADT. All pts were treated with empty rectum and full bladder, according to a written protocol Daily set-up control with CBCT was conducted and the number of repositioning due to inadequate preparation were recorded. During treatment pts were evaluated weekly and by three months from the end of RT, for acute toxicity (according to CTCAE version 4.03).

Results: Among the 193 pts treated, 140 have never been repositioned (72,54%), 29 pts have been repositioned once (15,03%), 4 pts have been repositioned more than three times and only 1 the maximum number recorded (n=8). Among 95 pts in the post-operative setting , acute GU toxicity recorded were: G0=12,63%, G1=49,47%, G2=37,74% and G3=3,16%; more important toxicity were nocturia (G3 in 3 pts and G2 in 28 pts) and urinary frequency (G2 in 14 pts), Acute GI and rectal toxicity was mild with G2 as a maximum grade in 4 patients (diarrhea in 2 pts, hemorrhoids and incontinence in 1 pts respectively), and none G3. Of 98 pts treated with radical intent, acute GU toxicity recorded were G0=6,12%, G1=37,76%, G2=46,94% and G3=9,18; more important toxicity were nocturia (G3 in 8 pts and G2 in 32 pts) and urinary frequency (G3 in 3 pts and G2 in 30 pts). Acute GI and rectal toxicity was G2 in 7 pts (diarrhea in 3 pts, hemorrhoids in 2 pts, hematochezia and tenesmus in 1 pt respectively), and G3 in 2 pts.

Conclusions: According to our results, moderate hypofractionated RT (also in the post-operative setting) seems to be feasible and safe, with a good toxicity profile. Moreover we recorded a good compliance to protocol for reproducible filling bladder and empty rectum, useful tool for the reproducibility of treatment and dose delivering to target and OARs.




A) Acute Genito-urinary toxicity in patients treated with RT for prostate cancer in post-operative setting.
B) Acute Gastrointestinal toxicity in patients treated with RT for prostate cancer in post-operative setting.
C) Acute Genito-urinary toxicity in patients treated with RT for prostate cancer with radical intent.
D) Acute Gastrointestinal toxicity in patients treated with RT for prostate cancer with radical intent

**Figure 1.**

**PO002**

## BILATERAL HIP PROSTHESES AVOIDANCE TECHNIQUE IN THE TREATMENT PLANNING FOR A CASE OF ENDOMETRIAL ADENOCARCINOMA

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Aims: Hip prosthetic implants - usually made of high density material - attenuate the incoming radiotherapy (RT) treatment beams and scatter the dose, with subsequent dosimetric uncertainty at the soft tissue interfaces and in the evaluation of dose uniformity inside the planning target volume (PTV). Furthermore, artifacts on images are usually caused by prostheses. Therefore, a standard practice is the avoidance of these prosthetic materials in the treatment planning. We report the case of an endometrial adenocarcinoma occurred in a patient with bilateral hip prostheses treated with a technique of hip prostheses avoidance (HPA).

Methods: A 76-years old woman with bilateral hip prostheses and an history of left breast cancer (2003) treated with mastectomy, chemotherapy, radiotherapy and hormonal therapy, underwent in 2018 surgery (hysteroannessectomy) for uterine prolapse: the histologic diagnosis was endometrioid adenocarcinoma G3 with no endovascular invasion, pathological stage pT1bNx. An external beam RT treatment plan with bilateral HPA was implemented. A total dose of 50 Gy in 25 fractions was prescribed to pelvic nodes and tumor bed, followed by a HDR-brachytherapy boost on the vaginal cuff (10 Gy in 2 fractions).

Results: At first, a contouring of the artifacts generated by the hip prostheses was done to assign them the water density. The HPA plan was implemented with a mixed technique: a VMAT technique for the upper region of PTV and a 3D conformal RT technique with 5 static beams (three obliques and two AP/PA beams) to cover the lower regions of PTV. VMAT and 3D beams had the same isocenter, to shorten the treatment time and to avoid unfavorable overlap. A good target coverage was achieved: V95 was 98%, Homogeneity Index (Dmax/Prescription dose) was 1.04. A satisfactory dose-sparing of the organs at risk (OARs) was also obtained. Imaging with daily KV was scheduled. Monitor Units were 248 + 458, the overall time for treatment delivery was 2 minutes and 20 seconds. Low grade acute toxicity (diarrhea G1) was observed. A Computed Tomography performed three months after the completion of RT confirmed absence of disease. No late adverse event was reported.

Conclusions: We propose a technique for HPA planning to allow good target coverage and HI, with an adequate sparing of OARs. Short delivery times and an adequate image-guidance support patient's compliance and treatment accuracy.

## PO003

### ATTITUDES AND PRACTICE TOWARDS INTENSITY-MODULATED RADIATION THERAPY TECHINQUES IN THE TREATMENT OF MEDIASTINAL LYMPHOMAS: A NATIONWIDE, MULTICENTER SURVEY BY ASSOCIAZIONE ITALIANA DI RADIOTERAPIA ED ONCOLOGIA CLINICA (AIRO) AND FONDAZIONE ITALIANA LINFOMI (FIL)

A. Di Russo[1], S. Meregalli[2], M. Buglione Di Monale[3], E. Bastia[3], P. Ciammella[4], G. De Marco[5], V. De Sanctis[6], A.R. Filippi[7], B. Lanfranchi[5], M. Levis[8], S. Vagge[9], U. Ricardi[8], G. Simontacchi[10]

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Aims: To report the results of a nationwide, multicenter survey investigating the practice of Intensity-Modulated Radiation Therapy (IMRT) techniques in the treatment of mediastinal lymphomas (ML).

Methods: In October 2018, a 25-items questionnaire was sent to all Italian Radiation Oncology Departments on behalf of Fondazione Italiana Linfomi (FIL). Centers were asked to provide data on the use of IMRT techniques in the irradiation of ML (HL and NHL), collecting specific information about radiation treatment prescription and delivery.

Results: 43/195 Centers completed the survey. The median amount of irradiated of ML was 16 pts/year/Center. IMRT is currently adopted in 95,3% of ML cases, according to the facilities of each Center: 56% VMAT, 34% IMRT, 10% Tomo-therapy. 92% of responders used Image-fusion with pre-chemotherapy diagnostic imaging to define target volumes. Organ-at-Risk (OAR) are systematically contoured, and lungs, heart, breasts, and esophagus are considered the most relevant. 100% of responders took into account the dose constraints to OAR with 63% of these using ad hoc "low dose" constraints derived by medical literature (81%) or single institution experience (19%). In 91% of treatments, Image-guidance modalities were used to verify treatment set-up. Respiratory gating was used by 21% of responders. 91% of partecipating Radiation Oncologists are favourable to the standardization of the adopted radiation techniques to treat mediastinal lymphoma in daily practice and 98% consider useful a manuscript on specific dose constraints for lymphoma radiotherapy.

Conclusions: Radiotherapy plays a significant role in the treatment of lymphoma, with high efficacy but still long term potential toxicity. The use of state-of-art treatment planning and delivery modalities could play an important role to improve quality of life and survival in lymphoma patients, however no guidelines in IMRT dose constraints have been published. According to most of AIRO Radiation Oncologists participating to this survey, a manuscript on specific dose constraints for ML radiotherapy should be published.

## PO004

### HELICAL TOMOTHERAPY IN THE TREATMENT OF UNFIT BLADDER CANCER PATIENTS: A MONO-INSTITUTIONAL STUDY UPDATE (2011-2018)

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Aims: To evaluate the use of Helical Tomotherapy (HT) in the treatment of bladder cancer. The HT system employs a compact 6 MV Linac-based on CT ring gantry to rotationally deliver intensity modulated fan beams. Patients are translated through-out the gantry on a treatment couch, resulting in helical irradiation geometry. The HT unit also contains a mega-voltage CT detector array located opposite the radiation source for pre-treatment verification, allowing accurate re-positioning. This technique permits to precisely target tumors while minimizing impact on surrounding healthy tissue: this could be very interesting for unfit bladder patients, to reduce GU and GI toxicity.

Methods: 38 patients (age: 51-89) with bladder cancer were treated in our institution from 2011 to 2017 with HT. None of these patients were fit for surgical indication due to concomitant medical conditions. None of these patients had concomitant chemotherapy due to medical conditions. 21/38 (55%) of these patient had positive lymphonodes. CT axial scanning was performed at 5-mm intervals: for this purpose a CT Multislice GE Healthcare Discovery 590HT was used. The radiation oncologists contoured the volumes of interest (CTV) according to the RTOG guidelines. The planning target volume (PTV) was generated from the CTV volume by adding a 3 mm margin in all directions. Accurate delineation of organ at risk was performed. In these patients, we used several radiotherapy schedules, according to volume and site of cancer and considering performance status of the patients. Treatment plans were evaluated on a dedicated TPS.

Results: 31/38 of these patients ended scheduled radiotherapy: 4 patients ended early treatment for cardiac condition, 1 for diabetes complications, 2 patients died. Median follow up was about 11 months (range 2-41). All patients had acute GU toxicity: 20 patients (53%) had G1, 13 patients (34%) had G2 and 5 patients (13%) had G3. Late GU toxicity was seen in 8 patients (21%) as G1 and in 3 patients (7%) as G2. 21 patients (55%) had GI toxicity: 15 patients (40%) had G1, 6 patients (16%) had G2. Late GI toxicity was seen in 5 patients (13%) as G1. OS was 68% at 1 year, 55% at 2 years and 38% at 3 year.

Conclusion: HT is a safe and feasible technique to treat unfit patients with bladder cancer. All patients had acute GU toxicity, but it was acceptable for the greatest part of them. Acute GI toxicity was acceptable too. Late toxicity, both GU than GI, was never ≥G3. The OS is surely influenced by the poor clinical concomitant conditions of the patients too.

## PO005

### VOLUME CHANGES AFTER PROTONTHERAPY IN VESTIBULAR SCHWANNOMA: CONTROL RATE, TOXICITY AND HEARING PRESERVATION

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Aims: The purpose of this study was to evaluate the control rate of vestibular schwannomas (VS) after treatment with protontherapy radiosurgery (SRS) or conventional protontherapy (SRT) by using a validated volumetric measuring tool, toxicity and hearing preservation.

Methods: Retrospectively, 15 VS patients treated with active beam protontherapy based SRS or SRT were analyzed. Baseline and follow-up magnetic resonance imaging scans were analyzed with volume measurements on contrast enhanced T1-weighted (1 mm thickness) and three-dimensional constructive interference in steady-state (3D-CISS) magnetic resonance imaging. The volume measurements were performed on axial coupes, using a computer system fitted with specialized software: Raystation TPS v7.0; volumetric VS analysis was performed in cubic centimeter. Significant growth was defined as a volume change of 19.7% or more. Toxicity was assessed according to CTCAE version 4.03; hearing preservation rates was evaluated using the Gardner-Robertson grading system as determined by audiogram results. Eleven patients (73%) received 50.4 GyRBE in 28 fractions, 4 patients (26%) performed protontherapy SRS (12 GyRBE in single fraction).

Results: At the median follow-up of 24 months (range 9-53), significant shrinkage was seen in 20%, stable VS in 53%, and significant growth in 27% of the patients. In 46% of all patients, transient swelling was observed. However, in the significant growth group no additional treatment was required. No significant shrinkage was observed in protontherapy SRS group. Registered acute side effects include G1 (10%) fatigue, G1 (14%) muffled, G2 (14%) headache, G2 (7%) nausea. There were no G 3 or higher acute toxicities. Registered late side effects include G 1 (7%) and G2 (14%) dizziness, G2 (7%) vertigo, G2 (7%) nausea, facial nerve deficit (House Brackmann scale G2) (7%). Absolute hearing, normal facial and trigeminal preservation rates were 67%, 86% and 93% respectively.

Conclusions: Active beam protontherapy is feasible and safe treatment for patients with untreated VS. Good control rates are reported for protontherapy based SRS or SRT in VS, in which the lower rate of radiological growth control is attributed to the use of the more sensitive volume measurements. Transient swelling is a common phenomenon and should not be mistaken for treatment failure. Longer FU is necessary to assess definitive efficacy and toxicity.

## PO006

### STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) FOR CARDIAC ARRHYTHMIA: A NEW THERAPEUTIC OPTION?

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Aim: Despite of therapeutic efforts, cardiovascular diseases are still the first cause of mortality on a global scale. In this context, Stereotactic Ablative Radiaotherapy (SABR) is used in non-oncologic indications, recently even for cardiac arrhythmias. Thus, aim of the present review is to analyze preclinical, early clinical evidences and future direction of the latter new treatment approach.

Method: A collection of available data regarding SABR and cardiac arrhythmias was made, by Pubmed research and 2 independent researchers, including preclinical and clinical data. A review of ongoing trials was conducted on ClinicalTrials.gov.

Results: Preclinical research conducted in animal models showed that a safe and efficacy non-invasive treatment approach for cardiac arrythmias could be represented by SABR with a median time of response around 2-3 months. The technique doesn't condition the results, while the treatment dose plays a crucial role. The position of arrhythmogenic foci is a relevant aspect, considering that in the most studies the atrioventricular node would seem more radiosensitive than the other cardiac electric zone. Clinical data, such as published case series, case reports and early prospective studies, have already suggested the feasibility, efficacy and safety of SABR (25Gy in one session) for refractory ventricular arrhythmias. The first prospective single arm study-phase I/II-has shown that through cardiac SABR in single dose of 25Gy using respiratory motion control and image-guided delivery with the support of non-invasive electrophysiology study, a significant reduction of ventricular arrhythmias with modest short-term risks is obtained. The non-invasiveness of the therapy is fundamental in this approach and the safe delivery treatment requires a multidisciplinary adequate work team. The potential clinical applicability of the hybrid Magnetic Resonance -Linac for cardiac ablation remains investigational. Two ongoing trials

(NCT03819504 and NCT03601832) will provide further information on the feasibility and safety of non-invasive SABR in ventricular tachycardias.

Conclusion: Considering the ongoing trials of SABR and new technological improvements in radiotherapy and in arrhythmias non-invasive mapping systems, the future analyses will improve the reliability of those preliminary results.

## PO007

### CARBON ION RADIOTHERAPY (CIRT) IN AXIAL BONE AND SOFT TISSUE SARCOMAS TREATED AT CNAO: PRELIMINARY RESULTS

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Aims: To evaluate preliminary results of carbon ion radiotherapy (CIRT) in patients with axial bone and soft tissue sarcomas treated with curative intent at the National Center for Oncological Hadrontherapy (CNAO).

Methods: From January 2013 to September 2018, 54 patients with axial bone and soft tissue sarcomas were treated with curative intent with CIRT using active scanning beam at CNAO . Median age was 50 years (range 19-79), M/F=32/22. Tumor site was pelvis in 50% of cases (n=27), thoracic region in 24% (n=13), cervical spine in 15% (n=8) and lumbar spine in 11% (n=6). 76% (n=41) of patients had primary disease, while 24% (n=13) had recurrent disease. Before CIRT, surgery was performed in 47% of cases, including positive margins (R1) in 8 patients, and macroscopic residual disease (R2) in 17. Histologic subtypes were mainly chondrosarcoma in 39% (n=21) and osteosarcoma in 24% (n=13). Pre-treatment chemotherapy was administered in 40% of cases (n=22); no patient received previous RT. All patients were treated with CIRT for a median total dose of 73.6 Gy[RBE] (70.4 - 76.8 Gy), in 16 fractions (4 fractions per week) with a median daily dose of 4.6 Gy[RBE] (range: 4.4-4.8 Gy). Toxicity was assessed following CTCAE v4.0 scale. Time-to-event data were analysed with Kaplan-Meier method and log-rank test.

Results: Median follow-up was 24 months (range, 4-61). Four patients were lost at follow-up. Acute toxicities were mild, with no G>2 event reported and no treatment interruption needed. For late toxicity, only G3 neuropathy was observed in 4% of cases (n=2). With a median time to local progression of 13 months (3-35), 15 local failures were detected, resulting in 1- and 2-years local control rates of 84.8% and 67.4%, respectively. Distant progression occurred in 12 patients, with 1- and 2-years progression free survival (PFS) rates of 97.5% and 92.2%. Fifteen patients died resulting in 1- and 2-years overall survival (OS) rates of 87.1%% and 75.4%, respectively. At statistical analysis, GTV>1000 cc was found to be predictive of local failure (p=0.04), pre-treatment chemotherapy was found to be significantly related to PFS and OS (p=0.02 and p=0.016); also, recurrent disease and distant progression were significantly related to OS (p=0.019 and p=0.0013).

Conclusions: Our preliminary results of CIRT for axial bone and soft tissues sarcomas are promising in terms of clinical outcomes and acceptable toxicity. A longer follow-up is warranted.

## PO008

### STEREOTACTIC BODY RADIOTHERAPY FOR SPINE METASTASES USING ELEMENTS SPINE SRS BRAINLAB• DEDICATED SOFTWARE

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Aim: Stereotactic ablative radiotherapy (SBRT) is a consolidate treatment approach in several cancer settings. Although SBRT is still under investigation for spinal metastases with promising results in terms of effectiveness and tolerability. In spinal SBRT, one of the most relevant issue is represented by inter-observer variability in target definition. Recently, specific tools for multi-imaging management, automated treatment volumes contouring and planning could allow clinicians to minimize uncertainties in spinal SBRT workflow. The aim is to report the feasibility of a Linac-based spine SRS/SBRT dedicated system (Element®, BrainlabTM Germany) in clinical practice.

Methods: Patient selection criteria were as follows: age ≥18 years, diagnosis of spinal metastases ≤3, life expectancy >3 months, controlled primary tumor or synchronous diagnosis and Spinal Instability Neoplastic Score (SINS) ≤ 12 points. All clinical target volumes (CTV) were defined and planned with the support of a dedicated system. The following organ at risks (OARs) were delineated: lung, esophagus, spinal cord, cauda equine, kidneys. Dosimetric constraints were defined as follow: spinal cord (0.1 cc) < 14 Gy and <21.9 Gy, cauda equine (0.1 cc) < 16 Gy and < 24 Gy, kidney (>200 cc) <8.4 Gy and <16 Gy, esophagus (1 cc) < 15.4 Gy and <25.2 Gy for single and 3 fractions schedules respectively; each lung V10<10%, V5<35%, V20<3% and mean dose ≤ 5 Gy (1 and 3 fractions). Dose prescription ranged between 12 Gy and 24 Gy (single and 3 fractions). Toxicity was assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.0.

Results: Between April 2018 and April 2019, 54 spinal metastases in 32 recruited patients were treated

with Linac-based SBRT, using the dedicated system for spinal target definition and planning. Dosimetric constraints to OARs were met in all cases. With a median follow-up of 4.2 months (range 3-11.6 months), local control at 3 months and 6 months were 94.1% and 85.6%, respectively. No adverse events higher than grade 2 were observed. Table 1 resumed patient characteristics.

**Table 1. Patients and disease characteristics.**

| | |
|---|---|
| Number of patients and spinal metastases | 32 and 54 |
| Sex (F/M) | 11/21 |
| Median age (range) | 68 (43-83 years) |
| Median performance status (range) | 1 (0-2) |
| Histology (%) | |
| Lung | 2 (6.2%) |
| Breast | 9 (28.1%) |
| Prostate | 15 (46.9%) |
| Others | 6 (18.8%) |
| Median number of spinal metastases for patients (range) | 1 (1-3) |
| Pre-treatment MRI | 5 (15.6%) |
| Pre-treatment PET-CT | 22 (68.8%) |
| Pre-treatment combined radiological exams | 5 (15.6%) |
| Vertebra (%) | |
| Cervical | 7 (13.0 %) |
| Dorsal | 36 (66.7%) |
| Lumbar | 11 (20.3%) |
| Sacral | 0 |
| Anatomical site (%) | |
| Vertebral body | 27 (50%) |
| Vertebral body + spinal process | 1 (1.9%) |
| Vertebra body + peduncle | 8 (14.8%) |
| Vertebral body + spinal process + peduncle | 4 (7.4%) |
| Peduncle | 8 (14.8%) |
| Spinal process | 4 (7.4%) |
| Full vertebra | 2 (3.7%) |
| Spinal Instability Neoplastic Score (SINS) | |
| Median (range) | 5 |
| 0-6 | 22 (68.7%) |
| 7-12 | 10 (31.3%) |
| Pre-treatment Visual Analogue Scale (VAS) | |
| Median (range) | 0 (range 0-8) |
| First follow-up VAS | 0 (range 0-7) |
| Post-treatment VAS | |
| Median (range) | 0 (range 0-7) |
| Systemic therapy associated to SBRT (no; %) | |
| None | 8 (25.0 %) |
| Hormone therapy | 16 (50%) |
| Chemotherapy | 4 (12.5%) |
| Target therapy | 0 |
| Immunotherapy | 4 (12.5%) |

Conclusions: This preliminary experience shows that, with respect to acute toxicity and early clinical response, Linac-based SRS/SBRT using a dedicated system is a feasible and effective approach. Moreover, this technique demonstrated to be an intriguing tool to minimize potential inter-observer variability, time to treatment preparation and offering an accurate target definition and planning.

**PO009**

## 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 intrauterine brachitherapy

Methods: We included 24 pts with LACC (range 29-82 years) that referred to our institution between 2013 and 2019. Pts were treated with concomitant CRT and subsequent brachytherapy. FIGO STAGE: 1/24 was IB1, 3/24 were IIA, 14/24 IIB, 4/24 IIIB and 2/24 IVA. 10/24 pts had regional lymph node involvement and 1 pt had also positive lombo-aortic lymph nodes. 19/24 pts underwent radiotherapy and concomitant weekly chemotherapy with Cisplatin (40 mg/mq$^2$), 3 pts received also neoadjuvant chemotherapy and 2 patients only radiotherapy. 14/24 pts were treated with IMRT tecnique and 10 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 lombo-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, 2 pt 25 Gy, 16 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 brachitherapy all pts performed early-PET: 18/24 were negative and 6/24 positive. 2/18 (11.1%) pts with negative early-PET showed a relapse: 1 pelvic nodal relapse after 15 months and 1 cervical, annexial and nodal relapse after 5 months from the end of brachytherapy. 3/6 pts (50%) with positive early PET-TC had progressive/relapse disease: 2 pts showed systemic (lung-heart) progressive disease after respectively 3-4 months 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.

## PO010

### VMAT VERSUS IMRT FOR HEAD AND NECK CANCER IRRADIATION: COMPARISON OF DOSIMETRIC AND TOXICITY ISSUES

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Aims: Over the last decades progressive implementation of IMRT technique lead to improve critical structure sparing with good target coverage particularly in head and neck cancers (HNC). In spite of its efficiency in dose conformity, IMRT is burdened by an increased treatment delivery time and higher monitor units (MUs); VMAT could overcome this, but comparative studies are lacking. The aim of our retrospective study was to compare VMAT and IMRT treatment plans for HNC focusing on target coverage, doses to organs at risk (OARs) and on radiation-induced toxicity.

Methods: Clinical and dosimetric data of 24 HNC (oropharynx, oral cavity, larynx, cutaneous, parotid and unknown primary) treated with IMRT (14) and VMAT (10) were recorded. Dose-Volume histograms (DVHs) were utilized to obtain doses to PTVs (high dose, high risk and low risk) and OARs including spinal cord, brain stem, parotids, mandible, esophagus. IMRT and VMAT plans comparison considered dosimetric parameters for all structures, monitor units per fraction (MU/fx), conformal index (CI), homogeneity index (HI), gradient index (GI) and delivery time. Radiation-induced toxicities were recorded according CTCAE v4.3 scale.

Results: Nine of 24 HNC patients received definitive radiotherapy (IMRT=5, VMAT=4) with a total dose of 66-70 Gy and 15 postoperative (IMRT=9, VMAT=6) with a total dose of 60-66Gy. Mean follow up was 12,74±10 months. Overall, VMAT provided similar target coverage, CI, HI and GI as shown in Table1. Statistically significant differencein favor of VMAT plans was observed forhigh-dose PTV coverage (D98%VMATwas 93,27±2,41and D98% IMRT91, 66±1,99, p=0,014), CI of high-dose PTVs (CI VMAT 0,9614±0,0182 and CI IMRT 0,9115±0,0753, p=0,031) and low-risk PTV coverage (D2% VMAT was 83,60±2,71 and D2% IMRT 85,22±6,55, p=0,019). There were no differences in sparing OARs. In addition, VMAT plans had a lower number of monitor units on average (MU=734.08±206.62) than IMRT plans (MU=1075.41±231.17). Mean delivery timewith VMAT and IMRT was 9.24 and 3.29 minutes, respectively. Rates of toxicity in IMRT and VMAT group were similar, with G3 acute mucositis in 2 and 3 cases, respectively; G3 acute and late dysphagia was observed in one case in both groups.

Conclusions: Our results seem to show that compared to IMRT, VMAT plans can achieve similar target coverage and OARs and normal tissues sparing, with a slight gain for small PTVs besides a significant reduction in delivery time and MU/fx.

**Table 1. Dosimetric results for PTV-HD, PTV-HR and PTV-LR.**

**Dosimetric results for the PTV-HD (66-70)**

| Parameter | IMRT | VMAT | p |
|---|---|---|---|
| D98 (%) | 91,66±1,99 | 93,27±2,41 | 0,014 |
| D2 (%) | 105,37±0,97 | 105,08±1,03 | 0,268 |
| HI | 0,1391±0,0237 | 0,1175±0,0246 | 0,153 |
| CI 95% | 0,9115±0,0753 | 0,9614±0,0182 | 0,031 |
| GI | 13,50±4,64 | 14,76±6,41 | 0,310 |

**Dosimetric results for the PTV-HR (60-63)**

| Parameter | IMRT | VMAT | p |
|---|---|---|---|
| D98 (%) | 88,91±4,16 | 82,64±6,68 | 0,489 |
| D2 (%) | 94,48±0,97 | 95,37±6,09 | 0,393 |
| HI | 0,0625±0,0338 | 0,1426±0,0450 | 0,192 |
| CI 95% | 0,99±0,01 | 0,97±0,02 | 0,081 |
| GI | 6,74±1,31 | 5,78±1,55 | 0,242 |

**Dosimetric results for the PTV-LR (54-60)**

| Parameter | IMRT | VMAT | p |
|---|---|---|---|
| D98 (%) | 76,08±6,44 | 73,47±3,97 | 0,163 |
| D2 (%) | 85,22±6,55 | 83,60±2,71 | 0,019 |
| HI | 0,1085±0,0527 | 01286±0,0349 | 0,138 |
| CI 95% | 0,96±0,27 | 0,94±0,08 | 0,410 |
| GI | 4,57±1,15 | 4,13±0,8 | 0,171 |

PTV-HD: high-dose PTV; PTV-HR: high-riskPTV; PTV-LR: low-risk PTV;
CI: conformal index ; HI: homogeneity index , GI: gradient index

## PO011

### STEREOTACTIC BODY RADIOTHERAPY IN PANCREATIC CANCER: A NATIONAL SURVEY BY THE AIRO GASTROINTESTINAL STUDY GROUP ON INDICATIONS, VOLUMES DEFINITION AND DOSE PRESCRIPTIONS

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Aims: Currently, stereotactic body radiation therapy (SBRT) is intensively investigated in pancreatic cancer, thanks to the advantages of a short overall treatment time, minimal interruption of systemic therapy, and high ablative doses to the tumor. However, a great variability about indications, volume definition and doses are reported. Then, the Italian Association of Radiation and clinical Oncology (AIRO) study group of gastrointestinal malignancies proposed a national survey aiming to investigate this scenario.

Methods: In October 2018, a questionnaire was sent to all Italian Institutions performing pancreatic SBRT.

Results: Twenty-two centers joined the survey. Three (14%) of them treat more than 20 pancreatic cases/year. SBRT is performed for unresectable locally advanced pancreatic cancer (LAPC) and/or local recurrences in 100% and/or for neoadjuvant treatment in bor-

derline resectable (BR) disease in 45% of the centers. Clinical Target Volume is defined as the Gross Tumor Volume (without margins in 8 centers, 40%) delineated by a co-registration (90.9% of the centers) with diagnostic CT (90%), Magnetic Resonance Imaging (47%), and/or 18F-Positron Emission Tomography (42%).

A large diversity of fractionation schemes is reported between centers, as shown in the Table. Due to this variability, the prescribed tumor doses are converted to Biological Effective Doses (BED), assuming tumor and late reacting normal tissue (stomach and small bowel) a/b ratios of 10Gy and 3Gy, respectively. The majority of the centers (72%) delivers a 5-fraction schedule with a total dose of 25-30Gy, for both LAPC and BR patients. In the 80% of the centers the optimal prescription isodose level is chosen between 85-95%, with a heterogeneity contained between 110-120% of the prescribed dose. Dimensional criteria (>5cm) and tight margins to normal adjacent structures are declared as major limiting factors for dose prescription in 77% and 95% of the center, respectively.

Conclusions: SBRT has found a wide indication in the treatment of LAPC. Multimodal imaging remains a fundamental requirement for accurate volume delineation. Our analysis shows that highly effective doses (>75Gy BED10) are currently administered only in a small percentage of cases. Based on these results, a multicentric retrospective analysis aiming to evaluate the effectiveness of the most used 5-fraction schedules in LAPC patients is currently ongoing.

**Table**: Doses and fractionation schedules administered in the 22 centers joining the survey (in bold the most used). The prescribed tumor doses are converted to biological effective doses (BED) for tumor ($\alpha/\beta$=10) and late reactions of the stomach and small bowel ($\alpha/\beta$=3), respectively.

| DOSE (Gy) | FRACTION (n°) | BED $\alpha/\beta$=3(Gy) | BED $\alpha/\beta$=10(Gy) |
|---|---|---|---|
| 48 | 8 | 144 | 77 |
| 35 | 7 | 93 | 52 |
| 36 | 6 | 108 | 58 |
| 45 | 6 | 163 | 80 |
| 54 | 6 | 216 | 103 |
| **25** | **5** | **67** | **38** |
| **30** | **5** | **90** | **48** |
| 35 | 5 | 117 | 60 |
| 37.5 | 5 | 131 | 65 |
| 40 | 5 | 147 | 72 |
| 50 | 5 | 217 | 100 |
| 24 | 4 | 72 | 38 |
| 15 | 3 | 40 | 23 |
| 24 | 3 | 88 | 43 |
| 30 | 3 | 130 | 60 |
| 36 | 3 | 180 | 79 |
| 24 | 2 | 120 | 53 |
| 7 | 1 | 23 | 12 |
| 15 | 1 | 90 | 38 |

**PO012**

## WHICH TECHNOLOGY BEHIND STEREOTACTIC BODY RADIOTHERAPY IN PANCREATIC CANCER? A NATIONAL SURVEY CONDUCTED BY THE AIRO GASTROINTESTINAL STUDY GROUP FOCUSED ON PLANNING STRATEGIES, MOTION MANAGEMENT, ACCURACY AND DELIVERY

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Aims: Pancreatic stereotactic body radiotherapy (SBRT) relies on an extremely precise delivery of high dose/fraction to the tumor. Then, accurate protocols are mandatory. The Italian Association of Radiation and clinical Oncology (AIRO) study group of gastrointestinal malignancies proposed a national survey to investigate the currently clinical practice of pancreatic SBRT focusing on planning strategies, motion management, accuracy and delivery.

Methods: In October 2018, a survey was administered to all Italian Centers performing pancreatic SBRT.

Results: Twenty-two Institutes joined the study. The 14% of the centers treats more than 20 cases/year. Stereotactic body-frame is used in 4 centers (18%), whereas a frameless set-up (thermoplastic mask or vac-lok, 16 centers=73%) or not-customized devices (wing boards, 2 centers=9%) are performed in the most of the centers. Organ motion control methods are used in the 63% of the centers (Figure1A). Fiducial markers (2-3 in 50% of cases) are routinely placed for the target movement evaluation or a better localization in 19% of the centers. Computer Tomography (CT) simulation is performed administering iodinated (72%) or oral barium (43%) contrast medium. For Gross Tumor Volume (GTV) delineation a rigid (47%) or dynamic (37%) co-registration with diagnostic CT (90%), Magnetic Resonance Imaging (MRI, 47%), and/or 18F-Positron Emission Tomography (PET, 42%) is carried out in 90.9% of the centers. PET/CT or MRI are also used for simulation and/or planning in some centers (Figure1B). Clinical Target Volume is defined as GTV without margins in 8 (40%) centers. An individual Internal Target Volume is generated in 17 centers (77%). Intensity Modulated Arc Therapy (IMAT) is planned in 85% of the centers. A multifunctional LINAC or dedicated delivery systems (Cyberknife) are employed in 70% and 9% of the centers, respectively. Image-Guided Radiotherapy (IGRT) is performed in all centers before each fraction, and the 9% of them carries out the infraction error correction too.

Conclusions: This survey illustrates the current status of technical strategies for pancreatic SBRT in Italy.

A high quality of treatment is highlighted by organ motion management (including fiducials placement) and volume delineation based on diagnostic imaging, both in almost all centers. A shared agreement and consensus between centers to standardize this treatment approach could improve treatment outcomes in future clinical trials in this scenario.

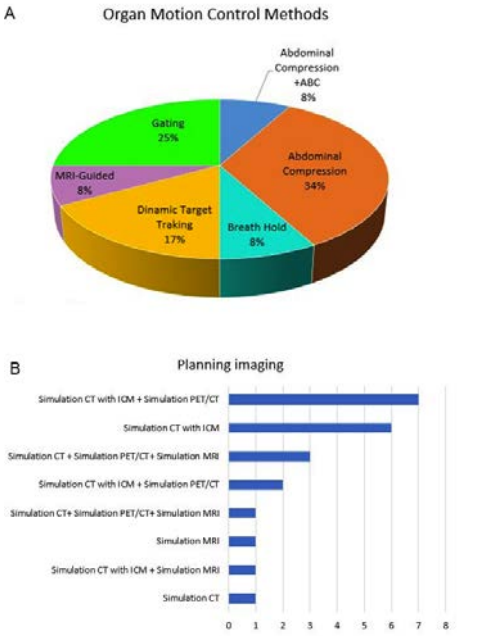


Figure 1: A. Organ motion control methods used in the several centers. (ABC: Active Breath Control. MRI: Magnetic Resonance Imaging). B. Simulation imaging used by the centers. (ICM: intravenous contrast medium)

**PO013**

## PELVIC INTENSITY MODULATED RADIATION THERAPY IN PATIENTS WITH COLIC DIVERTICULOSIS

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Aims: In the last few decades radiotherapy (RT) resulted an effective and widely used treatment for management of pelvic tumors. However, pelvic RT may be the cause of bowel radiation induced injury. Diverticulosis is a widespread disease with increased prevalence in developing world and in elderly patients. It is usually considered as a negative risk factor increasing radiation pelvic toxicity. The aim of this study was to assess the impact of diverticulosis on gastrointestinal toxicity in era of modern pelvic RT.

Methods: A retrospective dosimetric analysis was conducted on 32 patients with incidental diagnosis of uncomplicated colic diverticulosis in at least one of the staging exams (colonoscopy, CT, and/or MRI). All patients underwent pelvic irradiation (4500cGy, 180cGy for fraction) +/- boost prescription according to primary tumor. All treatments were delivered with Intensity Modulated Radiation Therapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT) between 2015 and 2018. Organs at risk (bowel bag and sigma) were delineated according to RTOG guidelines in the treatment field at least 1 centimeter above the Planning Treatment Volume (PTV). All patients with a follow-up shorter than 3 months were excluded. Gastrointestinal acute and late toxicity were recorded according to RTOG and EORTC/RTOG scales, respectively. Clinical data and dosimetric parameters for bowel bag and sigma were collected.

Results: Patients, tumor, treatment characteristics and detailed dosimetric parameters are shown in the Table 1. Overall, 12 patients (37%) experienced G1 acute intestinal toxicity (diarrhea) and 8 (25%) a G2 toxicity (diarrhea, proctitis), according to RTOG scale. None acute toxicity > G2 was recorded. With a median follow-up of 5 months (3-38), none subacute and late intestinal toxicity was reported. Median bowel bag and sigma volume into irradiated field were 2511,5cc (299,55-3679,4) and 78.7cc (25,03-289,17), respectively. Median V45 and Dmean of bowel bag resulted 57,94cc and 2511,5cGy; median V40, V50 and Dmean of sigma were 45,8%, 0,22% and 3749cGy.

Conclusions: Despite the small number of patients, VMAT and IMRT in patients with diverticulosis seems to be safe with acceptable toxicity. Dosimetric parameters showed that IMRT or VMAT are able to reduce the volume of irradiated bowel bag and sigma at doses > 40Gy. The study is still ongoing to confirm these results on a larger number of patients and a longer follow-up.

**Table 1.**

**Patients, tumor and treatment characteristics N (%)**

| | | | | |
|---|---|---|---|---|
| *Tumor site* | Gynecologic 15 (47) | Anal 3 (9) | Rectum 6 (19) | Prostate 8 (25) |
| *Median age* | 70 | 69 | 69 | 72,8 |
| *Diabetes* | 2 (6) | 0 | 1 (3) | 1 (3) |
| *Hypertension* | 8 (25) | 0 | 2 (6) | 4 (13) |
| *Acute intestinal toxicity G1* | 7 (22) | 1 (3) | 1 (3) | 3 (9) |
| *G2* | 4 (12,5) | 1 (3) | 2 (6) | 1 (3) |
| *Total Dose prescription (range, cGy)* | 4500-5400 | 5400-6000 | 5500 | 6800-7800 |
| *Concomitant chemotherapy /Hormonal therapy* | 7 (22) | 3 (9) | 6 (19) | 8 (25) |

***Dosimetric parameters***

| ***Bowel bag*** | | | | ***Sigma*** | | | |
|---|---|---|---|---|---|---|---|
| | Min | Max | Median | | Min | Max | Median |
| V5 (cc) | 299,6 | 3563,6 | 1133 | V5 (%) | 69,63 | 100 | 100 |
| V15 (cc) | 281,9 | 2584,1 | 884,7 | V15 (%) | 48,75 | 100 | 100 |
| V30 (cc) | 103,3 | 979,9 | 33,41 | V30 (%) | 16,51 | 100 | 83,7 |
| V40 (cc) | 61,1 | 497,2 | 191,83 | V40 (%) | 4,21 | 96,24 | 45,8 |
| V45 (cc) | 7,16 | 182,58 | 57,94 | V50 (%) | 0 | 66,12 | 0,22 |
| D2cc (cGy) | 4433 | 6831 | 4675,5 | D2 cc (cGy) | 4262 | 6832 | 4753,5 |
| Dmean (cGy) | 1098 | 3821 | 2511,5 | Dmean (cGy) | 176,88 | 4571 | 3749 |
| Volume (cc) | 299,55 | 3679,4 | 2511,5 | Volume (cc) | 25,03 | 289,2 | 78,7 |

**PO014**

## ULTRA-HIGH B2000 VERSUS B1000 DIFFUSION-WEIGHTED MRI IN LOCALLY ADVANCED RECTAL CANCER TREATED WITH NEOADJUVANT CHEMO-RADIOTHERAPY: A QUALITATIVE AND QUANTITATIVE COMPARISON

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Aims: T2 weighted MRI is the gold standard for locally advanced rectal cancer (LARC) staging submitted to neoadjuvant chemoradiotherapy (CRT). Diffusion-Weighted (DWI) images are able to improve treatment response assessment. Our study aimed to investigate the potential benefit of ultra-high DWI, comparing qualitatively and quantitatively b=1000 s/mm2 (b1000) and b=2000s/mm2 (b2000) value, for tumors detectability and conspicuity.

Methods: Thirty-three non-mucinous rectal cancer patients were retrospectively analyzed, with 42 3T MRI performed as diagnostic and/or restaging after neoadjuvant CRT. An expert radiologist (Reader 1) and an in training one (Reader 2) delineated the tumor and assessed the presence of tumor conspicuity (how much the tumor is bright respect to the background) on b1000 and b2000, comparing signal intensity distribution of the tumor and the surrounding tissue. Distribution normality was tested via Shapiro-Wilk test; b1000 and b2000 images were compared using Mann-Whitney test. Inter-observer agreement (IOA) was calculated with Cohen's Kappa and Intraclass Correlation Coefficient (ICC).

Results: Twenty-four patients with 29 MRI were finally analyzed: 18 (62%) diagnostic and 11 (38%) restaging MRI. Of these 11, 6 (21%) showed pathologic complete response and 5 (17%) residual tumor at pathology. Two restaging exams were excluded because of artefacts, leaving 9 (31%) evaluable restaging MRI. On the 18 baseline MRI, both readers correctly identified tumors in all b1000 and b2000 images. On the 9 restaging MRI, both readers correctly identified all tumors, except in a case in which it was correctly identified only on b2000. For patients with a detected tumor on DWI, mean overall conspicuity scores were higher for b2000 compared to the b1000 (3.57 vs 2.85 for Reader 1, $p=0.001$; 3.0 vs 2.45 for Reader 2, $p=0.002$). IOA agreement was good for both b-values ($k=0.71$ for b1000, $k=0.65$ for b2000). In the tissue surrounding the tumor, the mean signal intensity was significantly lower using b2000 ($p<0.05$) respect to b1000, in which it was significantly higher ($p<0.05$). The IOA for the signal intensity in the tumor bed improved from b1000 to b2000 (ICC=0.60 and 0.79, respectively).

Conclusions: Ultra-high b2000 DWI has the potential to improve tumor conspicuity in LARC patients. This could be more beneficial in the restaging, where the differentiation between complete and no/partial response is particularly important for conservative strategies.

**PO015**

## VOLUME DELINEATION IN CERVICAL CANCER WITH T2 AND DIFFUSION-WEIGHTED MRI: AGREEMENT ON VOLUMES BETWEEN OBSERVERS

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Aims: Standard treatment for locally advanced cervical cancer is represented by external beam radiotherapy (EBRT), concurrent chemotherapy and brachytherapy. T2-weighted MRI is the gold standard for tumor volume delineation. As for others tumors, functional Diffusion-Weighted MRI (DWI) images, in combination with T2-MRI, are able to improve lesion detection. The aim of our study was to evaluate the difference in GTV delineation based on T2 weighted and Apparent Diffusion Coefficient maps (ADC-MRI), evaluating volumes and inter-observer agreement between a radiologist and a radiation oncologist, in order to improve volumes delineation in cervical cancer patients.

Methods: We evaluate 37 cervical cancer patients, who underwent diagnostic 1.5T MRI. Imaging study including axial T2 weighted MRI and ADC maps, calculated with the use of minimum 2 different b values. Median age was 55 years (range: 28-94). According to FIGO classification, 2 (5.4%) patients were staged 1B1, 6 (16.2%) patients 2A1, 17 (46%) 2B, 2 (5.4%) 3B and 10 (27%) patients staged 4A. Two observers, one radiologist and one radiation oncologist delineated GTV on T2 (T2GTV) and ADC (ADCGTV) sequences, blinded and independently from each other. GTV volume (cm3) was measured for T2 and ADC for each observer, and evaluated using the t-test. Observer agreement was assessed using DICE index, Bland-Altman analysis (mean difference, 95% limits of agreement), coefficient of repeatability (CR) and intraclass correlation coefficient (ICC).

Results: Mean T2GTV and ADCGTV volumes were 43.84±71.47cc and 37.28±68.92cc for radiologist, and 43.4±70.44cc and 36.65±69.21cc for radiation oncology, respectively. Significant larger volumes were obtained using T2 compared to ADC ($p<0.001$ and $p<0.001$ for both observers). Concordance plots for T2 and ADC between observers are shown in Figure 1,

respectively. Mean DICE index, ICC and CR are 0.86, 0.998 and 7.984 for T2GTV, and 0.84, 0.999 and 5.496 for ADCGTV, respectively. The Bland-Altman plots show some outliers out of the limits of agreements (Figure 1), but globally the methods for the two observers are in accordance, conforming to the CR coefficients.

Conclusions: ADC resulted in smaller volumes compared to T2 weighted MRI in GTV delineation, with an almost perfect agreement between radiologist and radiation oncologist. It could be an option to evaluate the role of ADC for target contouring, with an acceptable variability between different observers.

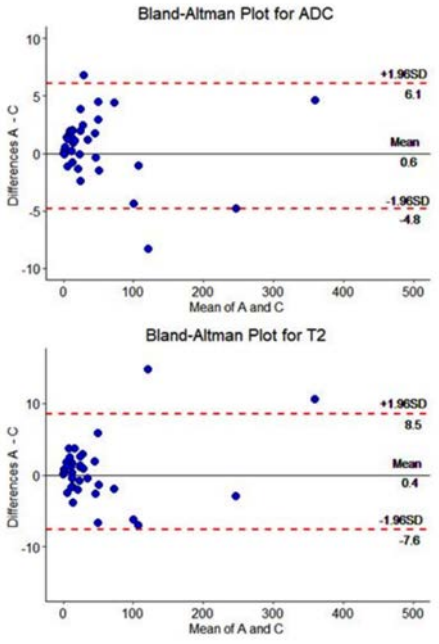


**Figure 1.** Bland-Altman concordance plot between radiologist and radiation oncologist against their mean for $T2_{GTV}$ and $ADC_{GTV}$, respectively. The lower and upper 95% limits of agreements are represented as dotted lines; the mean difference is represented as a continuous line. $T2_{GTV}$ [panel left; mean difference 0.6 (95% limits of agreement -4.8; 6.1)] and in $ADC_{GTV}$ [panel right; mean difference 0.4 (95 limits of agreement -7.6; 8.5)].

## PO016

## DO WE NEED SIGMA SPARING CONSTRAINTS IN ERA OF INTENSITY-MODULATED RADIATION THERAPY FOR PROSTATE CANCER? A MONO-INSTITUTIONAL ANALYSIS OF DOSE-VOLUMES PARAMETERS AND GASTROINTESTINAL TOXICITY

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Aims: Intensity and/or volumetric modulated radiotherapy (IMRT, VMAT) have demonstrated to significantly reduce high doses to rectum and bladder, and related acute and late toxic effects, and currently represent the standard technique in the treatment of prostatic cancer. Moreover, the wide atlases availability allows a high accurate definition of treatment volumes and organs at risk (OARs) with likely outcomes improvement. Currently, according to RTOG atlas, sigma represents an OAR in prostate radiotherapy. However dose constraints for sigma are to date not available. In this context the aim of this study was to analyze sigma dose-volume parameters and intestinal (GI) toxicity in prostate cancer patients treated with IMRT/VMAT.

Methods: A retrospective evaluation of all patients with sigma included in the treatment field (at least 2 cm above the Planning Target Volume, PTV) treated in our institution, and with a minimum follow-up of 6 months, was conducted. Clinical data, early and late GI toxicity (RTOG scale) and dose-volume parameters were collected and analyzed. V15, V30, V40, V45, V50, V60, V70, Dmax, Dmean and median volume of sigma were evaluated.

Results: Fifty-eight patients with prostate acinar adenocarcinoma treated from 2015 to 2018 were analyzed; median age was 72 (range 45-81). Hormonal therapy was administered in 43 patients (74%). Treatment intent was exclusive, adjuvant or salvage in 17 (29,3%), 18 (31%) and 13 (biochemical: 20,7%; macroscopic recurrence: 1,7%) patients, respectively. According to treatment doses (66-70Gy vs 72-78Gy), and volumes (whole pelvis vs no-whole pelvis) sigma dose-volume parameters were evaluated in 4 subgroups of patients (Table 1). Overall, limited volumes of sigma in treatment field was reported in all subgroups. The median follow-up was of 18,45 months (range 6-39,5). Overall, early and late Grade 2 GI toxicity (diarrhea, tenesmus, rectal bleeding, fecal incontinence) was reported in 10,3% and 1,7% patients, respectively. None early and/or late GI toxicity > grade 2 was reported.

Conclusions: Our results on a limited number of patients did not show Grade > 2 GI toxicity and high doses (V50%, V60%, V70%) were delivered only to small volumes of sigma, although specific constraints for sigma were not applied during planning optimization. These results highlights the ability of IMRT/VMAT to reduce toxicity. The study is still ongoing to confirm these results on a larger number of patients and a longer follow-up.

**Table.** Sigma and Planning Target Volume (PTV) parameters evaluated in 4 subgroups of patients according to treatment doses (66-70Gy vs 72-78Gy), and volumes (whole pelvis=WPRT, vs no-whole pelvis=NO WPRT).

| | 66-70 Gy (33 patients) | | | 72-78 Gy (25 patients) | | | WPRT (20 patients) | | | NO WPRT (38 patients) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sigma | Minimum | Maximum | Median | Minimum | Maximum | Median | Minimum | Maximum | Median | Minimum | Maximum | Median |
| V15 (cc) | 1,11 | 123,52 | 29,1 | 0,74 | 153,11 | 29,09 | 3,71 | 153,11 | 28,43 | 0,74 | 67,21 | 28,19 |
| V30 (%) | 2,18 | 100 | 45,67 | 9,81 | 100 | 48,98 | 25,32 | 100 | 45,55 | 2,18 | 92,21 | 45,55 |
| V40 (%) | 0 | 98,6 | 31,8 | 0,48 | 100 | 32,03 | 16,48 | 100 | 31,78 | 0 | 79,13 | 31,78 |
| V45 (%) | 0 | 95,52 | 18,07 | 0 | 68,38 | 19,01 | 6,23 | 95,52 | 17,6 | 0 | 63,38 | 18,54 |
| V50 (%) | 0 | 89,48 | 8,02 | 0 | 62,15 | 10,04 | 0 | 89,48 | 8,72 | 0 | 62,15 | 9,97 |
| V60 (%) | 0 | 78,35 | 2,49 | 0 | 49,84 | 3,04 | 0 | 78,35 | 2,49 | 0 | 49,84 | 2,96 |
| V70 (%) | 0 | 1,4 | 0 | 0 | 9,5 | 0 | 0 | 1,66 | 0 | 0 | 9,5 | 0 |
| Dmax (cGy) | 3642 | 7769 | 6751 | 4173 | 8384 | 6772 | 4878 | 7857 | 6759 | 3642 | 8384 | 6764 |
| Dmean (cGy) | 510 | 6188 | 3127 | 579 | 5680 | 3205 | 2159 | 6188 | 3159 | 510 | 5680 | 3095 |
| Sigma Volume (cc) | 4,33 | 123,52 | 37,84 | 2,04 | 167,88 | 38,77 | 3,71 | 167,88 | 37,95 | 2,04 | 89,31 | 37,84 |
| PTV D2% | 100,87 | 106,13 | 103,63 | 101,12 | 104,1 | 103,49 | 101,12 | 104,22 | 103,58 | 100,7 | 104,1 | 103,63 |
| PTV D98% | 93,21 | 98,67 | 94,98 | 93,21 | 96,61 | 95,22 | 93,57 | 97,84 | 95,29 | 93,21 | 96,61 | 95,23 |

**PO017**

## STEREOTACTIC RADIOTHERAPY AND AUTOMATIC TABLE REPOSITION

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Aim: Analyze and correct the positioning errors in the 6 freedom degrees of the treatment table, translation (Y, X, Z) and rotation (coronal, sagittal, transversal), in patients with intra and extracranial disease treated with stereotactic radiotherapy.

Methods: From March to May 2019 four patients were treated with stereotactic radiotherapy for metastatic disease. Patient A with three brain metastases of breast cancer origin; patient B with a paravertebral metastasis and with a pelvic lymphnode metastasis of prostate cancer origin; patient C with a paraesophageal lymphnode metastasis of lung cancer origin; patient D with a pelvic lymphnode metastasis of prostate cancer origin. All patients underwent daily IGRT verification and in all patients automatic table translation and rotation correction were performed for each radiotherapy session. All patients had a specific immobilization system and all patients were treated with the "Elekta VERSA HD" linear accelerator equipped with the "HexaPOD" automatic table rotation system.

Results: An average was made in all freedom degrees for every patient treated. Patient A: avg translation Y=0.13cm, X=0.1cm, Z=0.07cm; avg rotation coronal 0.93°, sagittal 1.26°, transverse 2.03°. Patient B: avg translation Y=0.4cm, X=0.42cm, Z=0.48cm; avg rotation coronal 1.54°, sagittal 1.84°, transverse 0.26°. Patient C: avg translation Y=1.22cm, X=0.22cm, Z=0.62cm; avg rotation coronal 1.52°, sagittal 1.84°, transverse 0.26°. Patient D: avg translation Y=0.13cm, X=0.23cm, Z=0.33cm; avg rotation coronal 2.2°, sagittal 1.7°, transverse 0.43°. The average for every shift on all treated patients were made: avg translation Y=0.47cm, X=0.24cm, Z=0.37cm, coronal avg rotation 1.55°, sagittal 1.72°, transverse 0.87°.

Conclusions: In our experience, although limited to a small number of patients, the automatic movement of the table, in the 6 degrees of freedom, is a valid support to guarantee a more accurate positioning of the patient treated with stereotactic radiotherapy. Due to type of different errors linked with the patient collaboration, operator experience, to the immobilization system used, to the irradiated body district, it's necessary use this process for every single session.

**PO018**

## ROLE OF 18F-FDG-PET/CT IN ADJUVANT TREATMENT OF ENDOMETRIAL CANCER

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Aims: Aim of this study was to define the role of 18-Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography (18F-FDG-PET/CT) in the adjuvant treatment of endometrial cancer.

Methods: High risk endometrial cancer is defined by some characteristics, based on pathological International Federation of Gynecology and Obstetrics (FIGO) staging, grading and histotype, that determine the proper adjuvant treatment (radiotherapy and/or brachytherapy and/or chemotherapy) in order to reduce the chance of relapse. Surgery provides a lymphadenectomy, that sometimes has not been done: the absence of it or an insufficient lymphadenectomy are considered further risk factors that may change the adjuvant treatment. Patients who referred to our center after surgery for endometrial cancer and that performed 18F-FDG-PET/CT between 2008 and 2018 were included. All patients would have been treated with radiotherapy because of the presence of at least one risk factor. The primary end-point was to investigate how often and in what way the 18F-FDG-PET/CT has changed the adjuvant treatment of high-risk endometrial cancer. Secondary objective was to analyse correlations between patients' risk factors and FDG-PET/CT data.

Results: 58 patients were included. In 24 patients (41.4%) the 18F-FDG-PET/CT was positive at different sites, as pelvic disease, pelvic or paraaortic lymph nodes, metastases or an association of them. 6 patients (10.3%) were not submitted to radiotherapy and they did other treatments, because of the evidence of metastatic disease or for medical decisions. 18 patients underwent to radiotherapy and 14 of them also to brachytherapy treatment. Between patients treated with radiotherapy, in 12 cases (20.7% of the total) the radiotherapy treatment was redefined according to PET.

Results: 10 patients received also a boost (sequential or concomitant) to the 18F-FDG-PET/CT positive area, 1 patient had a brachytherapy boost and in a patient the treatment volume was modified. All the 34 patients (58.6%) with negative 18F-FDG-PET/CT have performed the radiotherapy treatment.

Conclusions: According to international guidelines, the role of 18F-FDG-PET/CT in the adjuvant setting of endometrial cancer is not still clearly defined. In intermediate-high risk endometrial cancer, 18F-FDG-PET/CT is important in the adjuvant setting to adequately treat patients: based on PET findings, we reported 31% of cases in which the planned adjuvant treatment was changed.

**PO019**

## COMPARISON BETWEEN SIMULATION PET-CT AND FUSION WITH DIAGNOSTIC PET-CT IN HEAD AND NECK RADIOTHERAPY PLANNING. EFFECTS ON TARGET VOLUME DETERMINATION

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Aims: To evaluate volumetric discrepancies between Gross Tumor Volume (GTV) delineated on simulation PET-CT (sPET-CT) and simulation CT fused with diagnostic PET-CT (dPET-CT), in patients with head and neck (H&N) cancer.

Methods: Twenty consecutive H&N cancer patients underwent to sPET-CT, in treatment radiotherapy set-up (flat top, mould), using a specific optimized PET acquisition protocol (2 beds, matrix 400x400, 6 minutes/bed). All patients also underwent to whole body dPET-CT (matrix 200x200, 2.5 minutes/bed) that was co-registered and fused with planning CT using a rigid algorithm (mutual information intensity-based metrics). Both on sPET-CT and dPET-CT primary GTVs were delineated manually (mGTV) and using an automated threshold method at 50% and 40% of the intralesional SUV max (50%tGTV, 40%tGTV). GTVs differences were analyzed in terms of volumetric absolute values, DICE similarity index (DSI), Jaccard Index (JI) and distances from centroids.

Results: Mean distance between centroid of 50%tGTVs on sPET-CT vs Co-registered PET-CT was 0.94 cm (0.25-2.17cm). Comparing these volumes, low mean values for JI (0.2 [0-0.5]) and DSI (0.3 [0-0.8]) were found. Figure 1A. Despite different acquisition protocol, 50%tGTV obtained from sPET-CT and dPET-CT, showed a high correlation in terms of absolute volume (Pearson correlation coefficient R=0.97); analogous considerations were reported for 40%tGTV. The 50%tGTVs were, by definition, smaller than 40%tGTVs in the totality of cases, both on dPET-CT and sPET-CT, notably, the mean volumetric reductions were of 40% and 37%, p<0.005. Similarly, 50%tGTVs were smaller than mGTVs in the totality of cases, with mean volumetric reductions of 63% and 69%, p<0.005. Figure 1B. The 40%tGTVs were smaller than mGTVs in 16/20 cases for dPET-CT and in 19/20 cases for sPET-CT, p<0.005.

Conclusions: Shift errors related to the image fusion process among series in different set-up, negatively influenced similarity between target volumes. The high correlation (R=0.97) between threshold GTVs suggests reproducibility of the automatic based contouring method; we observed agreement between optimized sPET-CT protocol and standard dPET-CT protocol in terms of intralesional SUV values. In these preliminary evaluations, sPET-CT could be considered an optimization in Radiotherapy workflow for H&N cancer management to reduce image fusion uncertainties and to standardize GTV delineation.

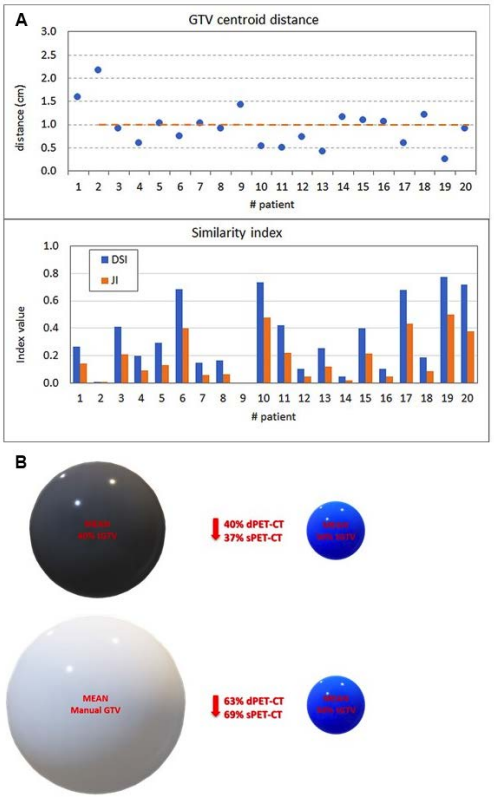


**Figure 1.**

**PO020**

## SIMULATION PET-CT BASED DIRECT PLANNING IN HEAD AND NECK RADIOTHERAPY. PRELIMINARY OUTCOME RESULTS AND TREATMENT PLANNING IMPLICATIONS

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Purpose: To evaluate the impact of a simulation PET-CT (sPET-CT) and direct planning protocol in head and neck (H&N) cancer radiotherapy (RT): we report early clinical outcome and treatment planning implications.

Methods: Sixteen consecutive H&N cancer patients underwent to an optimized protocol of sPET-CT in RT set-up. Gross Tumor Volume (GTV) was delineated using automated threshold method at 50% of the intra-lesional SUV max. Clinical Target Volume (CTV) was obtained adding a 9 mm isotropic margin, respecting anatomical boundaries. In the same patient cohort, we compared the dosimetric differences between plans optimized on sPET-CT and the former standard (whole body diagnostic PET-CT -dPET-CT- fused with simulation-CT using a rigid algorithm). On simulation-CT fused with dPET-CT, CTVs were obtained from manually delineated GTVs plus margins as previously described. Volumetric modulated arc therapy (VMAT) plans were designed considering also elective nodal irradiation. We compared target coverage, conformity index (CI), organs at risk (OARs) dose differences between VMAT plans elaborated on dPET-CT and sPET-CT. To evaluate early clinical outcome, PET-CT and/or CT plus clinical examination, were performed 3 and 6 months after RT.

Results: All 16 enrolled patients showed GTV evidence on PET-CT. Subsites involved were: oral cavity (4), oropharynx (5), larynx (6), and hypopharynx (1). Dose prescription ranged from 66 to 70 Gy. 11/16 patients had concurrent chemotherapy. All patients completed RT. At 6 months mean follow-up, 12/16 patients showed a complete response at PET-CT and/or CT plus clinical examination; 2/16 showed a partial response and 1/16 disease progression. Planning comparison showed a good coverage of targets generated from sPET-CT when introduced into the plans optimized on dPET-CT in 14/16 cases (v95%>95%) but with a decrease of CI in all cases (mean reduction 18%, range 7%-35%). Comparing plans optimized on dPET-CT vs sPET-CT, a slightly but costant dose reduction to OARs was observed in sPET-CT cases.

Conclusion: In our cohort, sPET-CT could be considered an optimization in RT planning. H&N patients undergone to sPET-CT direct planning protocol showed good early responses to treatment. Longer follow up and larger series are needed to confirm these data. We reported adequate coverage of sPET-CT volumes in plans optimized on conventional dPET-CT volumes at the expense of lower CI and a potential reduction of OARs dose in sPET-CT plans.

**PO021**

## THE ROLE OF CYBERKNIFE→ STEREOTACTIC RADIOTHERAPY IN THE TREATMENT OF ORBITAL PRIMARY AND SECONDARY TUMORS: A MONOISTITUTIONAL EXPERIENCE

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Aims: Orbital lesions are rare but responsible for severe symptoms such as visual deficits, pain, ocular motility disorders with negative impact on the patient's quality of life. Their proximity to critical structures makes treatment difficult. Stereotactic radiotherapy (SRT) with CyberKnife® (CK) System can be a valid treatment option. The aim of this study is to evaluate the safety and efficacy of this type of therapy.

Methods: From December 2013 to February 2019, 15 consecutive patients with primary or secondary orbital lesions were treated in our Institute with CK RT. We evaluated: local control (LC) as the sum of complete response (CR), partial response (PR) and stable disease (SD) according to RECIST criteria; median overall survival (OS) and disease free survival (DFS) from the date of CK SRT procedure; toxicity using CTCAE scale. Statistical analysis was performed to find the factors influencing the development of toxicity. A p-value<0.05 was considered statistically significant.

Results: Patients and treatment characteristics are summarized in Table 1. The median follow-up was 7 months (1-44 months). OS and DFS were 48 months (5-212) and 7 months (1-44), respectively. During follow-up 2 patients died due to neoplastic cachexia. Before therapy, 11 patients were symptomatic, the most frequent symptoms were pain and vision disorders. After treatment one of the 4 non-symptomatic patients developed symptoms, instead of the 11 symptomatic patients 5 improved, 5 remained stable, 1 had a worsening of the visus. We observed SD in 13 patients (86.7%) and PR in two cases (13.3%). Treatment was well tolerated and only 1 patient stopped treatment due to seizures. Toxicity ≤G2 was observed in 7 patients. No statistically significant relationship was observed between characteristics of patients as well as age, sex, type of lesion and the occurrence of toxicity using chi-square.

Conclusions: This study highlights how the SRT of orbital lesions with CK System is safe, effective and

able to control visual symptoms with a positive impact on the quality of life of patients.

**Table 1. Patients and treatment characteristics.**

| Patients characteristics | |
|---|---|
| Sex | F: 10 (66.7%)<br>M: 5 (33.3%) |
| Age (median) | 61 years (6-81) |
| Karnofsky performance status (median) | 80 (70-100) |
| Lesion | Primary: 7 (46.7%)<br>Secondary: 8 (53.3%) |
| Histology | Breast: 5 (33.3%)<br>LNH: 3 (20%)<br>Meningioma: 2 (13.2%)<br>Sarcoma: 1 (6.7%)<br>Bladder: 1 (6.7%)<br>Melanoma: 1 (6.7%)<br>Hemangiopericytoma: 1 (6.7%)<br>Unknown primary: 1 (6.7%) |
| Affected eye | Left: 8 (53.3%)<br>Right: 6 (40%)<br>Bilateral: 1 (6.7%) |
| Orbital localization | Roof: 4 (26.7%)<br>Floor: 5 (33.3%)<br>Lateral wall: 3 (20%)<br>Medial wall: 3 (20%) |
| Symptomatic lesion | Yes: 11 (73.3%)<br>No: 4 (26.7%) |
| Pre-radiotherapy biopsy | Yes: 7 (46.7%)<br>No: 8 (53.3%) |
| **Treatment characteristics** | **median (range)** |
| Total prescription dose | 20 Gy (18-25) |
| Number of fractions | 5 (1-5) |
| Prescription isodose % | 80% (77-80) |
| GTV volume | 3.9 cc (0.58-19.81) |
| Ipsilateral eye Dmax | 2069 cGy (356-2526) |
| Ipsilateral lens Dmax | 191.25 cGy (19.99-2025.49) |
| Ipsilateral optic nerve Dmax | 211.3 cGy (28.49-2135.46) |
| Optic chiasm Dmax | 317 cGy (4-1275) |
| Brainsteam Dmax | 193 cGy (4.85-2401) |

## PO022

### UPDATE ON ACUTE AND LATE TOXICITY OF HYPOFRACTIONATED RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER: INTENSITY – MODULATED RADIOTHERAPY VERSUS TOMOTHERAPY

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Aims: To evaluate the incidence of acute and late toxicity after hypofractionated radiotherapy using Linac intensity-modulated radiotherapy (IMRT) compared with helical Tomotherapy (HT).

Methods: From September 2016 to October 2018, 160 consecutive patients with localized prostate cancer (cT1-2, GS< 8, PSA<10 ng/ml) were randomized to Linac IMRT and to helical Tomotherapy. 80 patients were treated with Linac IMRT and 80 with TOMO. Patients were monitored before therapy, weekly during therapy, 2 weeks, three and six months after radiotherapy was completed, using RTOG GI and genitourinary toxicity grading scale. Patients received radiotherapy schedule according to histology reports following international guidelines. Doses were prescribed to planning target volumes (PTVs) as the followings: 72 Gy (2.4 Gy/fx) to PTV-whole prostate and 64.5 Gy (2.15 Gy/fx) to PTV-prostate and seminal vescicles in 30 fractions with SIB technique. Dose to abdominal cavity, both femoral heads, bladder and rectum were constrained below each tissue tolerance.

Results: Median age of the patients was 72.5 (range 55-86 years). At the end of the treatment (6 weeks), 23/80 (29%) patients in the TOMO group vs. 28/80 (35%) patients in the Linac IMRT group had G1-G2 grade of GI toxicity (p=0.009), while 3/80 (4%) patients in the TOMO group vs. 6/80 (7.5%) patients in the Linac IMRT group had G3 grade of GI toxicity. 39/80 (49%) patients in the TOMO group vs. 45/80 (56%) patients in the Linac IMRT group had G1-G2 grade of GU toxicity (p=0.04), while 2/80 (2.5%) patients in the TOMO group vs. 5/80 (6%) patients in the Linac IMRT group had G3 grade of GU toxicity. No G4 grade of GI and GU toxicity was showed. After 6 months from the end of the treatment, no patients in the TOMO group vs. 3/80 (4%) patients in the Linac IMRT group had G1-G2 grade of GI toxicity, while 2/80 (2.5%) patients in the TOMO group vs. 4/80 (5%) patients in the Linac IMRT group had G3 grade of GU toxicity.

Conclusions: Acute toxicity is very low. Most of the recorded symptoms decrease over time. A small increase in mild toxicity, statistically significant, was observed in the Linac IMRT group when compared with TOMO group. Our study confirmed that Tomotherapy allows for safe moderate hypofractionation, offering a shorter overall treatment time, a lower rate of acute and late toxicities and providing potentially more economic health care.

## PO023

### NOVEL "BAYESIAN PENALIZED LIKELIHOOD" (Q.CLEAR) PET RECONTRUCTION ALGORITHM FOR TARGET DELINEATION IN OROPHARYNX CANCER

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Purpose: Image acquisition factors affect the performance of PET for radiotherapy planning. The Ordered Subset Expectationn Maximization algorithm (OSEM) is usually employed in clinical routine. It led to an enhanced contrast but amplifies noise in the image. The novel Bayesian penalized likelihood (Q.Clear, GE Healthcare) recontruction algorithm has been shown to reduce noise in recontructed image and improve signal-to-noise ratio with respect to OSEM. We investigated the effect of the Q.Clear recontruction algorithm on analysis of oropharynx cancer patients examined with 18F-FDG PET-CT, and determined its effect on target definition.

Methods and Materials: High-resolution 18F-FDG PET-CTs performed for radiation therapy simulation in eight patients with locally advanced oropharynx cancer were reconstructed using the new algorithm and compared to OSEM reconstruction. Lesion maximum standardized uptake value (SUVmax), mean background SUV (SUVbg), signal-to-background ratio (SBR), total lesion glicolysis (TLG), and primary tumor volume segmentation applying a threshold of 40% of SUVmax (T40), were collected. The T40s were evaluated and compared with the final GTVs edited by radiation oncologist after auto-contouring with known diagnostic informations including findings by other imaging modalities and endoscopy. Percentage volume error (%VE) was used as performance measures. Data were analyzed quantitatively using paired Student's t-test.

Results: Comparing Q.Clear to OSEM, there were significative increments in lesion SUVmax and SBR using Q.Clear (mean ΔSUVmax 2.39, p = 0,0024; mean ΔSBR 1,95, p=0,03). The average lesion T40s decreased from 9,51 $cm^3$ to 7,72 $cm^3$ (p=0,009) after application of the Q.Clear algorithm, with no significant differencies in TLG and SUVbg. Comparing T40 to GTV volumes defined by radiation oncologist, the%VE was significantly higher using Q.Clear than standars OSEM reconstruction (61% and 42%, respectively; p = 0,006).

Conclusions: Q.Clear reconstruction algorithm increased the lesion SUVmax and SBR. Primary tumor volume segmentation applying a threshold of 40% of SUVmax does not appear to be suitable for target volume segmentation in patients with oropharynx cancer when using the novel Q.Clear technology. Fixed and adaptive thresholds for auto-segmentation may vary across different reconstruction methods.

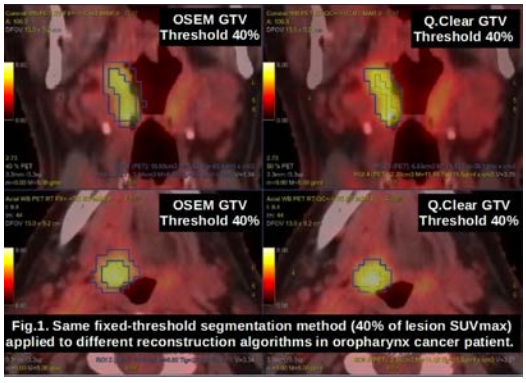


Fig.1. Same fixed-threshold segmentation method (40% of lesion SUVmax) applied to different reconstruction algorithms in oropharynx cancer patient.

**Figure 1.**

**PO024**

## CLINICAL OUTCOMES USING ONCE-DAILY PARTIAL BREAST IRRADIATION (OD-APBI) IN PATIENTS WITH INVASIVE LOBULAR CARCINOMA (ILC): PRELIMINARY RESULTS

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Aims: According to the update of the Consensus Statement of the ASTRO of January 2015, invasive lobular carcinoma (ILC) is not yet considered suitable criteria fot the enrollment of pts in the APBI arm. The purpose of this study is compare clinical outcome of pts with either invasive lobular carcinoma (ILC) or invasive ductal carcinoma (IDC) after treatment with once-day partial breast irradiation (OD-PBI).

Methods: From December 2010 to December 2018, 347 pts with invasive breast cancer (mean age: 65,2 yrs; range 50-86) underwent OD-PBI (38,5 Gy/10 daily fractions) delivered by Helical-Tomotherapy. We present results on 162 pts with a minimum follow-up of 55 months including 17 ILC cases. Of these 8 pts (47%) were pure ILC, 2 pts (11%) had a minimal/focal extensive intraductal component EIC (<5%), and 7 pts (42%) had associated focal LIN 1/2 component (<5%). Clinical, pathologic, and treatment-related factors were compared between ILC and IDC groups. Local recurrence (LR), regional recurrence (RR), axillary failure (AF), distant metastases (DM), disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS) were analyzed.

Results: ILC pts had similar age compare to IDC pts (mean age: 62,8 mths vs 64,9 mths; p=0,633); had slightly smaller tumors (DM: 10,4 mm vs 11,1 mm; p=0,60), and no patient received sistemic adjuvant chemotherapy. 11% of pts with ILC and 12% pts with IDC had lymph-node positive (p=0,992). In both groups the most frequent genetic sub-type was Luminal A-like (82% vs 69%). In ILC pts a trend was noted with a G2/G3 degree of tumor differentiation (G1:18% vs G2/G3:82%, p=0,08), while in the IDC cohort there is a less variability (p=0,73). Median FU was similar (6.3 yrs for ILC pts and 6.4 yrs for IDC pts; p=0,78). No differences were seen in 5-year actuarial rates of LR (0% vs. 0%), AF (0% vs. 0%), RR (0% vs 0%), DM (0% vs 0%), CSS (100% vs 100%) or OS (94,2% vs. 97.%, p=0,78) between the two groups. One pt with IDC developed a contralateral breast tumor 12 months after the end of the OD-PBI. Since no recurrence event was detected, age, tumor size, receptor status, chemotherapy, N-Stage and ILC histological type were not associated with LR,RR and AF.

Conclusions: No differences were seen in the rates of LR, RR or AF between ILC and IDC pts after OD-

PBI with good local control in both groups. These results support the continued enrollment of ILC pts in Phase III trials evaluating the efficacy of APBI.

**PO025**

## PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER (LARC): PREDICTIVE FACTORS OF NODAL RESPONSE TO NEOADJUVANT RADIO-CHEMOTHERAPY (RTCT)

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Aims: Preoperative RTCT followed by total meso-rectal excision (TME) is the standard of cure in patients (pts) with LARC. After neoadjuvant RTCT the rate of complete pathologic response (pCR) range between 15%-30% and many studies are trying to find predictive factors of response in order to select pts who could benefit from intensified loco-regional treatments or organ-preserving options. The primary endpoint of this retrospective analysis was to identify predictive factors of nodal response to neoadjuvant RTCT, which could be used in the next future for treatment decision making.

Methods: We analyzed retrospectively the data of 119 pts affected by LARC (100% cT3-T4 and 90,7% cN+) treated with neoadjuvant RTCT (50.4 Gy in 28 FF + capecitabine 1650 mg/mq/day) followed by TME, between January 2008 and December 2018. Based on MR-images, we analyzed nodal characteristics at diagnosis (clinical nodal stage, number of nodes with lower diameter ≥5mm and their distance from mesorectal fascia) trying to correlate these factors with the pathological nodal response. We also analyzed the time between surgery and the end of RTCT (> or < 8 weeks) and its correlation with nodal response.

Results: All pts completed the planned radiotherapy and underwent surgery. The mean time between the end of RTCT and surgery was 7, weeks (range: 6-8). Twenty-five pts (21%) had metastatic nodes at the pathological examination; twenty of them (80%) were clinically staged as N+ by our calculation (nodes ≥5mm at pelvic MR). The analysis showed a strong correlation with one of the parameters analyzed: the number of nodes ≥ 5 mm either as a continuous variable (p= 0,004) or as a dichotomous variable (number of nodes <3 vs ≥4; p<0,0001).

Conclusions: Know predictive factors of pathological response in pts affected by LARC treated with neoadjuvant RTCT could be important to decide to modify the locoregional treatments itselves. We decided to focusing our study on the analysis of predictive factors of nodal response only; based on our results, we could assume that pts with a greater number of large nodes at diagnosis (≥5mm ) are more likely to have positive lymph nodes at histological finding and could

therefore benefit from an increase in loco-regional treatments. In our study we did not find a correlation between the interval RTCT-surgery and the nodal response, probabily because this parameter was too homogeneous in our cohort of pts.

**PO026**

## 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 2018, 95 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, 55 G2 and 40 G3 at pretreatment biopsy. All patients had endoscopy and RM. The majority of patients had also an Endoscopic Ultrasound. At staging 22 patients had T3N0, 38 T3N1, 18 T3N2 and 17 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). 81 patients had radical anterior rectal resection, 14 pts a “Miles” surgery.

Results: After neoadjuvant treatment 66 pts had G0-1 rectal toxicity, 27 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 21 pts had a T0N0 (19/85 22%), 25 T1N0 (25%) 30 T2N0 (33%), 14 patient. T2N1 (14%). 90/95 /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.

## PO027

### MRI DELINEATION OF EMERGING ORGANS AT RISK IN MALE PELVIC FLOOR IN PROSTATE RADIOTHERAPY: TOWARDS DEVELOPMENT OF CONTOURING ATLAS FOR DAILY PRACTICE

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Aims: Advances in prostate cancer radiotherapy (RT) are related to improved imaging and accurate target volume delineation. Beyond well-established organs at risk (OARs), need for delineation of new structures, that can affect quality of life, is emerging. Magnetic Resonance Imaging (MRI) provides an optimal anatomical definition of prostate and pelvic floor structures with increasing role in RT treatment planning. The aim of our study was to define boundaries of the emerging OARs on MRI.

Table 1. Critical OARs boundaries identified on T2 sequence 3T-MRI

| OARs | Boundaries |
|---|---|
| Internal Anal Sphincter (IAS) | It arises from anorectal junction till anal orifice, concentrically surrounded by EAS, delimiting the anal mucosa |
| External Anal Sphincter (EAS) | It arises from PRM till anal orifice, internally including IAS |
| Puborectal Muscle (PRM) | It arises from LAM till the anorectal junction, with IAS medially and the dorsal part of pubic body and IRF laterally, with IRF surrounding it posteriorly |
| Levator Ani Muscle (LAM) | It arises from the cranial limit of the pubic bones to PRM, with the rectum-ano medially and the dorsal part of pubic body, obturator muscle fascia and IRF laterally |
| Internal Obturator Muscle (IOM) | Ischio-pubis and IRF surround the IOM |
| Ischio-Rectal Fossa (IRF) | It arises from: LAM, gluteus maximus, IOM till the level of the anal verge; laterally it is delimited by IOM, ischial tuberosity and gluteus maximus muscles |
| Penile Bulb (PB) | On axial plane, oval-shaped hyperintense midline structure anterior to rectum and posterior to CC |
| Corpus Spongiosum (CS) | On axial plane, hyperintense structure arises from bulbous spongiosum, posterior to CC and extends anteriorly to form glans penis |
| Corpus Cavernosum (CC) | On axial plane: hyperintense structure surrounded by a hypointense membrane, with extension from penis root to penis shaft, anteriorly to CS |
| Preprostatic Sphincter (PS) | On axial plane, the most hypointense tract of the bladder neck around urethra:<br>• the upper limit is the lower face of bladder bottom<br>• the lower limit is the upper face of prostate |
| Prostate-Membranous Sphincter (PMS) | On axial plane, hypointense structure surrounding the membranous portion of urethra, extending from prostate apex to penis root |
| Urethra (U) | On axial plane<br>Preprostatic: hypointense structure with extension from bladder neck to prostate<br>Prostatic: hypointense structure crossing through prostate; it is seen in the central portion of the posterior part of prostate<br>Membranous: hypointense ring surrounded by PMS<br>Bulbous: hypointense tubular structure in the midline within the bulb of corpus spongiosum coursing within penis root<br>Penile: hypointense structure extends from penoscrotal junction to external meatus |
| Bladder Neck (BN) | On sagital plane, hypointense funnel-shaped with craniocaudal extension from bladder floor to urethra |
| Neurovascular Bundles (NVBs) | On axial plane: hypointense round/elliptic-shape region, placed on both sides of prostate at hours 5 and 7 within the periprostatic fat tissue, between rectum and prostate |

Methods: After an accurate literature review, the structures of interest were identified. A 3Tesla prostate MRI simulation using the same set-up (rectal and bladder filling) and immobilization system (CIVCO combifix) of RT delivery was performed. Three patients were analyzed. Radiation oncologists jointly with radiologists identified and contoured critical structures visible on T2 sequences (axial, coronal and sagittal planes).

Results: Identified structures were: Internal Anal Sphincter (IAS), External Anal Sphincter (EAS), Puborectal Muscle (PRM), Levator Ani Muscle (LAM), Internal Obturator Muscle (IOM), Ischio-Rectal Fossa (IRF), Penile Bulb (PB), Corpus Spongiosum (CS), Corpus Cavernosum (CC), Preprostatic Sphincter (PS), Prostate-Membranous Sphincter (PMS), Urethra (U), Bladder Neck (BN), Neurovascular Bundles (NVBs). Boundaries of these structures are reported in Table 1.

Conclusions: MRI was useful and feasible to identify and contour emerging male pelvic floor structures. This atlas could be employed for evaluation of OARs sparing in the era of high-conformal RT.

## PO028

### USE OF F-DOPA-PET IN RADIOTHERAPY PLANNING IN PATIENTS WITH GRADE IV GLIOBLASTOMA

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Aims: Recurrence of malignant glioma after resection and adjuvant RT is frequently observed, which suggests marginal or out-of-field recurrence, especially in patients with 0-6 methylguanine DNA methyltransferase promoter methylation. Thus, the target volume should be well defined so that infiltrative lesions with high tumor cell density will not be erroneously left untreated. The impossibility to use the MRI in the planning phase, due to the presence of a pacemaker, led us to the use of metabolic images for a better definition of the volumes, in patient with partial resection of the cerebral lesion.

Methods: A single-institutional experience: A 82-year-old patient who underwent partial resection due to a massive lesion of the left fronto-temporal region, histologically confirmed to be a high-grade malignant neural neoplasm (grade IV Glioblastoma according to the WHO classification).Histological examination did not show methylation of the MGMT gene; no mutations in IDH1-2 genes. A PET-CT was performed with F-dopa and a rigid fusion with CT images for radiotherapy planning.

Results: An exclusive radiotherapy treatment was performed according to the hypofractionated scheme, with a dose prescribed at PTV of 40.05 Gy- dose per day of 270 cGy. The rigid fusion of morphological-functional images has resulted in a PTV of 218.90 cc. The radiotherapy treatment was well tolerated, the patient 45 days after the end of the radiotherapy treatment performed instrumental control with CT, which shows morphological reduction of the lesion, to be reassessed with a new metabolic control.

Conclusions: According to the available data, (18)F-FDOPA PET is a viable radiotracer for imaging and treatment planning of gliomas 18F-DOPA PET SUV max may more accurately identify regions of higher-grade/higher-density disease in patients with GLIOMA. Using SUV-based thresholds to define high-

grade portions of disease may be valuable in delineating radiotherapy volumes. Future incorporation of 18F-DOPA PET into clinical practice for RT planning will evaluate the influence of 18F-DOPA PET on local control and survival outcomes. Future studies will investigate the role of 18F-DOPA PET with relative cerebral volume in perfusion MRI for targeting the most aggressive disease components.

## PO029

### AN ATLAS OF EMERGING FEMALE PELVIC ORGANS AT RISK DEFINED ON MAGNETIC RESONANCE IMAGING IN RADIOTHERAPY PLANNING SET-UP

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Aims: Pelvic Radiotherapy (RT) is widely used for neoadjuvant, adjuvant or definitive treatment. Improvement of new RT techniques requires accurate definition of organs at risk (OARs). Magnetic Resonance Imaging (MRI), thanks to a better soft tissue definition, provides an optimal identification of pelvis anatomical structures. The aim of this study is to produce a MRI-based RT atlas for delineation of new emerging OARs in female pelvic region, considered most relevant for RT practice.

Methods: After an accurate literature review, the structures of interest were identified. 3Tesla-MRI simulation was performed according to our protocol for pelvic cancer treatments: full bladder and empty rectum. Radiation oncologists jointly with radiologists identified and contoured selected structures visible on T2 sequences (axial, coronal and sagittal planes).

Results: Identified emerging OARs are: • Internal Anal Sphincter (IAS) is the innermost muscle layer of anal canal, visible as a direct continuation of the circular smooth muscle of rectum, with an intermediate signal intensity. • External Anal Sphincter (EAS), PuboRectal Muscle (PRM), and Levator Ani Muscle (LAM): EAS forms the outer muscle layer of anal canal and it continues cranially with the PRM and LAM, respectively. LAM anchors the sphincter complex to the inner side of the pelvis. All this muscles appear hypointense. • Internal Obturator Muscle (IOM) originates from the obturator foramen, surrounded by the ischium and pubic bone and IRF. • Ischio-Rectal Fossa (IRF) triangular shaped, is represented by fat and connective tissue • Bladder Neck (BN) is well represented on sagittal plane as the hypointense funnel-shaped lower portion of the bladder, anterior to the vagina, continuing caudally in the urethra. • Labia Majora and Minora (LMM) appear hyperintense with the same signal intensity as surrounding soft tissue. • Vagina (V) is a hypointense structure with a rumpled lumen that forms an H or W appearance in cross sections, due to apposition of the vaginal walls. • Cervix (C) is a circular structure, from the junction of vaginal canal to the uterus, presenting higher signal intensity than vagina The anatomo-radiological boundaries identified to recognize these structures are shown in Table 1.

Conclusions: MRI was useful and feasible to identify and contour emerging female pelvic floor structures. This atlas could be employed for evaluation of OARs' sparing in the era of high-conformal RT.

**Table 1. Critical OARs boundaries identified onn T2-sequence 3T-MRI.**

| OAR | Cranial | Caudal | Anterior | Posterior | Medial | Lateral |
|---|---|---|---|---|---|---|
| **Internal Anal Sphincter (IAS)** | Anorectal junction | Anal orifice | External Anal Sphincter | External Anal Sphincter | Anal mucosa | External Anal Sphincter |
| **External Anal Sphincter (EAS)** | Puborectal muscle | Anal orifice | - | - | Internal Anal Sphincter | Central perineal tendon |
| **Pubo Rectal Muscle (PRM)** | Levator ani muscle | Anorectal junction | Parasymphyseal area, passing beside the urethra, vagina and anorectum | IRF | Internal Anal sphincter | Dorsal part of pubic body, IRF |
| **Levator Ani Muscle (LAM)** | Cranial limit of the pubic bones | Puborectalis muscle | Parasymphyseal area | - | Rectum-Anus | Dorsal part of pubic body, obturator muscle fascia, IRF |
| **Internal Obturator Muscle (IOM)** | Greater trochanter | Ischiopubic bone | Ischiopubic bone | IRF | IRF | Ischiopubic bone |
| **Ischio-Rectal Fossa (IRF)** | Levator ani, gluteus maximus, obturator internus muscles | At the level of the anal verge | Where the Obturator Internus Muscle, Levator Ani and Anal Sphincter muscles fuse | A transverse plane joining the anterior edge of the medial walls of the gluteus maximus muscle | Rectum-anus | Obturator Internus, Ischial tuberosity and gluteus maximus muscles |
| **Bladder Neck (BN)** | Bladder floor | Urethra | Pubic bone | Vagina | - | - |
| **Vagina (V)** | Cervix uteri | Vaginal introitus | Urethra | Mesorectum | - | - |
| **Cervix (C)** | Uterine orifice | Vagina | Bladder wall | Rectum (Douglas fossa) | - | - |
| **Labia Majora Minora (LMM)** | Pubic mound | Vaginal vestibula | Clitoris | Perineum | Clitoris | - |

## PO030

### DOSIMETRIC EVALUATION OF TWO MONO-ISOCENTRIC TECHNIQUES FOR STEREOTACTIC RADIOSURGERY OF MULTIPLE BRAIN METASTASES

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Aims: In this study we report our initial experience in using a mono-isocentric technique with multiple non-coplanar dynamic conformal arcs, Elements Multiple BrainMets Stereotactic Radiosurgery (SRS) from BrainLab, for the treatment of multiple brain metastases (MBM) and we compare it with the single-isocenter RapidArc volumetric-modulated arc therapy (VMAT) from Varian in terms of plan quality, risk of radionecrosis and number of monitor units (MU).

Methods: The automated planning software Elements Multiple BrainMets SRS uses the single-isocenter dynamic conformal arcs technique to treat up MBM. From November 2018 to March 2019, 7 patients have been treated with a total of 64 lesions (4-13 targets per patient) and an average total volume of 4.7 cc (range 1.1-6.4 cc); dose prescriptions were 18-22 Gy. For each patient, two mono-isocentric non-coplanar plans (Elements and VMAT) were calculated and analyzed by means of Paddick conformity index (CI), to evaluate plan quality, brain volume receiving 10 and 12 Gy (V10, V12), that are significantly correlated to the risk of radionecrosis, and MU. The treatment unit used for

this work is a Varian Novalis-TrueBeam STx linear accelerator equipped with a high-definition multi-leaf collimator and an X-ray image guidance system including a six degrees of freedom robotic couch (ExacTrac).

Results: Elements and VMAT plans had very similar CI values. It is well known that SRS plans showing a V10>10.5 cc or V12>8 cc are at higher risk for symptomatic radionecrosis and should be considered for fractionated treatment. We found a statistically significant difference in V10 and V12 between Elements and VMAT plans ($p<0.05$). In the Elements plans we obtained a 62% and 56% reduction in V10 and V12, respectively, compared to the VMAT plans. Although the average value of MU was higher for VMAT in comparison to Elements plans, the differences were not significant, but Elements benefits from short planning time in comparison with VMAT (on average 2 minutes against 40 minutes, respectively).

Conclusions: In this preliminary study, we found that the monoisocentric cranial Elements planning system is highly efficient for treatment planning of MBM and produces SRS plans of comparable quality to the VMAT plans. The advantages of Elements are the significantly reduced values of V10 and V12, with positive impact on the risk of radionecrosis, and the shortening in planning times. Further studies are required to confirm these data.

**Table 1. Mean values calculated over 64 treated lesions.**

| | Elements | VMAT | p-value |
|---|---|---|---|
| V10 (cc) | 21.6 | 57.4 | 0.03 |
| V12 (cc) | 13.9 | 31.6 | 0.04 |
| CI | 1.64 | 1.62 | 0.90 |
| Number of MU | 11330 | 12007 | 0.69 |

## PO031

### CAN DIFFERENT METHODS OF RECTUM DELINEATION INFLUENCE TOXICITY IN VMAT TREATMENT PLANNING OF PROSTATE CANCER?

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Aims: To compare different methods for rectum contouring as organ at risk in curative hypofractionated volumetric modulated arc therapy (VMAT) for prostate cancer (PCa) patients in terms of dose-volume histograms (DVHs) and dose constraints.

Methods: From January 2017 to March 2019, 50 patients with localized PCa received VMAT in hypofractionated regimen (67.5 Gy/25 fractions) and were retrospectively analyzed. The rectum was delineated using 2 different lengths and 3 different cross-sections and DVHs were evaluated. The 3 different cross-sections were: whole rectum (WR) including the rectal contents, whole rectal wall (WRW) and anterior rectal wall (ARW), excluding the rectal contents. 2 different lengths were used for the above 3 volumes: long (L), from cranial border starting at where the rectum turned horizontally into the sigmoid to the caudal border 2 cm below the prostatic apex; short (S), from 1 cm above to 1 cm below the prostate. A total of 6 different volumes (S-R and L-R, S-WRW and L-WRW, S-ARW and L-ARW) were generated. We considered for the comparison: the rectum volumes (cc) and the volume receiving at least 50 Gy (V50), for the 6 rectum volumes. Rectal toxicity was evaluated according to CTCAE scales 4.02.

Results: As expected, in all cases the correlation between the different contouring of the rectum and the V50 or the corresponding volumes is statistically significant ($p<0.05$) for couples with the same section and different length. Dose constraint of V50<33% is satisfied for all patients except for 34 (68%) and 42 (84%)patients when considering S-ARW and L-ARW, respectively. Different rectum delineations influenced the dose constraint satisfaction. Generally, the ARW should be less affected by the degree of rectum filling but it is the most at risk of proctitis because included in the PTV. Grade 2 (G2) proctitis after 2 months from treatment was <3% and 98% of treated patients showed V50<47% for S-ARW. The ARW should be considered as organ at risk and appropriate dose constraint should be evaluated for it.

Conclusions: In this study we demonstrate that the method of rectum delineation significantly influence the dose to the rectum represented in the DVH. Delineation of the WR underestimate the dose exposure of the rectum compared to delineation of the RW or the ARW, with possible consequences in rectal toxicity. In our experience, when V50<47% for S-ARW, the risk of G2 proctitis is <3%. A longer follow-up is needed to define the late toxicity.

## PO032

### DOSIMETRIC COMPARISON BETWEEN FLATTENED AND FLATTENING FILTER-FREE PHOTON BEAMS FOR HYPOFRACTIONATED VOLUMETRIC-MODULATED ARC THERAPY IN PATIENTS WITH LOCALIZED PROSTATE CANCER

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Aims: To evaluate potential differences between flattened and flattening filter-free (FFF) beams in volumetric-modulated arc therapy (VMAT) for patients with localized prostate cancer, in terms of dosimetric indicators of plan quality, monitor units (MU), treatment time (TT) and gamma value (GV).

Methods: Fifty prostate cancer patients, previously

treated at our center using 2 arcs VMAT technique with 6 MV photon beams, were selected for re-planning. Eight VMAT plans were generated for each patient (400 plans in total) using a Novalis-TrueBeam STx linear accelerator, photon beams with and without flattening filter (6, 10 MV and 6, 10 MV FFF, respectively), 2 arcs or single arc. Prescription dose was 67.5 Gy/25 fractions. Comparison was performed by means of conformity and homogeneity index, dose-constraints for organs at risk (OAR) (rectum, bladder, right and left femoral head), MU. All plans were delivered on a cylindric phantom equipped with p-type diodes (Delta4, ScandiDos) to measure GV (a method to quantitatively compare measured and calculated dose distributions) with 3%/3 mm criterion and TT.

Results: Small differences were detected between the 4 beams in target conformity and homogeneity; 2 arcs plans showed a more homogeneous ($p<0.01$) dose distribution than 1 arc plans and better conformity for 10 MV and 10 MV FFF beams ($p<0.05$). Dose-constraints for OAR were always satisfied. As expected, a significant increase in MU ($p<0.001$) was observed with FFF beams compared to conventional beams, both for planes with 2 arcs and 1 arc; on the other hand a reduction in TT was obtained for FFF beams, due to the higher dose-rate. Using 1 arc and 10 MV FFF, total MU were increased by 12% and TT was reduced by 45% compared to 10 MV; moreover for 10 MV FFF the average TT for 1 arc was halved compared to 2 arcs (50%, $p<0.001$). Although remaining above the threshold value of 95%, we obtained GV lower for FFF beams compared to flattened beams ($p<0.001$). This may be due to the increase in MU for FFF beams, which results in an increase in the plan complexity.

Conclusions: FFF beams resulted in dose distributions similar to flattened beams. 10 MV FFF beam in single arc plans provided the best compromise between plan quality and time saving. A clinical trial could be useful to demonstrate FFF beams benefits for patients with prostate cancer and further analysis is necessary to establish whether FFF beams are clinically applicable for any patient's plans.

**Table 1. Mean values of conformity and homogeneity index, number of MU, treatment times and gamma values for plans with one and two arcs.**

| | 2 arcs | | | | 1 arc | | | |
|---|---|---|---|---|---|---|---|---|
| | 6 MV | 6 MV FFF | 10 MV | 10 MV FFF | 6 MV | 6 MV FFF | 10 MV | 10 MV FFF |
| Conformity Index | 0.89 | 0.89 | 0.90 | 0.89 | 0.88 | 0.88 | 0.88 | 0.88 |
| Homogeneity Index | 0.06 | 0.06 | 0.06 | 0.07 | 0.07 | 0.07 | 0.07 | 0.07 |
| Monitor Units | 1078 | 1194 | 929 | 1057 | 1060 | 1145 | 932 | 1044 |
| Treatment Times (s) | 118 | 106 | 113 | 105 | 106 | 57 | 97 | 53 |
| Gamma 3%,3mm | 99.8 | 97.8 | 99.9 | 97.2 | 99.7 | 97.8 | 99.6 | 97.8 |

## PO033

### NEW IMAGING FOR OPTIMIZATION OF HYPO-FRACTIONATED RADIOTHERAPY TREATMENTS IN PATIENTS WITH PROSTATE CANCER

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Aims: The use of next-generation imaging modalities based on multiparametric-MRI (mpMRI) and PET-tc (with 11C-Choline or recently 68Ga-PSMA) open a new era for diagnosis, localization,staging and detection of recurrences of clinically significant prostate cancer and it also opened up opportunities for focal treatments.

Methods: Our clinical experience of the last five years has validated the use of mpMRI and PET-tc to optimize hypofractionated radiotherapy treatments for curative purposes, for targeted treatments of lymphonodes or skeletal metastases and for reirradiation, in patients (pts) with recurrence prostate cancer. 102 pts were treated. 13 pts have performed radical hypofractionated radiotherapy treatment and mpMRI was used to give a greater dose to the sick area through a sequential boost. 11 pts performed reirradiation, in these cases mpMRI and PET-tc were useful to identify sites of intraprostatic recurrence, allowing to limit the dose in these same sites only. 78 pts with 143 isolated lymphonodes, detected through PET-tc scan, were treated with stereotactic radiotherapy (SBRT). All targets delineation were performed on Plan CT-mpMRI/PET-tc fusion.

Results: Median follow-up was 40 months, 84% pts were still alive, 14% was dead and 2% was lost in FU. DFS, OS and LC at 2 and 5 year were 53%, 94% and 98%, and 20% 61% and 94% respectively. Any severe acute or late toxicity was not observed.

Conclusion: Increasingly, clinical management and decision making in prostate cancer are influenced by technologies such as new imaging techniques (mpMRI) or nuclear medicine studies (PET-tc) that can be used in the diagnosis of primary cancer as well as the staging and detection of recurrence or metastatic disease. In planning phase, is possible to combine these new imaging techniques to guarantee targeted and aggressive radiotherapy with greater therapeutic efficacy.

## PO034

### ROLE OF STEREOTACTIC BODY RADIATION THERAPY IN ELDERLY AND VERY ELDERLY PATIENTS WITH INOPERABLE PANCREATIC CANCER: EVALUATION OF PROGNOSTIC FACTORS AND CLINICAL OUTCOME

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Aims: This study assessed the efficacy, feasibility,

safety of SBRT in elderly and very elderly patients with inoperable pancreatic cancer. We also evaluated the impact of co-morbidities on overall survival (OS), progression free survival ( PFS) and local control (LC).

Methods: Between November 2010 to October 2018, 66 elderly and very elderly patients with inoperable pancreatic tumor were treated with SBRT in our Institution. Outcome analysis of elderly population (range 75-79 years old) and very elderly patients ( ≥ 80 years) were focused on age, perfomance status evaluated according to Karnosky (KPS) and on co-morbidities assessed according to Charlson Comorbidity Index (CCI). SBRT was admistered in 6 fractions with the prescription dose ranging from 30 to 45 Gy on primary tumor. Local control, overall survival, PFS and toxicities were assessed.

Results: 66 patients (28 elderly and 38 very elderly) were analyzed in this retrospective study. The median age was 80 years (range 75-92). Forty-nine patients (74%) presented a moderate CCI (score 6-8); 17 (26%) patients had severe CCI (score 9-13). KPS 1or 2 in all patients. Fifteen (23%) patients received chemotherapy before SBRT. Median follow-up was 14 months. Local control was 80% at 1 year. On univariate analysis (P<0.01) lesion size was statistically significant for LC. Median progression free survival and overall survival were 8 and 13 months, respectively. The CCI was significantly affecting overall survival (P<0.02). No relevant acute toxicity (≥ G3) were recorded.

Conclusion: Stereotactic body radiotherapy is a non-invasive and safe treatment for elderly and very elderly patients with inoperable pancreatic cancer and it could be a promising therapeutic option particularly in patients with moderate CCI.

**PO035**

## THE USE OF 4D-CT IN HYPOFRACTIONATED TREATMENT OF LUNG NODULES: A MONOCENTRIC EXPERIENCE

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Aims: The use of 4D-CT is strongly recommended in patients (pts) with lung lesions who are not eligible for gating or breath-hold techniques. In this retrospective study we analyzed the results in terms of local control and toxicity (fibrosis) of lung hypofractionated radiotherapy (RT) delivered to internal target volume (ITV).

Methods: Between July 2017 and July 2018, 32 pts (mean age 74 y, range: 61-91) with 38 lung lesions (provenance: 22 lung, 14 colonrectum, 1 kidney, 1 esophagus) were treated with hypofractionated RT, in Pisa University Hospital. They underwent 4D-CT by which we were able to define an ITV, irradiated with FFF-TrouBeam accelerator. In this analysis we evaluated the differences in terms of ITV-volume between medium-apical and basal nodules. We also analyzed the preliminary results in terms of local control and fibrosis, trying to find a correlation with the delivered dose and the planning volume. In order to conform the delivered dose, we calculated the equivalent dose in 2 Gy (EQD2) considering an alfa-beta ratio of 5, 5, 3 and 2 for cancer of colonrectum, esophagus, lung and kidney, respectively.

Results: The mean volume of GTV and ITV was 14,17cc (range: 0,30-139,44) and 19,96cc (range: 0,57-182,72), respectively. The ratio between ITV-volume and GTV-volume (mean:1,85; range: 1,05-4,64) was statistically related with the involved lobe (lower vs medium-upper; p:0,026). After a mean follow-up of 9,6 months (range: 2,2-16,1), 18 (50%), 7 (19,4%) and 2 (5,5%) nodules were in response, in stable disease and in progression, respectively; the local response was not evaluable in 9 lesions because of the fibrosis and 2 pts were lost in follow-up. The local control (complete/partial response vs stable/progression disease) was statistically related to a value of EQD2 ≥103 (p:0,048). Seventeen lesions showed a lung reaction to radiotherapy (fibrosis) at follow-up CT scans. This reaction was not statistically related to ITV-volume(p:0,350) and to the age (p:0,438) but was strongly related to EQD2 as a continuous variable (p: 0,015).

Conclusions: The volume of ITV changes according to the involved lobe due to the greater movement of basal lesions but it appear not related to local control and lung fibrosis, maybe because of pts with bigger ITV were treated with other techniques (gating or breath-hold). Instead, the dose delivered (optimized in EQD2) appear related to both local control (EQD2 ≥103 shows better results than lower value) and fibrosis.

**PO036**

## GROSS TUMOR VOLUME DEFINITION IN PROSTATIC CANCER ON DWI AND T2W MMRI SEQUENCES

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Aims: T2 weighted sequence is the most significant diagnostic tool to highlight the presence of neoplastic lesions (hypointense areas or nodules); diffusion-weighted axial scans (DWi) is a fundamental parameter in multiparametric MRI (mMRI). The purpose of the present study is to evaluate the differences between the gross tumor volume(GTV) of prostatic neoplastic lesions obtained on T2 weighted MRI sequences and diffusion-weighted scans (DWI).

Methods: We retrospectively analyzed 7 patients with prostatic tumor who performed mMRI of the pelvis. The MultiPlan® System was used to delineate GTV on DWI and T2w MRI sequences. Statistical analysis

with t Student test have been performed to evaluate the presence of statistically significative differences between the GTV obtained with both mMRI sequences.

Results: All patients had prostatic lesions with a P-RADS between 4 and 5, and the presence of prostatic cancer was confirmed by histopathological examination. In 2 cases the lesion sites were exclusively the peripheral zone; in 2 cases the transition zone and the peripheral zone; in 2 cases the transition zone, the peripheral zone and the seminal vesicles; in 1 case the peripheral zone and the seminal vesicles; in 4 cases there was involvement of the prostatic capsule with bulging of its profile. 7 lesions showed low signal in the T2 weighted images, restricted water diffusion in DWI images (b value=2000); only 4 of these were characterized by high and persistent impregnation in the Dynamic contrast enhanced (DCE) study. Table 1 shows the GTV mm³ obtained on the MRI sequences under examination. The difference between the volumes recorded on both sequences was found to be not significant on t Student test (t=1,161; P=0,268).

Conclusions: This preliminary experience does not allow to draw definitive conclusions. We suggest that both sequences should be used to define the GTV.

**Table 1.**

| | GTV-T2 mm³ | GTV-DWI (b2000) mm³ |
|---|---|---|
| 1st case | 17219 | 17448 |
| 2nd case | 14879 | 14216 |
| 3rd case | 5095 | 13466 |
| 4th case | 15209 | 23257 |
| 5th case | 6514 | 5591 |
| 6th case | 10710 | 20187 |
| 7th case | 7710 | 7677 |

## P0037

## COMPARISON OF DEEP-INSPIRATION BREATH-HOLD AND FREE-BREATHING TECHNIQUES IN LEFT BREAST CANCER IRRADIATION: A DOSIMETRIC EVALUATION IN 66 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).

Methods: 66 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 ($D_{meanheart}$), to the ipsilateral lung ($D_{meanlung}$) and to the left anterior descending coronary artery ($D_{meanLADCA}$), the volume receiving 20 Gy ($V_{20Gylung}$) and the volume receiving 30 Gy ($V_{30Gylung}$) for the ipsilateral lung, the volume receiving 20 Gy for LADCA ($V_{20GyLADCA}$) in conventional schedule, the volume receiving 19 Gy for LADCA ($V_{19GyLADCA}$) in hypofractionated schedule, the maximum dose for LADCA ($D_{maxLADCA}$) and heart ($D_{maxheart}$). Moreover 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.

**Table 1. Organs at risk $D_{mean}$ and $D_{max}$ in free breathing (FB) versus deep inspiration breath hold (DIBH) techniques. Ipsilateral lung volumes receiving more than 20 Gy ($V_{20Gylung}$) and 30 Gy ($V3_{0Gylung}$) in FB versus DIBH. LADCA volumes receiving more than 20 Gy and 19 Gy for the conventional and the hypofractionated schedules, respectively. Total ipsilateral lung volumes ($V_{lung}$).**

| | Technique | Mean dose (Gy) | SD | Mean dose difference (Gy) | Mean dose reduction (%) | p-value |
|---|---|---|---|---|---|---|
| $D_{meanheart}$ | FB | 2.47 | 1.34 | 1.17 | 47.3 | 0.0000 |
| | DIBH | 1.30 | 0.59 | | | |
| $D_{maxheart}$ | FB | 40.28 | 10.18 | 18.87 | 46.9 | 0.0000 |
| | DIBH | 21.41 | 15.39 | | | |
| $D_{meanLADCA}$ | FB | 15.45 | 9.88 | 9.74 | 63.0 | 0.0000 |
| | DIBH | 5.72 | 5.76 | | | |
| $D_{maxLADCA}$ | FB | 38.31 | 11.23 | 18.89 | 49.3 | 0.0000 |
| | DIBH | 19.42 | 15.19 | | | |
| $D_{meanlung}$ | FB | 7.49 | 2.53 | 1.08 | 14.4 | 0.0064 |
| | DIBH | 6.41 | 1.90 | | | |
| | **Technique** | **Mean volume (%)** | **SD** | **Mean volume difference (%)** | **Mean volume reduction (%)** | **p-value** |
| $V_{20Gylung}$ | FB | 12.81 | 5.22 | 2.19 | 17.1 | 0.0076 |
| | DIBH | 10.63 | 3.97 | | | |
| $V_{30Gylung}$ | FB | 10.79 | 5.06 | 1.96 | 18.2 | 0.0115 |
| | DIBH | 8.82 | 3.63 | | | |
| $V_{20GyLADCA}$ | FB | 28.50 | 27.19 | 21.44 | 75.2 | 0.0007 |
| | DIBH | 7.06 | 16.98 | | | |
| $V_{19GyLADCA}$ | FB | 34.84 | 26.21 | 29.59 | 84.9 | 0.0000 |
| | DIBH | 5.25 | 11.74 | | | |
| | **Technique** | **Mean volume (cc)** | **SD** | **Mean volume difference (cc)** | **Mean volume increase (%)** | **p-value** |
| $V_{lung}$ | FB | 1326.6 | 370.3 | 969.9 | 73.1 | 0.0000 |
| | DIBH | 2296.5 | 506.1 | | | |

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. A positive correlation was found between MHD and mean heart dose difference. The MHD showed an average relative reduction of 81% ($p<0.001$). Average Dmeanheart also reduced from 2.5 Gy to 1.3 Gy in FB and DIBH, respectively (47.3%) and we reported an average Dmaxheart reduction of 47% ($p<0.001$). Average $D_{meanLADCA}$ was reduced from 15.4 Gy to 5.7 Gy with a statistically

significant mean dose reduction of 63%. Average $D_{maxLADCA}$ decreased from 38.3 Gy to 19.4 Gy ($p<0.001$). In the conventional and in the hypofractionated schedules, $V_{20GyLADCA}$ and $V_{19GyLADCA}$ showed an average relative volume decrease of 75% and 85%, respectively. A 100% reduction in $V_{20GyLADCA}$ and $V_{19GyLADCA}$ was recorded in 58.6% and 57% of patients respectively.

Conclusions: Our study confirms the DIBH technique advantage in reducing cardiac and pulmonary doses for LBC patients and further research is warranted to evaluate potential long-term clinical implications.

## PO038

### PAIDEIA (PACEMAKER AND IMPLANTED CARDIOVERTER DEFIBRILLATOR MANAGEMENT IN RADIATION THERAPY) SURVEY, PROMOTED BY THE YOUNG GROUP OF THE ITALIAN ASSOCIATION OF RADIATION ONCOLOGY (AIRO)

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Aims: Cardiovascular diseases and cancer rate is growing up, favoured by population aging. In this context, the number of patients with a cardiac implantable electronic device needing radiotherapy is increasing. The correct management of these patients is crucial, with a general lacking knowledge and clear recommendations. Aim of this survey, promoted by the Young Group of AIRO, was to estimate the awareness within the Italian Radiation Oncologist community on this issue.

Methods: The PAIDEIA Project Working Group designed a 22 item-based questionnaire, shared among the Members of the AIRO Yung Working Group and validated by two external reviewers. Three domains of interest were investigated: a first part about general information on respondent; a second tier about knowledge on devices and their management; a last domain about clinical practice and routinely behaviour. The survey was proposed during the AIRO National Congress in 2015, then submitted to the radiation oncologists community both on line, employing the Internet-based Survey- Monkey platform (www.surveymonkey.com) and on a paper version,The survey analysis was conducted before the publication of the Italian recommendations on this topic,[1] therefore the answers were not conditioned by guidelines and were compared to the recommendations.

Results: A total of 113 questionnaires were collected anonymously and analysed (online: 50; paper: 63). The age of the 44% of the respondents was between 30-35 years old. A good level of awareness was expressed by analysing the answers, but with a non-homogeneous adherence to the different published guidelines and recommendations. A low rate of multidisciplinary approach, accounting a preliminary cardiological evaluation, was expressed, in line with some others already published surveys; nevertheless, a needed focus on specific treatment factors and patient-centred point of view emerged.

Conclusions: A generally good awareness of this topic was shown, without homogeneous application of guidelines and recommendations, probably due to the absence of a clear route to follow. A larger prospective data collection could be helpful to establish a correct management of these patients.

**Reference**

1. Zecchin M, Severgnini M, Fiorentino A, et al (2018) Management of patients with cardiac implantable electronic devices (CIED) undergoing radiotherapy: A consensus document from AIAC, AIRO, AIFM. Int J Cardiol 15 (255):175-183.

## PO039

### POST HIGH INTENSITY FOCUSED ULTRASOUND (HIFU) RADIOTHERAPY WITH SALVAGE INTENT IN LOCALLY RELAPSED PROSTATE ADENOCARCINOMA: A MONO-INSTITUTIONAL ANALYSIS

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Aims: The main objective of the present study was to evaluate tolerance, feasibility and biochemical control rates of salvage external beam radiotherapy (EBRT) in patients with local relapse from prostate cancer after HIFU as primary treatment.

Methods: This is a retrospective analysis of 20 patients with prostate adenocarcinoma treated with 1 or more HIFU sessions between 2008 and 2018. All patients presented biochemical failure after HIFU (according to the Stuttgard definition) and choline-PET or PSMA-PET was performed for restaging and treatment planning in most of cases. The median interval between HIFU and EBRT was 37 months and the median PSA before EBRT was 5.0ng/ml. Salvage EBRT was performed with moderate hypofractionation schedule in 28 fractions (n=13) or with extreme hypofractionation schedule in 5 fractions (n=7) by means image-guided volumetric modulation arc therapy (VMAT-IGRT). All patients were treated with EBRT to the residual prostate. In case of moderate hypofractionation the median dose was 71.4Gy (range 71.4-

74.2Gy) and 6 patients concomitantly received pelvic lymphnode EBRT (range 50.4–51.8Gy). In case of extreme hypofractionation, the residual prostate with a median dose of 32.5Gy (range 30–35Gy) was irradiated. Six patients (30%) received androgen deprivation therapy. Primary endpoints were acute toxicity and biochemical disease-free survival. Genito-urinary (GU) and rectal and bowel toxicity (GI) were scored by CTCAE 4 scale. Biochemical response was assessed by ASTRO Phoenix criteria.

Results: The median follow-up was 24 months. The median PSA nadir after EBRT was 0.16 ng/ml with a median time to nadir of 17 months for moderate hypofractionation and 6 months for extreme hypofractionation; 50% of the patients reached a PSA nadir <0.2ng/ml. No grade 3 or higher toxicity was observed. Only 3 patients presented with grade 2 acute GI toxicity (actinic proctitis), out of them 1 was treated with extreme hypofractionation. Twelve (60%) patients experienced acute grade 1 GU toxicity: 8/13 of men treated with moderate hypofractionation and 4/7 of men treated with extreme hypofractionation. At the time of follow-up only 3 patients (15%) had a biochemical progression.

Conclusions Our data confirm the feasibility and the low toxicity of salvage EBRT with both schedules of treatment after HIFU failure. The findings of low toxicity and good biochemical control rates are encouraging, but larger number of patients and a longer follow up are needed.

## PO040

### IMPACT OF 18-F-FET-PET ON TARGET VOLUME DEFINITION IN RECURRENT HIGH-GRADE GLIOMA PATIENTS

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Aims: To evaluate the differences between 18-F-FET-PET, T1 weighted contrast-enhanced (T1 CE) MRI and T2w flair-MRI in Gross Tumour Volume (GTV) definition in previously treated recurrent high-grade glioma (HGG) patients.

Methods: Six patients with recurrent HGG were included in this study. All patients underwent, previous informed consent, both to 18-F-FET-PET and T1 CE - T2w-MRI scan. In all the cases the workspace dedicated to the registration of multimodal imaging of TPS MultiPlan® was used to define the GTV. Descriptive statistical analysis was done. A paired samples t-Student test was done to assess significant differences.

Results: There were six male patients (median age 62, range 37-75). The median cc value of GTV in T2w-MRI was 26.98 (range 6.82/164.97); the median cc value of GTV in 18-F-FET-PET was 26.47 (range 6.19/171.1). 18-F-FET-PET has a high specificity and sensibility in defining recurrent HGG. Recent guidelines suggest the inclusion of volumes that are hyperintense on T2 fluid-attenuated inversion-recovery (FLAIR) Magnetic Resonance Images (MRI) in order to do primary contouring in recurrent HGG. Table 1 shows the volumes in these six cases. There were no statistically significant differences in the two groups (t= 0,330; P=0,755).

Conclusions: This preliminary study does not allow to draw definitive conclusions. More data are needed to validate the use of FET-PET in radiation volume definition in recurrent HGG patients.

**Table 1.**

| | GTV T2w-MRI* | GTV 18-F-FET-PET* |
|---|---|---|
| 1st case | 34,80 | 6,19 |
| 2nd case | 61,82 | 75,93 |
| 3rd case | 19,16 | 10,23 |
| 4th case | 164,97 | 171,1 |
| 5th case | 6,82 | 12,46 |
| 6th case | 13,17 | 40,49 |

**All the value were reported in cc (cubic centimetres)*

## PO041

### CLINICAL RESULTS OF PROTON THERAPY FOR PRIMARY LIVER TUMORS

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Aims: Liver cancer represents the sixth most commonly diagnosed cancer and the fourth leading cause of cancer death worldwide in 2018. Hepatocellular carcinoma (HCC) accounts for 90% of all liver cancers, most of the remaining being intrahepatic cholangiocarcinoma (ICC). Among the therapeutic options available for primary liver cancer, radiotherapy has a narrow therapeutic window due to the low-radio-tolerance of the liver and the need for high doses of radiation for disease control. In this context, proton therapy (PT) with its unique physical properties, allows for a better sparing of heathy tissue (i.e. non invoved liver) compared with x-ray therapy, and represents a valid option for liver cancer treatment. Here we report the first results of our center with the use of PT in the treatment of primary liver cancer.

Methods: All, consecutive patients treated since the implementation of liver target treatment technique were included. The choice of PT was made in a multidisciplinary board for all patients. Active scanning proton therapy using single Field Optimization technique was used. Patient's setup consisted of expiration breath hold with the use of Active Breath Coordinator device (Elekta™, Sweden). Three CT were acquired for the estimation of intra-fraction liver position reproducibi-

lity. The Clinical Target Volume consisted of a 5-10 mm expansion of the Gross Tumor Volume. Target and OARs prescription doses were chosen according to Hong 2016. Response to PT was grade according to both RECIST and modified RECIST criteria for HCC. Toxicity was graded according to the CTCAE vers. 5 scale.

Results: Between January 2018, and March 2019 17 patients (13 HCCs, 4 ICCs) were treated. Median age was 68 y (range 55-79). Child Pugh (CP) Score for HCC patients was A5 in seven patients, A6 in four patients and B7 in two patients. Median delivered dose was 58,05 Gy in 15 fractions (range 58,05-67,5) The median GTV volume was 31,65 cm3 (range 1,54 - 789,08 $cm^3$), the median dose provided to the not involved liver volume was 13,43 Gy (range: 5,87 to 22,03 Gy). Treatment was well tolerated with no ≥ G2 Toxicities. CP score improved in 3 patients, worsened (1 point) in three patients, no changes were observed in the other 7 HCC patients. No radiation induced liver disease was observed so far. With a median Follow-up of 6 months (range1-15), all lesions treated are controlled (Figures 1 and 2). Regional, Liver progression was observed in 7 patients (41%). 15 (88%) patients are alive; two patients affected by synchronous double tumor (non Hodgkin lymphoma and non small cell lung cancer) were dead.

Conclusions: Our first results confirm PT as a feasible and very promising option for primary liver cancer, both in HCC and ICC patients. The better non involved liver sparing guaranteed by PT allows for its integration with other treatment modalities (*i.e.* TACE) in order to maximize local and locoregional control in unresectable HCC.

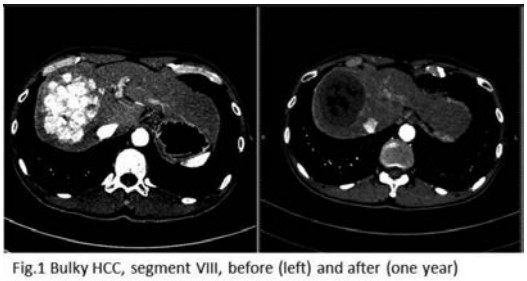

Fig.1 Bulky HCC, segment VIII, before (left) and after (one year) protontherapy treatment, 58,05 Gy in 15 fractions

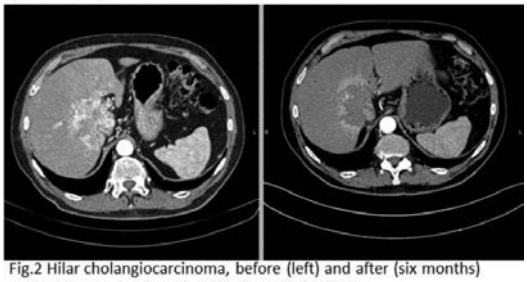

Fig.2 Hilar cholangiocarcinoma, before (left) and after (six months) protontherapy treatment, 58,05 Gy in 15 fractions

**Figures 1 and 2.**

**PO042**

## THE USE OF HYDROGEL IN MODERATE HYPOFRACTION IN PROSTATE CANCER: IS A TREATMENT SAFE? MONOISTITUTIONAL EXPERIENCE OF UOC RT IN CT

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Aim: Moderate hypofraction is non inferior to conventional fractionation and is recommended as a new the standard of care for EBRT of localized prostate cancer. The rectum is a dose-limiting structure when treating prostate cancer, given its close proximity. The physical shift of the rectum allows a greater proportion of the organ to be spared high dose and has resulted in reduced rectal toxicity. We report our experience regarding use of hydrogel in moderate hypofractionated for prostate cancer to reduce rectal toxicities.

Materials and Methods: From September 2018 to April 2019 we have enrolled 17 pts with prostate adenocarcinoma low-medium risk. The inclusion criteria were stage T1-2 GS ≤7, PSA≤10 ng/ml. All patients had 3 gold fiducial markers implanted a trans perineal technique prior to hydrogel placement. A MRI and CT scans were acquired after implantation to enable delineation of the prostate, the adjacent rectal wall and the Hydrogel.The CT images were deformable registered with the MRI scans by auto matching with dedicated software. Depending on the prognostic risk group the CTV was defined as the prostate only (CTV1), the prostate with the base of the seminal vesicles (CTV2) or the prostate with the whole seminal vesicles (CTV3). The bladder, femoral heads, rectum were delineated as solid organs. The prescription dose PTV was 62 Gy/20fx. The VMAT plan consisted of a singol arc and the isocenter set at the center of PTV. The coverage dose was 95-99% of target. Hydrogel resulted in ≥7.5-mm prostate-rectal separation in 95.8% of patients with consequent reduction of the dose to the rectum. Patient positioning was verified with kv Cone Beam-CT. The toxicities was evaluated according RTOG scale.

Results: All patients completed the treatment without break. Median follow-up time was 5 months (range: 3-8 months). Acute toxicities, during treatment G1-2: 0%, and after 3-6 months we recorded gastrointestinal toxicities (proctitis) G1-G2 0%.

Conclusions: Injection of hydrogel into the prostate-rectal interface resulted in dose reductions to rectum for >95% of patients treated. Our experience demonstrate that hydrogel is a device safe and doesn't get worse QdV and its use allows the hypofraction radiotherapy prostate cancer respecting rectum-constraints. We do not yet know what the results will be with regards to late toxicity, but numerous studies affirm that early rectal toxicities is a predictor factor for late toxicities.

PO043

## FRACTIONATED GAMMA KNIFE RADIOTHERAPY IN LARGE VOLUME INTRACRANIAL MENINGIOMAS: A SAFE AND EFFECTIVE TREATMENT

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Aims: Morbidity and mortality in surgery for large-volume intracranial meningiomas is still high. Gamma Knife Radiosurgery (GKS), today, represents feasible alternative treatment for patient with meningioma. Single session GKS for these patients increase the risk of radiation-induced toxicity. The new version of Gamma Knife, "Icon", which uses thermoplastic masks, has encouraged the use of fractionated GKS (FGKS) as an increasingly favorable treatment option. In this study, we report our results on the efficacy and safety of FGKS for large meningiomas.

Methods: Twelve patients treated with Gamma Knife "Icon" at our institute, from may 2018 to february 2019, received MR imaging for preplanning before treatment session. The median tumor volume was 20 $cm^3$ (range 6.6-35 $cm^3$). It was used thermoplastic mask as immobilization system with a "patient-marker" to control the positioning intra session. For each treatment fraction, a daily CBCT was performed to verify the actual tumor position. Treatment plan is automatically corrected for any discrepancy in patient position by registering the pretreatment CBCT to the reference image in Leksell Gamma Plan. During treatment, we recorded the intrafractional patient motion. The median prescription dose was 7 Gy in 3 fractions (range 6-8 Gy).

Results: The mean follow-up duration was 6 months (range, 6~9). There was no mortality. All pts performed MRI brain s/c mdc after 6-12 months to the end of FGKS. The tumor volume was stationary in 10 patients after 6 months to the end of GFKS, in 2 pts recorded progression disease. The signs and symptoms recorded were regression complete of headache in 8 patients, 4 patients (33.3%) showed transient cranial neuropathy after FGKS, spontaneously resolved; 3 patients presented perilesional edema to first follow up with MRI brain, treated with cortisone therapy; 1 patients showed visuals disturbances; 1 patient, with sclerosis multiple, presented walking problems unreliable GFKS-related.

Conclusions: Patients with large meningiomas that cannot be subjected to surgery find a good alternative in the fractionated gamma knife with good tumor control and lower complications rates. Further studies of large cohorts with long term follow-up are required to clarify the efficacy in the tumor control and functional outcome as well as radiation toxicity.

PO044

## TECHNIQUE IMPLEMENTATION AND INITIAL CLINICAL RESULTS OF PROTONTHERAPY FOR LYMPHOMAS

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Aims: Radiotherapy (RT) is currently part of consolidative treatment for Lymphoma malignancies. Patients undergoing RT experience late toxicities due to radiation dose to organs at risk such as heart, coronary vessels, esophagus, thyroid and lungs. The risk of radiation-induced secondary cancer is also not negligible for long-term survivors. Due to its unique physical properties, Proton therapy (PT) can reduce toxicity to uninvolved tissues compared to conventional photon RT. Limited data exist demonstrating the clinical benefit of proton radiotherapy for both Hodgkin (HL) and Non Hodgkin Lymphoma (NHL) patients. Here we present the results of PT treatment technique implementation in our center along with the clinical results of the very first patients.

Methods: Patient's setup consisted of deep (80% of maximum) inspiration breath hold (BH) with the use of Active Breath Coordinator device (Elekta™). Three CT were acquired for the estimation of intra-fraction position reproducibility. The Clinical Target Volume was contoured according to the International Lymphoma Radiation Oncology Group (ILROG) guidelines. The Internal Target volume consisted of the union of the CTVs contoured on the three CT. The Planning Target Volume was a 5-7 mm ITV isotropic expansion. Active scanning proton therapy using single Field Optimization technique with simultaneous integrated boost was used. The final alignment was made with 2 acquisition of orthogonal kV images during BH. The images were aligned to reference digitally reconstructed radiographs using the sternum, the clavicles and the vertebral bodies for alignment. Treatment was monitored with an optical tracking system (VisionRT™). It was used as safety system to stop the delivery if the patient was unable to hold his breath.

Results: Between May, 2018, and May, 2019, four patients (3 HL, 1 NHL) were treated. All patients underwent standard chemo-immunotherapy before PT. Patients were referred for PT for mediastinal bulky disease. One patient presented congenital aortic stenosis. Median PTV volume was 693 cm3 (653-1280).Treatment dose were 36-40, 36-40, 30, 30-36 in 1,8-2 Gy per fraction, respectively. Median average heart dose was 3 Gy (2,3-4,8). Treatment was well tolerated with no acute ≥G2 toxicities. Median FUP was 7,5 months (1-12). No late toxicities were observed so far. All patients are free of disease at last FUP.

Conclusions: The potential of PT to reduce acute

and late sequelae in comparison with conventional RT should be considered into multidisciplinary Lymphoma boards and included into a risk adapted treatment strategy for lymphoma patients eligible to receive consolidative RT. In our center, the implementation of a photon-proton treatment comparison in collaboration with the patients' referring radiotherapy center is currently under development with the aim of identifying patients with a true benefit of advanced technique.

## PO045

### TRIPLE-NEGATIVE BREAST CANCER: AN OBSERVATIONAL , MONOCENTRIC, RETROSPECTIVE ANALYSIS

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Backgroun: Triple-negative breast cancer (TNBC) is a very aggressive and poor prognostic subset of breast cancer, associated with a higher risk of early recurrence and distant metastasis occurrence. The purpose of the present retrospective, observational, single institution study was to evaluate the patterns of care of patients affected by TNBC.

Materials and Methods: We collected data of 164 patients with primary TNBC treated in our Institution between January 2008 and January 2018. All patients were stage I-III tumor, operable, which had received adjuvant/neoadjuvant chemotherapy with or without postoperative radiotherapy. We examined TNBC patients with respect to demographic data, BRCA mutation presence, clinico-pathological parameters, adjuvant/neoadjuvant chemotherapy and radiotherapy regimens. We analyzed disease-free survival rates (DFS), overall survival (OS), and predictive factors of outcomes.

Results: At a median follow up of 5.2 years, 6,6% LR 13,25 DM 7,83 deaths. The median age was 56 years 13.2% received neoadjuvant chemotherapy, with one had complete pathological response (pCR), 69.9% adjuvant chemotherapy and 75.9% radiotherapy, 20,5% using conventional fractionation and 50% hypofractionation. 67.5% were treated on the whole breast while 6.1% on the chest wall and regional nodes. The local recurrence-free survival (LRFS) was 33.4 months and the distant-free survival (DFS) was 20.2 months. Univariate analysis showed a statistically significant favorable effect on patients who did not receive neoadjuvant chemotherapy (p=0.0037; HR 0.23 95%CI 0.02 to 0.45), patients who had a lower pT (p<0.0001), earlier postsurgical stage (p=0.0100) and those treated on the whole breast only (p=0.0272). Concerning PFS, a statistically significant advantage was found in patients who did not have neoadjuvant chemotherapy (p=0.0182), with lower postsurgical stage (p=0.0001), in patients who had extensive surgery (p=0.0012), and those who had done hypofractionated treatment (p=0.0007). Fractionation was also statistically significant at multivariate analysis (p=0.0001).

Conclusions: Prognosis of TNBC is strongly dependent by stage at diagnosis, showing a relapse interval and an extremely short PFS. Current strategies of treatment are widely uneffective.

## PO046

### CORRELATION BETWEEN INITIAL MRI-BASED TUMOR VOLUME AND CLINICAL COMPLETE RESPONSE IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY: UPDATED ANALYSIS OF 52 CASES

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Aims: The aim of this analysis was to evaluate the volumetric tumor regression at MRI after neoadjuvant chemo-radiotherapy (nCRT) in patients (pts) with locally advanced rectal adenocarcinoma (LARC) planned for radical surgery. The final goal was to identify pts with the highest probability of achieving a complete clinical response after nCRT, in the context of an organ preservation strategy, based on the findings of basal MRI.

Methods: Between 6/2013 and 12/2017, 51 pts with a histological diagnosis of adenocarcinoma of the rectum (T3-4 N0-2), were examined reviewing MRI studies performed before and after nCRT at Niguarda Cancer Center. We made the contouring of GTV on axial-T2 MRI sequences in order to quantify the tumor volume (cc) before and after nCRT, to evaluate a correlation between tumor volume and the probability to achieve a complete clinical response, with standard neoadjuvant radiochemotherapy.

Results: The median GTV pre-nCRT was 26.4 cc (range 2.41-195.26 cc). All pts had a tumor volume regression post-nCRT greater than 21% (range 21-100%, median 76%). Twelve pts achieved a complete radiological response (100% of volumetric reduction). The median GTV of this group pre-nCRT was 8 cc (range 2.41-24.39cc). No complete radiological responses were observed in tumors greater than 25 cc.

Conclusions: Based on these preliminary data it is possible to assume that the tumor volume is a significant predictor for a complete radiological response after nCRT, regardless of the stage of T. If these data will be confirmed in further analyses, this parameter could become a useful factor to identify a more favorable group of pts to be managed with an organ preservation approach (i.e., omission of surgery). We could also assume that in larger tumors a program of dose escalation of nCRT is needed to increase the probability of achieving a complete response.

## PO047

### COMBINED USE OF 4DCT WITH CONTRAST MEDIUM AND TRIPHASIC CT IN THE PLANNING OF SBRT TREATMENTS IN HEPATOCELLULAR-CARCINOMA: IMPLEMENTATION OF A CLINICAL PROTOCOL

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Aims: The advent of SBRT, technological innovations and the evolution of imaging methods have allowed RT to be a therapeutic option in patients with unresectable HCC. We aimed to determine the usefulness of an institutional simulation protocol to optimize SBRT planning using a threshold of 20 mm for target volume.

Methods: Six cases of HCC were included in the analysis. Lesions diameter was 26 mm in one, and <20mm (range from 7 to 15mm) in the others. For all patients, processing of an ""UnTagRec""-CT (UTR-CT) i.e. a 3DCT obtained from all the sinogram data of a 4D-CT without Contrast Medium (CM) was carried out irrespective of the lesion's diameter. For HCC ≤20mm, a Triphasic CT-scan with CM was performed and the GTV derived from the 3 phases was identified on the UTR-CT, and an isotropic margin of 1 cm was added to create a PTV. For HCC >20mm, patients underwent a 4D-CT with CM including the entire liver volume, and an ITV was obtained by the sum of 6 different GTVs outlined on the respiratory phases. An isotropic PTV of 7 mm was then created. All patients were administered a five-fractions SBRT by means of VMAT and IGRT, to a total dose ranging from 30 Gy to 50 Gy (median 50Gy). Liver, intestinal and skin toxicity was assessed by CTCAE 4.0 scale.

Results: The methodology herein employed was proved to be effective in identifying targets with high precision, and the contouring process was substantially facilitated. None of the patients experienced a ≥G2 acute gastrointestinal toxicity. G2 acute skin toxicity occurred in one of the patients. All patients in both groups completed SBRT without any interruptions.

Conclusions: The use of this institutional simulation protocol was helpful in optimizing SBRT planning for HCC, which resulted in an excellent toxicity profile. Our findings show that for lesions >20mm, 4D-CT with CM can easily identify both the target and the organs at risk. A Triphasic CT-scan with CM might be useful for identifying smaller lesions. A prospective validation of this approach on a larger patients population is warranted.

## PO048

### IMPACT OF BREATH-HOLD TECHNIQUE ON ACUTE CORONARY EVENT EXCESS CUMULATIVE RISK IN LEFT BREAST IMRT: A DOSIMETRIC ANALYSIS

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Aims: Cardiac toxicity is a major concern for left breast tangential field irradiation. Recent analyses reported a strong relationship between volume of the left ventricle receiving 5 Gy (LV-V5) and mean heart dose (MHD) with acute coronary event (ACE). Moderate deep inspiration breath hold (mDIBH) during radiation delivery may reduce the cardiac dose. We quantified the impact of mDIBH during left-sided breast irradiation on potential reduction of ACE excess cumulative risk.

Methods: 20 patients who underwent adjuvant tangential IMRT with mDIBH were analyzed. All patients underwent CT simulation in both free breathing (FB) and mDIBH. The Elekta ABC spirometer was used for respiratory control and breath-hold length of 20–30 s. A simultaneously integrated boost plan was created with prescription doses of 50 Gy to whole breast and 60 Gy to the tumor bed in 25 fractions. ACE cumulative risk was calculated using the prediction model developed by van den Bogaard (JCO, 2015) depending on MHD, LV-VH, patient age and pretreatment risk factors. In particular, for each patient ACE cumulative risk was calculated simulating all pretreatment risk factors.

Results: The use of mDIBH resulted in target coverage with no significant statistical differences with respect to FB plans. Median MHD was 3.7 Gy (range:2.8-6.2 Gy) in FB and 2.5 Gy (range:1.6-4.1 Gy) in mDIBH ($p<0.05$), resulting in absolute and relative reduction of 1.3 Gy (range: 0.2-2.5 Gy) and 35.0% (range: 4.7-53.6%), respectively. Median LV-V5 was 34.6 cc (range: 13.0-67.2 cc) with FB and 11.5cc (range: 0.0-35.7 cc) with mDIBH ($p<0.001$), resulting in absolute and relative reduction of 19.9 cc (range: 1.8-

43.8 cc) and 67.3% (range: 8.3-100%), respectively. The impact of mDIBH on ACE cumulative risk becomes increasingly remarkable with patients' age. For patients age >60 years, dose reduction in MHD translated in ACE 9-year excess cumulative risk decrease from 1.4% to 1.0% for patients without risks and from 7.0% to 4.9% for patients with pretreatment risks (diabete, hypertension, …), respectively. Similarly, dose reduction in LV-V5 translated in ACE 9-year excess cumulative risk decrease from 1.6% to 0.9% for patients without risks and from 5.4% to 2.9% for patients with pretreatment risks.

Conclusion: ABC mDIBH technique resulted in a significant reduction of MHD and LV-V5 for left sided breast radiotherapy. Excess risk of ACEs can be remarkably reduced, in particular for patients age >60 years.

**PO049**

## DOES AUTOMATED VMAT PLANNING IMPROVE PLAN QUALITY IN HEAD-NECK CANCER? A COMPREHENSIVE DOSIMETRIC EVALUATION

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Aims: Treatment plans for head-neck are highly complex due to large irregular shaped target volumes, multiple dose prescription levels and to several OARs close to the target. We assessed the performance of the Pinnacle automated inverse-planning algorithm and we compared automatically generated VMAT plans (AP) with the historically clinically accepted manually-generated ones (MP).

Methods: Twelve patients treated with VMAT-SIB for bilateral head-neck cancer were re-planned with the Auto-Planning engine implemented in Pinnacle TPS v.16.0. The PTV1 included the primary tumor, PTV2 and PTV3 included the high-risk and low-risk lymph-nodal areas, respectively. PTV1, PTV2 and PTV3 were simultaneously irradiated over 30 daily fractions at 67.5Gy, 60.0Gy and 55.5 Gy, respectively. Three metrics were defined for plan evaluation: 1) a healthy tissue conformity index (H) to describe the overall plan conformity, 2) a merit function (M) to describe the targets coverage and a penalty function (P) to evaluate the sparing of critical organs. A plan quality index (PQI) was introduced to consolidate the three metrics H, M, P into a single figure defined by the Euclidean distance between the points (H,M,P) and (1,1,1). PQI=0 represents the ideal scenario. Healthy-tissue integral dose (ID) was also evaluated. A Wilcoxon paired test was performed for plan comparison with statistical significance set at $p<0.05$.

Results: Scores of PQI for MP and AP plans were 1.036±0.092 and 0.956±0.074 (p=0.003), respectively. For the targets coverage M, MP and AP attained 0.852±0.011 and 0.857±0.005 (p=0.110) showing no differences in targets coverage. For H index, MP and AP attained 0.367±0.048 and 0.406±0.032 (p=0.003) showing a significant improvement of AP plans in dose conformity. For P index, MP and AP attained 0.195±0.095 and 0.267±0.084 (p=0.003) showing a significant improvement of AP plans in OARs sparing. AP plans provided a significant decrease in Integral Dose of 7% (p=0.003). Increase of AP plans quality was always accompanied by a reduction of plan variability. The mean number of MUs was higher for AP (586 vs. 451, p=0.002), suggesting an increased degree of fluence modulation.

Conclusions: The Pinnacle Auto-Planning module was able to produce highly consistent treatment plans for this complex anatomical site. AP supplied an overall increase of plan quality, together with a reduction of variability. The planning time was substantially reduced with Auto-Planning down to one hour.

**PO050**

## PET AS PROGNOSTIC VALUE IN CERVICAL CANCER MANAGEMENT. A MONOISTITUTIONAL EXPERIENCE

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Aims: Cervical cancer is the second most common gynecological cancer worldwide. In locally advanced cervical cancer,18F-FDG PET/CT has become important in the initial staging, particularly in the detection of nodal and distant metastasis, metastasis, all stage variables correlated with treatment implications and prognostic value. The aim of this study is analyzed the role of18F-FDG PET/CT in uterine cervical cancer as predictive value for progression free survival in our mono-institutional experience.

Methods: From January 2011 to May 2018 we retrospectively analyzed a total of 64 pts who underwent PET-CT scan pretreatment and after 3 months end of treatment with LACC FIGO Ib2-Iva. Pts treatments schedule were CT and EBRT with IMRT or Tomotherapy, followed by BRT. BRT treatment was planned with MRI or CT scan. Time intervals are reported as median and inter quartile range (IQR).

Results: We consider pts with positive pretreatment PET (50 pts positive on cervix 81%, 29 pts positive on nodes (pelvic and paraaortic) 46%) who repeated PET

after therapy in order to evaluate metabolic response. who repeated PET after therapy in order to evaluate metabolic response. Median time from 1st to 2nd PET is 5 months and 3 weeks (IQR 18 days). Here we reported Results: COX model adjusted for age, FIGO and time from first to second PET, HR = 7.86 (95%CI 1.93 - 31.97), p=0.004. Events (progression or death) occurred about 8 time faster in patients with positive cervical uptake at second PET compared to patients with negative. COX model adjusted for age, FIGO and time from first to second PET, HR = 6.98 (95%CI 1.23 - 39.70), p=0.028. Events (progression or death) occurred about 7 time faster in patients with positive nodes at second PET compared to patients with negative .

Conclusions: In our experience a negative PET-TC after 3 months from end of treatment, was significantly correlated with an improved disease-free survival. With the limit of unbalanced number of group's pts, the results seem to have a higher predictive value than the classical prognostics parameters and may be useful to identify high-risk groups at time of the first revaluation and to tailor the following therapeutic approach in this type of cancer.

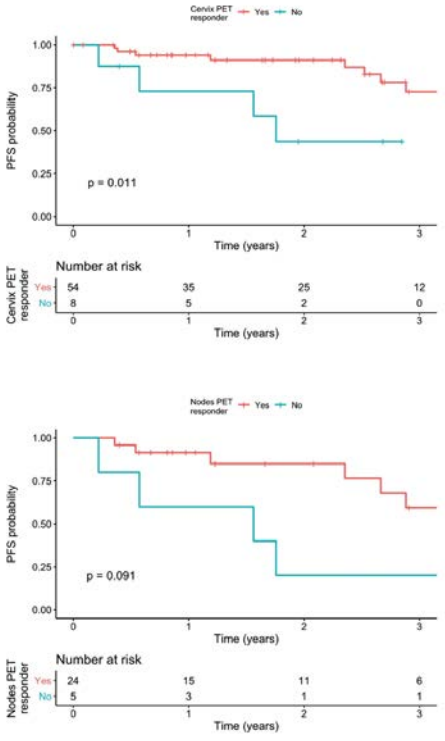


**Figure 1.**

**PO051**

## STEREOTACTIC BODY RE-IRRADIATION WITH CYBERKNIFE SYSTEM FOR LOCALLY RECURRENT PROSTATE CANCER AFTER PRIMARY RADIATION THERAPY

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Aim: Local recurrence management in prostate cancer after primary Radiotherapy isn't still defined. There are no guidelines regarding prostate re-irradiation, however stereotactic body radiotherapy (SBRT) is an interesting limited sites treatment option; we present our experience of re-irradiation with Cyberknife system (CK) for localized prostate cancer failure.

Methods: Between April 2016 and April 2019, 10 patients with instrumental recurrence on prostatic gland were treated with CK in our Institute. Patients were underwent to primary radiation therapy at average total dose of 65,3 Gy (range 38-76 Gy); at time of biochemical relapse (PSA nadir + 2 ng/ml according to Phoenix criteria), they were underwent at instrumental re-staging with pelvic multi-parametric MRI and/or a total body Fluorocholine-PET/TC or PSMA-PET/TC. They were treated by no-monoisocentric CK-SBRT radioablation that, thanks to intraprostatic fiducial markers and real-time tracking system, allowed to reduce doses to organ at risk (OAR). We evaluate biochemical control and adverse events with PSA levels and EORTC/RTOG criteria every 3 months for the first two years and then every 6 months for the following ones after re-treatment.

**Table 1.**

| | | | | | | |
|---|---|---|---|---|---|---|
| Number of patients | 10 | Age at recurrence (y) | Median (range) 73(61-88) | | | |
| Age at diagnosis (y) | Median (range) 65.5(54-70) | PSA-DT at reirradiation (mo) | Median (range) 7.5 (3.2-24.5) | | | |
| PSA at diagnosis (ng/mL) | Median (range) 7.19(4.7-345) | Interval time primary RT and re-irradiation (y) | Median (range) 2(06-10) | | | |
| AJCC cT-stage<br>T1c<br>T2a<br>T2b<br>T3a<br>T3b | 2<br>2<br>3<br>3<br>0 | Months follow-up | Median (range) 12(0-24) | | | |
| NCCN risk class<br>low<br>intermediate<br>High | 1<br>2<br>7 | GTV<br>Average<br>median | (cm3)<br>36.84<br>42.85 (22.67-65.52) | | | |
| Gleason score<br>≤6<br>7(3+4)<br>7(4+3)<br>≥8 | 6<br>0<br>0<br>4 | Constraints bladder<br>V50%< 40%<br>V100%< 10% | median (range)<br>18.65 (3-34)<br>3.95(0-8) | | | |
| PSA nadir after RT (ng/mL) | Median (range) 0.66(0-2.54) | Constraints Rectum<br>V50% < 50%<br>V80% < 20%<br>V90% < 10%<br>V100% < 5% | median (range)<br>20.1(13.68-33.8)<br>6.35(3.7-14)<br>3.9(2.0-9.1)<br>1.3(0.4-4.4) | | | |
| Radiological staging<br>PET-CT (choline/acetate)<br>PET-PSMA<br>MRI<br>Bone scan | 4<br>2<br>3<br>1 | Genitourinary Toxicity (RTOG) | Under-RT (Gbe) | 3 mo(%e) | 6 mo(%e) | 12 mo(%e) |
| | | 0 | 40% | 43% | 83% | 80% |
| | | 1 | 50% | 43% | 17% | 20% |
| | | 2 | 10% | 14% | 0% | 0% |
| | | 3 | 0% | 0% | 0% | 0% |
| Time between 1° RT and 1° relapse (y) | Median (range) 10 (3-12) | Gastrointestinal Toxicity (RTOG) | Under-RT (Gbe) | 3 mo(%e) | 6 mo(%e) | 12 mo(%e) |
| | | 0 | 40% | 71% | 67% | 80% |
| | | 1 | 60% | 29% | 33% | 0% |
| | | 2 | 0% | 0% | 0% | 20% |
| | | 3 | 0% | 0% | 0% | 0% |
| Technique Primary RT<br>3DCRT<br>IMRT<br>BT | 7<br>2<br>1 | PSA level (ng/ml)<br>Median (range) | Pre-RT (Gbe)<br>3.25<br>(0.38-16.98) | 3 mo(%e)<br>0.93<br>(0.15-3.43) | 6 mo(%e)<br>0.7<br>(0.04-3.3) | 12 mo(%e)<br>0.67<br>(0.14-2.52) |

Results: Median time between primary radiotherapy and CK-SBRT was 10 years. At time of first diagnosis, 7 patients were classified as NCCN high-risk class, 1 patient as low-risk, 1 as favorable and 2 as unfavorable intermediate-risk class. At time of recurrence, 9/10 patients used or had been treated with long-term androgen deprivation therapy (ADT) (median duration 35

months). We delineated prostate (GTV), PTV (GTV + 3 mm posterior and 5 mm in all other direction) and OARs. CK-SBRT prescription total dose was 30 Gy (6Gy in 5 fraction) at 80% isodose line for all patients. Treatment and patients characteristics are summarized in Table 1. The median time of follow-up was 9 months (range: 3-24 months). Median overall survival (OS) was 9 months, 9-months biochemical recurrence-free survival rate was 100%. Treatment was well tolerated. Urinary and rectal toxicity are showed in Table1.

Conclusions: SBRT re-irradiation with Cyberknife System after primary RT showed favourable results in term of biochemical control with low toxicity. Our study shows that SBRT may be a promising option in local recurrence prostate cancer patients previously irradiated. Longer follow-up is needed to confirm these results.

**PO052**

## SALVAGE THERAPY OF HIGH GRADE GLIOMA RECURRENCES WITH CYBERKNIFE TECHNIQUE

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Aims: Recurrence represents the main pattern of failure in the treatment of High Grade Glioma (HGG), after a primary treatment which includes surgical resection, adjuvant chemotherapy and radiotherapy. The recent development of radiotherapy techniques able to deliver high dose of radiation in small volumes sparing the surrounding organ at risk, has opened the possibility to reirradiate the recurrent tumor in a high hypofractionated regime while minimizing the risk of radiation induced side effects. In this study we present the experience of the Cyberknife Centre of Mater Dei Hospital (Bari, Italy) in the treatment of HGG recurrences with Cyberknife (CK) technique. We have evaluated the efficacy and the toxicity of a CK treatment with a follow-up of 34months.

Methods: From March 2016 to July 2018, we have treated 25 pts. (15♂, 10♀). The median age was 60 yrs. The histology was: 21 Glioblastoma, 3 Anaplastic Astrocytoma, and 1 Oligodendroglioma. Primary treatment consisted in surgery, radiotherapy and chemotherapy in all pts. except one who received only radiotherapy and chemotherapy. The dose prescribed (with Cyberknife) varies from 12Gy to 35 Gy, to the 78-80%, in one to three fractions depending on the dimension and localization of the target. The biologically equivalent dose (BED) is equal to 50-60 Gy considering an $\alpha/\beta$ =10 for the cerebral tumor.

Results: The treatment was generally well tolerated. Acute side effects of the therapy included nausea, vomiting and headache; vertigo and seizures are less frequent. These symptoms were transient and generally responded to medication with steroids. Late toxicity is correlated to the high risk of radiation induced complications deriving from brain reirradiation. The cumulative total dose tolerated by the brain was kept below 100Gy (normalized to 2Gy/fraction, $\alpha/\beta$ ratio 2): exceeding this limit could lead to the development of radiation necrosis, cranial nerve neuropathies, vascular injuries (including carotid artery stenosis) and severe edema. The median relapse free survival and overall survival were not reached after a median follow-up of 15 months.

Conclusions: Our results demonstrate that Cyberknife technique is a suited technology to reirradiate HGG Glioma recurrences leading to a good local control disease with low toxicity.

**PO053**

## MALIGNANT GYNECOLOGICAL MELANOMA TREATED WITH CARBON ION RADIOTHERAPY AT CNAO

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Aims: Gynecological malignant mucosal melanoma (g-MMM) is considered to be a radioresistant tumor with poor regression after photon beam radiation therapy (RT) that have a mostly palliative role. For their biological and physical advantages, carbon ion radiotherapy (CIRT) may be superior to photons for managing radioresistant tumors, such as g-MMM. We analyzed early clinical outcomes of CIRT in the first patients with g-MMM treated at the National Center of Oncological Hadrontherapy.

Methods: Between 2016 and 2018, 9 patients (pts), with a median age of 68 years, and histologically proven g-MMM were treated with CIRT after surgery or in exclusive settings. Patient, tumor and treatment details are described in Table 1. They had 7 vaginal (VaM), 1 cervical (CM) and 1 vulvar (VuM) MMM. One pt with VaM had been previously irradiated with photons; 8 pts are considered inoperable for local extension and 1 pt underwent to adjuvant CIRT on the small pelvic space after radical surgery without lymphadenectomy. Two pts underwent to neoadjuvant and sequential anti-PD-1 immunotherapy. Because of the large volume of macroscopic disease, the CM and VuM patients were irradia-

ted with up to a total dose of 28 GyRBE in 3 fractions and 68.8 GyRBE in 16 fractions, respectively, to the Clinical Target Volume (CTV) defined as the Gross Tumor Volume (GTV) + uterine cervix and corpus for the CM and GTV + vulva for the VuM. Except adjuvant case, for VaM the small pelvic space including GTV was irradiated with up to a total dose of 38.7-43 GyRBE followed by a GTV boost of up to a total dose of 68.8 GyRBE in 16 fractions. All patients were treated with synchrotron-based scanning carbon ion beams (pencil beam scanning and spill-by-spill active energy variation). Early clinical and toxicity profile (according to CTCAE V4.03- scale) were evaluated.

Results Treatment was well tolerated and no interruption was needed. For the evaluable pts, toxicity profile was favorable and no G≥2 acute/late toxicities were observed. Overall, for pts with a follow-u p≥ 3 months, the median LC ranged from 3 to 13 months (< for VuM and CM), the median MFS and the median OS was 6.5 (range: 3-23) and 10 months (range: 3-31) respectively. Data are still ongoing.

Conclusion: Because of the high rate of distant metastasis and unsatisfactory survival benefit, a more conservative treatment approach, instead of extensive surgery, may be warranted. We think that CIRT could be a treatment choice for patients with g-MMM.

**Table 1. Patient, tumor and treatment characteristics.**

| | Subgroup | Value |
|---|---|---|
| Age, years | Median (range) | 68 ( 52-83) |
| Tumor site | Vagina<br>Vulva<br>*Cervix uteri* | 7<br>1<br>1 |
| Molecular features | *NRAS* mutation<br>c*KIT* mutation | 1(Vulvar melanoma)<br>1 (Vaginal melanoma) |
| Previous treatment | Surgery<br>Radiation therapy with photons | 1 (Vaginal melanoma)<br>1(Vaginal melanoma) |
| GTV volume, cc | CM<br>VuM<br>VaM median (range) | 380.96<br>305.65<br>26.8 (1.2-133.07) |
| Total dose | CM<br>VuM<br>VaM (radical treatment)<br>VaM (adjuvant treatment) | 24 Gy RBE(3 fraction)<br>68.8 Gy RBE (16 fractions)<br>68.8 Gy RBE (16 fractions)<br>43 Gy RBE (16 fractions) |
| Anti-PD-1 immunotherapy | VaM (neoadjuvant and sequential) | 2 |

VaM: vaginal melanoma, VuM: vulvar melanoma, CM: cervical melanoma

## PO054

### RE-IRRADIATION WITH CARBON ION RADIOTHERAPY FOR PELVIC RECTAL CANCER RECURRENCES: CNAO CLINICAL EXPERIENCE

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Aim: The re-irradiation of locally recurrent rectal cancer (LRRC) presents challenges due to the proximity of critical organs such as bowel. Carbon ion radiotherapy (CIRT) could be a treatment option for conventionally difficult-to-cure patients (pts). Our purpose was to evaluate the clinical outcome (local control LC, metastasis free survival MFS and overall survival OS) and toxicity profile in previously irradiated patients with LRRC treated with CIRT.

Methods Between 2014 and 2018, a total of 14 pts (M:F= 12:2) with a median age of 58.5 years (range: 34-78) were treated with CIRT as re-irradiation for LRRC at CNAO. All pts had a history of, at least,a surgery for RC. Except a case in which radiotherapy (RT) was delivered for a prostatic cancer(total dose TD:76 Gy), previous pelvic RT ranged from 45 Gy to 50.4 Gy. Moreover, 1 pt received brachytherapy boost (TD: 20 Gy) after pelvic RT and 1 pt, at time of the first recurrence, underwent stereotactic radiotherapy (30 Gy in 6 fractions). Ten relapses were located in the presacral, 1 in perineal, 1 in perianal and 2 in pre-coccygeal region. Four pts received spacer implantation prior to CIRT to secure adequate distance between bowel and tumor. Clinical outcome and toxicity profile (according to CTCAE V4.03scale) were evaluated.

Results: Median interval between the two courses of RT was 65 months (range: 14 - 139). Median TD of CIRT was 60 GyRBE (range: 35-76.8; from 3 to 4.8 Gy RBE/fraction). All pts completed the scheduled treatment course. Median follow-up was 18 months. Acute toxicity was mild and mainly neuropathic: grade 2 (G2) neuropathic pain in 1 and G1 in 2 pts. The major late toxicities were peripheral neuropathy (20%, G2). No G≥3 acute/late reaction nor pelvic infections were observed. The 1-year and 2-year LC rates were 78% and 52% respectively, relapses occurred in 6 pts in close proximity to bowel. The 1-year and 2-year OS rates were 100% and 76.2% respectively. The 1-year and 2-year MFS rates were 64.3% and 43%. At statistical analysis, LC was not influenced by age, grading, GTV volume or total CIRT dose.

Conclusions: Re-irradiation with CIRT appears to be a promising, effective, and safe treatment option for LRRC. Further research is required to identify the long-term safety and efficacy in a larger number of pts.

## PO055

### REIRRADIATION WITH STEREOTACTIC BODY RADIATION THERAPY OF A LOCAL RECURRENCE OF PROSTATIC ADENOCARCINOMA AFTER CONVENTIONAL ADJUVANT RADIOTHERAPY

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A man of 79 in good general conditions (ECOG 0\1) presented with an increase of PSA levels. He was on androgen deprivation therapy (LHRH agonist plus Bicalutamide) after having been treated with radical

prostatectomy and postoperative radiotherapy for prostate cancer 19 years before. A 18-F choline PET-CT documented a local failure adjoining the urethral meatus. A rectoscopy was obtained to rule out significant radiation injuries caused to the rectal mucosa by the previous radiotherapy. Since the rectoscopy was negative, the patient was treated with image guided, stereotactic body radiation therapy to the site of disease relapse. A total dose of 25 Gy in 5 fractions of 5 Gy was administered. The treatment was quite well tolerated, except for mild tenesmus. After 6 months the patient is fit and well, he reports no symptoms of toxicity and PSA level is half as much as before treatment, so Bicalutamide is discontinued.

## PO056

### CHOOSING THE OPTIMAL GATED WINDOW FOR DEFINING TARGET VOLUME IN LUNG STEREOTACTIC ABLATIVE RADIOTHERAPY

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Aim: To compare retrospectively generated gated internal target volumes (ITV) and to evaluate whether gated ITVs can provide a reduction of planned target volumes (PTVs) than standard ITV expansions.

Methods: In this study, we retrospectively generated respiratory gated ITV and PTV for our cohort of patients that underwent 4DCT for thoracic radiotherapy at our Department betweeen august 2018 and february 2019. We calculated standard ITV and we calculated two gated ITVs (PTV30%-70% that included 30,40,50,60 and 70% and PTV80%-20% that included 80,90,100,10 and 20%, see Figure 1, A, B and C) to analyze the volumetric reduction. Further, we considered as significant a reduction >10% for the PTV and we analyzed the role of the localization and the size of the gross tumor volumes.

Results: We included 38 patients with a median age of 70 years (mean 68, SD± 13,4, range 43-89), 18 patients were females (47%) and 20 males (52%). Both the two gated PTVs (PTV 30%-70% and PTV 80%-20%) were significantly smaller than standard PTV (p-value<0,001 for both PTVs). Taking into consideration the volume of the GTV, we found a significant correlation with GTV30cc and the ITV30%-70% (Chi-square analysis, p:0,006) and with GTV5cc and the ITV80%-20% (p:0,003). We also found a correlation with the localization of the target lesion (mediastinal / central /peripheral lesion) for both the gated ITVs (respectively p: 0,030 for ITV 30%-70% and p:0,018 for ITV 80%-20%).

Conclusions: Gated ITVs plans could be useful for sparing of normal tissue. Our results show that this approach could be useful for smaller lesions and for certain localizations (island tumors).

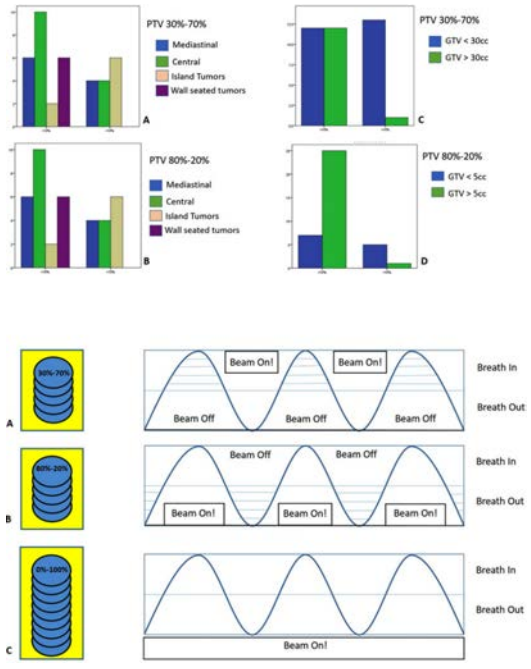


Figure 1.

## PO057

### 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 seventy-two

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. Sixty-one patients (85%) were glioblastoma (GBM) and 12 (15%) resulted anaplastic astrocytoma and anaplastic oligodendroglioma (Grade III WHO). Of them 50 patients underwent Stupp regimen and 22 pts were treated with short course radiotherapy (40,05 Gy in 15 fractions) according to Perry et.al protocol due to low KPS (unfit to Stupp protocol). The treatment was performed with LINAC Synergy of Elekta company using 3DCRT or VMAT technique.

Results: At analysis 47 pts (65%) were male and 25 (35%) female. The median KPS was 80 (range 50-100).

The median OS in all patients was 18 months and at the moment of abstract submission 27 patients are still alive. In patients underwent Stupp regimen the overall survival was 21 months and 4 years survival was 38%. 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. Finally, PTV > 265 cc was associated with lower OS compared to pts with PTV ≤ 264 cc (17 mths vs 24 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 < (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, total dose, PTV ≤ 264 cc, KPS, total tumor resection and CR after radiotherapy treatment were prognostic factors in terms of OS. Pts with low KPS underwent short course radiotherapy had a poor prognosis and only KPS ≥ 70 and association of TMZ with RT was influenced OS.

**PO058**

## THE INFLUENCE OF BREAST SIZE ON TOXICITY USING ISC TECHNIQUE FOR ADJUVANT RADIOTHERAPY

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Aims: To evaluate the results in terms of moist desquamation occurrence in women with large breast size (volume ≥1000 cm3) treated with adjuvant whole breast radiotherapy (WBRT) using the irregular surface compensator (ISC) technique.These results are compared with historical control group (CG) of patients treated with the traditional 3D field-in-field (FIF) technique.

Methods: All patients received adjuvant WBRT in 25 fractions to a total dose of 50 Gy, using ISC and FIF technique. Patients with negative prognostic factors received a boost of 10 Gy. Systemic adjuvant treatments were hormonal therapy (HT) and/or chemotherapy (CHT) and/or Trastuzumab. Toxicity was assessed using the Common Terminology Criteria for Adverse Events (CTCAE 4.03) scale. Chi-square test was used to assess differences between groups.

Results: Fifty-seven patients were included in the analysis. Thirty patients (52.6%) were treated with ISC technique and twenty-seven (47.4%) patients with FIF (see Table 1). Median age was 65 years (range 48-84). Median PTV cc was 1236.6 (range 1013.7 - 2110.8 cc). The incidence of moist desquamation was 37% and 63% in ISC and 3D-FiF group respectively (p=0.04, see figure 1). A total of 8 patients (14%) suspended radiotherapy course (median days 5; range 3-8), 3 in the ISC group, 5 in the 3D-FiF group.

Conclusions: ISC WBRT technique seems associated with a lower rate of moist desquamation in large breasted patients (CTV > 1000 cc) compared with the FIF technique and therefore can be employed in these patients.

**Table 1.**

| | ISC patients | 3D patients (Control Group) | p |
|---|---|---|---|
| Age (mean, yrs) | 64.4 | 63.8 | 0.159 |
| CTV (mean, cc) | 1392.8 | 1241 | 0.813 |
| Boost (n, %) | 18 (60) | 14 (52) | 0.535 |
| HT (n, %) | 28 (93) | 23 (85) | 0.139 |
| Concomitant Trastuzumab (n, %) | 6 (20) | 5 (18) | 0.582 |

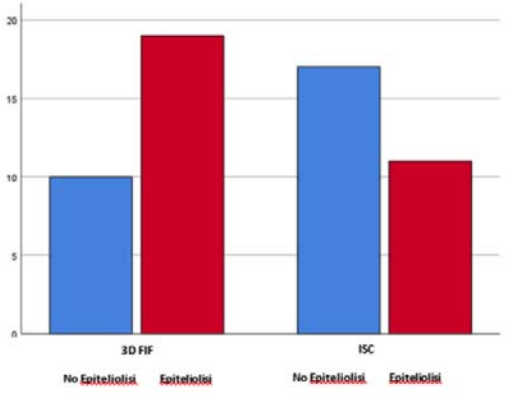


**Figure 1.**

**PO059**

## MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING (MPMRI) IN THE MULTIDISCIPLINARY WORK-UP AND FOR RADIOTHERAPY IN VERY HIGH RISK PROSTATE CANCER PATIENTS

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Purpose: Very high risk (VHR) prostate cancer is defined to: (1) GS 8-10 in combination with ≥ 1 other high-risk factor (PSA > 20 ng/mL and cT3-4) or (2) primary Gleason pattern 5 or ≥ 4 cores containing pattern 4. Here we describe our experience of main role of multiparametric magnetic resonance imaging (mpMRI) not only in multidisciplinary work-up but overall in radiotherapy of VHR patients.

Methods: We have reported 3 recent cases of VHR patients discussed on Multidisciplinary Uro-Oncologic Board. In our diagnostic work-up, patient was clinically examined with 1,5 T mpMRI done at staging prior to Androgen Deprivation Therapy (preADT) and at PSA nadir (preRT, after 6 months of ADT).

Results: In the first patient, preADT 41 cc prostate volume with DW restriction (tumoral focus) and preRT 12 cc without diffusion-weighted (DW) restriction and no more contact with rectal wall. In the second, preADT 37 cc and preRT 12 cc and no DW restriction. In the third, preADT 33 cc with DW restriction; preRT 22 cc and no DW restriction.

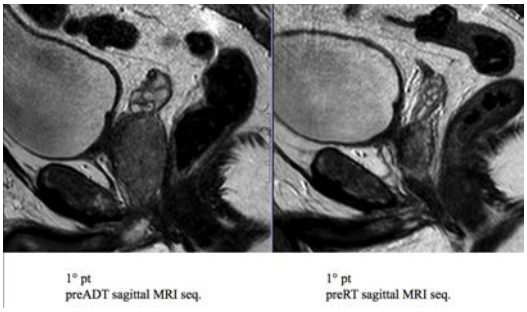


**Figure 1.**

Conclusions: Numerous studies have demonstrated the value of mpMRI in evaluating prostate cancer (PCa). (3,4) Pretreatment assessment with diffusion-weighted MRI (DW-MRI) showed tumor risk. MRI has high specificity but poor and heterogeneous sensitivity for local PCa staging(4). mpMRI can accurately detect small-volume significant tumors, localize and stage PCa(3). Furthermore, we could always evaluate dimensional reduction both organ and tumor with mpMRI. There was a significant rectal sparing on radiation planning. Therefore mpMRI improved quality of radiation treatment.

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**PO060**

## EVALUATION OF SETUP UNCERTAINTIES AND INTERFRACTION ORGAN MOTION IN SBRT FOR PANCREATIC CANCER USING INTRATUMORAL FIDUCIAL MARKERS

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Aims: To quantify systematic and random errors for stereotactic body radiation therapy (SBRT) of pancreatic cancer (PC) and to evaluate the interfractional pancreatic position variation using gold fiducial markers and daily cone beam computed tomography (CBCT) scans. We also analyzed the trend over time of the relative position of the markers to evaluate a possible migration and to validate their suitability for tumor localization.

Methods: For this work we will analyze data from 30 pts treated with SBRT for PC. All pts underwent fiducial markers position by endoscopical procedure prior to SBRT. Patients were treated with abdominal compression to reduce motion caused by breathing, digestion and heartbeat and CBCT has been acquired for every patient every day before starting treatment delivery. SBRT treatments were delivered over 5 consecutive days with Volumetric Modulated Arc Therapy (VMAT) technique. We analyzed CBCT for each treatment day and patient to evaluate systematic and random errors of treatment. In a first step, CBCT has been registered with the reference CT on bone anatomy to obtain the displacement from the starting position (the setup error). In a second step CBCT has been registered with the reference CT on the implanted fiducials to obtain the "pancreas displacement" from his planning position related to bone anatomy position.

Results: Preliminary results (derived by the analysis of the first five patients) show a systematic error of 2.5, 3.8 and 3.2 mm respectively for left-right, superior-inferior and cranio-caudal direction and a random error of 3.2, 5.1 and 3.4 mm. The interfractional variation of the markers position relative to bone anatomy can be < 8 mm, but these results and their significance must be confirmed by the analysis of all the treatments. The analysis of the relative position of fiducials seems to suggest that there is not a significant migration, also because radiotherapy is delivered in only five days.

Conclusions: If the analysis of the whole sample

will confirm these data, it will be possible to conclude that the use of implanted pancreatic markers improves the accuracy of PTV localization and the quality of SBRT treatment, allows a correct choice of margins between GTV and PTV, could allow a future dose escalation and could be advisable in all pancreatic treatments.

## PO061

### ABSTRACT WITHDRAWN

## PO062

### INTERNATIONAL PROSTATIC SYMPTOMS SCORE (IPSS) IMPROVEMENT AFTER VOLUMETRIC MODULATED ARC RADIOTHERAPY USING THE CLARITY 3D ULTRASOUND SYSTEM: OUR PRELIMINARY EXPERIENCE

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Aims: To evaluate the International Prostatic Symptoms Score (IPSS) improvement in patients after prostate radiotherapy using the Elekta Clarity Autoscan 3D ultrasound system.

Methods: We progressively analyzed 14 patients with a median age of 70 years treated with a curative therapy for prostate tumour at our Radiation Therapy Unit from January 2019 till April 2019. All patients were treated using Volumetric Modulated Arc Radiotherapy (VMAT), with the Elekta Clarity Autoscan 3D ultrasound system that offers live imaging of the target and surrounding anatomy during prostate treatment; this device is used to reduce intra and inter-fractions movements. All the patients were scored as intermediate risk according AJCC. For each patient, we calculated IPSS pre-treatment and 45 days after treatment; IPSS is a scale evaluation that allows an objective evaluation of the urinary symptomatology of the patient suffering from prostatic diseases.

Results: We included 14 patients with a median age of 70 years (mean 61.8 years, range 61-75 years). In 12/14 patients (85%) there was an average IPSS reduction of six points respect of the beginning of the treatment. In only one patient, there were a stationary state of IPSS. All the patients have reported a slight acute toxicity (G1 from RTOG scale evaluation) after treatment. At the first follow-up, 100% of our patients had a PSA reduction.

Conclusions: The Elekta Clarity Autoscan 3D ultrasound system has shown to be an interesting device, with a favorable acute toxicity profile. Further studied are needed to evaluate chronic toxicities with a long term follow-up.

## PO063

### TOTAL IRRADIATION OF THE SCALP AND FACE IN CUTANEOUS LYMPHOMAS, EXPERIENCE OF THE UNIVERSITY OF FLORENCE

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Aims: Aim of this study is to report on the use of total scalp and face irradiation in three patients affected by cutaneous lymphomas with an extensive involvement of the skin of scalp and face.

Methods: We analyzed the treatment plans and the clinical outcome of three patients with cutaneous lymphoma, 2 Mycosis Fungoides (MF) and 1 Follicular Lymphoma (FL). Patients underwent a CT scan using a thermoplastic head-shoulder mask. The clinical target volume (CTV) included the patient's entire skin surface of scalp and face (in the patient affected by Follicular Lymphoma both ears were not included in the CTV since were not involved by disease). The planning target volume (PTV) was obtained with an isotropic 3 mm expansion of the CTV. The prescription dose was 14 Gy for the two MF patients and 20 Gy for the FL patient in 2Gy fractions. They were treated with Helical TomoTherapy with daily IGRT with MVCT. A 2.5cm field width was used. An effective and robust template was generated for plan standardization. Ring structures around the PTV were contoured and used to improve gradient and conformity.

Results: Dosimetric parameters are reported in table 1. Despite the complex shape and superficial nature of the target, we obtained a good target coverage with the volume of PTV that received the 95% of the prescribed dose that ranged between 94,9% and 97,1%, with Dmax between 111,7-112,2%. The dose to the organs at risk resulted within the dose constraints except for the lens (average dose range 10,2-19,7Gy) and we obtained excellent dose gradient with low brain and hippocampal dose (average dose to hippocampus between 1,23 and 2,53Gy; dose to 40% of hippocampus between 1,09 and

2,65Gy). Two patients ended the treatment with excellent tolerance, the main acute side effects were grade 1 dysgeusia and grade 1 erythema. One MF patient will start the treatment in the coming days. The two patients experienced complete G2 alopecia, one patient completely recovered his hair about 6 months after the treatment. No other late side effects have been recorded so far. The MF patient had an almost complete response and has stable disease 10 months after the treatment. The FL patient has a partial response one month after the treatment. Conclusions: In selected patients with diffuse cutaneous lymphoma, the treatment of total scalp and face irradiation with TomoTherapy technique is feasible and effective with low toxicity.

**Table 1. Dosimetric parameters**

| | 95% coverage PTV dose | 100% coverage PTV dose | Max. Dose PTV | Lens L (average dose) | Lens R (medium dose) | Hippocampus L 40% volume | Hippocampus L (average dose) | Hippocampus R 40% volume | Hippocampus R (average dose) |
|---|---|---|---|---|---|---|---|---|---|
| Patient 1 | 13,29Gy, 94,9% | 8,17Gy, 58,4% | 15,75Gy, 112,5% | 11,05Gy, 78,9% | 10,27Gy, 73,4% | 2,39Gy, 17,1% | 2,3Gy, 16,4% | 2,65Gy, 18,9% | 2,53Gy 18,1% |
| Patient 2 | 19,37Gy, 96,9% | 12,76Gy, 63,8% | 22,33Gy, 111,7% | 19,74Gy, 98,7% | 17,29Gy, 86,5% | 1,24Gy, 6,2% | 1,23Gy, 6,2% | 1,23Gy, 6,2% | 1,22Gy 6,1% |
| Patient 3 | 13,6Gy, 97,1% | 8,17Gy, 58,4% | 15,75Gy, 112,5% | 14,54Gy, 103,9% | 13,9Gy, 99,3% | 1,09Gy, 7,8% | 2,3Gy, 16,4% | 1,09Gy, 7,8% | 2,53Gy 18,1% |

| | Eye L (average dose) | Eye R (average dose) | Parotid gland R (average dose) | Parotid gland L (average dose) | Lacrimal gland R (average dose) | Lacrimal gland L (average dose) | Brain (average dose)) | Brain V 80% prescription dose | Cochlea L (average dose) | Cochlea R (average dose) |
|---|---|---|---|---|---|---|---|---|---|---|
| Patient 1 | 8,46Gy, 60,4% | 8,22Gy, 58,7% | 10,17Gy, 72,6% | 10,06Gy, 71,9% | 8,63Gy, 61,6% | 8,51Gy, 60,8% | 3,42Gy, 24,4% | 1,96Gy, 14% | 2,83Gy, 20,2% | 2,63Gy, 18,8% |
| Patient 2 | 16,26Gy, 81,3% | 15,64Gy, 78,2% | 16,22Gy, 81,1% | 16,19Gy, 81% | 9,48Gy, 47,4% | 9,81Gy, 49,1% | 5,42Gy 27,1% | 1,25Gy, 6,3% | 1,44Gy, 7,2% | 1,45Gy, 7,3% |
| Patient 3 | 11,27Gy, 80,5% | 11,13Gy, 79,5% | 12,59Gy, 89,9% | 13,26Gy, 94,7% | 4,21Gy, 30,1% | 4,23Gy 30,2% | 3,83Gy, 27,4% | 1,25Gy, 8,9% | 1,59Gy 11,4% | 1,53Gy 10,9% |

## PO064

### PROGNOSTIC VALUE OF IMAGING (18FDG PET AND MRI) IN PREDICTING LOCALLY ADVANCED RECTAL CANCER RESPONSE TO NEOADJUVANT THERAPY

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Purpose. Prognostic value of imaging (18 F-FDG PET and High Resolution MRI) in predicting pathological response after neoadjuvant concurrent radiochemotherapy, followed by surgery. We report our experience at S. M. Goretti Hospital in these last years.

Materials and methods. From January 2010 to December 2018 we treated 53 patients diagnosed with locally advanced rectal cancer. 14 patients were females and 39 males. Median age at diagnosis was 65 years (range 47-83). Clinical stage was as follows: 12 pts stage IIA (T3N0) and 41 pts IIIB (T3-4 N1). All patients received a pre and post treatment staging including colonoscopy, computer tomography, magnetic resonance and a PET-TC simulation. Imaging data has been collected: tumor SUL-Peak, SUV max and MRI features. All patients received a dose of 50-50.4 Gy in 1.8-2 Gy per fraction to the pelvic area. Concomitant chemotherapy was based on protracted intravenous infusion 5 FU (220 mg/mq) in 9 pts, capecitabine (825 mg/mq twice daily) throughout radiotherapy course in 44 pts. Surgery was performed 6-8 weeks after radiotherapy course.

Results. After a median follow-up of 70 months (range 25-108 months), 55 patients are still alive and free of disease, 4 pts died of local progression of disease and systemic metastases, after 16, 18, 19 and 28 months of follow-up. Sfincter saving surgery was performed in 56% of patients eligible for abdominal perineal resection. Complete pathological response was reported in 14 patients (pCR: 26.4%) and correspons to a clinical complete response, as assessed by MRI and PET-TC parameters. 6 pts who had achieved a cCR after radiochemotherapy did not undergo subsequent surgery. They are still alive and free of disease. The treatment was well tolerated, moderate acute and late toxicity (G1-2 according to RTOG scale) were reported. No patient suffered a performance status worsening during the scheduled treatment.

Conclusions. MRI and PET-TC parameters correlate clinical and pathological response. Preoperative radiochemotherapy is a well tolerated and effective treatment.

## PO065

### EXCELLENT OUTCOMES FOLLOWING VMAT RADIATION THERAPY FOR SMALL CELL CARCINOMA OF THE PROSTATE: A CASE REPORT

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Aim: Small cell carcinoma of the prostate (SCCP) is a rare disorder accounting for less than 1% of all prostate cancers. The most popular approach involves both local control using surgery to the primary tumor and systemic treatments with chemotherapy, but few reports have addressed the role of radiotherapy. We evaluated the feasibility and toxicity of Volumetric modulated arc therapy (VMAT) radiotherapy for locally advanced SCCP.

Methods: In April 2014, a 76 years old patient with SCCP underwent a transurethral resection of the prostate (TURP) for obstructive urinary symptoms. The final pathology demonstrated findings consistent with primary SCCP. The metastatic workup did not reveal evidence of bone, nor visceral metastates, but right external iliac lymph nodes (diameter 2.8 cm) along with a tumor confined to the prostate, were detected and confirmed at pelvic magnetic resonance imaging (MRI). TNM classification was cT2N1M0. Initial PSA was 1.2 ng/mL. A moderately hypofractionated image-guided VMAT treatment with simultaneous integrated boost was planned delivering 68.75 Gy (2.75 Gy per fraction) to prostate, 55 Gy (2.2 Gy per fraction) to the seminal vesicles and positive nodes, and 45 Gy to negative pelvis lymph nodes, administered in 25 fractions.

Concomitant and adjuvant use of androgen deprivation therapy with LH-RH agonist was prescribed for a total duration of 5 years. Biochemical control was assessed using the Phoenix definition. Treatment related toxicities were recorded and scored using the CTCAE v.3.

Results: The tumor volume decreased remarkably by 2 months after VMAT at CT scan (diameter < 1 cm). Only a mild (Grade 1) acute genitourinary toxicity occurred. No late GU and GI events were experienced. Three months after VMAT, serum PSA had decreased to 0 ng/mL and was mantained for five years thereafter until last follow up (April 2019). No evidence of disease was found at restaging exams.

Conclusions: despite the poor prognosis, our patient exhibited excellent outcomes in terms of both tolerability and efficacy of the combination of ADT and VMAT radiotherapy for locally advanced SCCP. The rapid decrease in tumor size in both the prostate and the iliac nodes seems to suggest a similar high radiosensitivity to that of SCLC. A prospectic validation of this approach is warranted.

## PO066

### CLINICAL-DOSIMETRIC ASSESSMENT WITH THE PRODVH SOFTWARE OF PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY FOR MALIGNANT PLEURAL MESOTHELIOMA: A RETROSPECTIVE ANALYSIS

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Aims: To analyze overall survival (OS), acute and late lung toxicity in a retrospective cohort of patients undergoing adjuvant radiotherapy after extra-pleural pneumonectomy (EPP) for malignant pleural mesothelioma (MPM), with or without chemotherapy. To investigate possible correlations between dosimetric data and clinical outcomes and assess the role of 3 dimensional conformal RT (3DCRT) and intensity modulated RT (IMRT) in terms of coverage of target volumes and preservation of the major organs at risk (esophagus, lungs, heart)

Methods: Data of all patients (pts) treated with adjuvant RT after EPP for malignant pleural mesothelioma were reviewed. Overall survival (OS), acute and late lung toxicity (ALT and LLT) according to CTCAE V4.0 scale were analysed. Kaplan-Meyer curves and log-rank test were used for survival analysis, while chi-square test was calculated to compare the different variables. $P<0.05$ was considered significant. Furthermore, the data of all patients were evaluated with PRODVH, a homemade software developed to compare biologically equivalent DVHs and calculate mean DVH within clinically relevant groups (type of treatment, technique used, OAR and PTV)

Results: From 2005 to 2013 58 patients were treated with adjuvant RT after EPP for malignant pleural mesothelioma. The 3, 5 and 8 years overall survival rates resulted to be 48%, 34% and 18% respectively. Our study confirmed the relevant contribution of IMRT to local control after EPP. Local relapse free survival resulted to be 80%, 64% and 58% at 3, 5 and 8 years, respectively. Analysis of PRODVH showed that worse DVHs of OARs (lung, left coronary artery, pericardium and heart) are related with an increased risk of toxicity, in particular dyspnea .

Conclusions: IMRT following EPP achieved excellent local control for MPM, that might lead to the long-term survival in selected patients. However, treatment burden including acute and late toxicities should be considered in this treatment approach. Single plan DVH does not represent by itself the best approach to estimate treatment-related toxicity. PRODVH produces an average DVH giving more accurate information on the dosimetric features related with an increased risk of toxicity.

## PO067

### IMPACT OF SANTES® VAGINAL SUPPOSITORIES ON LATE VAGINAL TOXICITY IN THE RADIATION THERAPY FOR GYNECOLOGICAL CANCER

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Aims: Late vaginal toxicity represents a critical issue in patients undergoing to radiotherapy for ginecological cancer. In this series we evaluated the potential benefit of Santes® vaginal suppositories (hyaluronic acid, tocopheryl acetate, retinyl palmitate, semisybthetic glycerides) in 52 patients who underwent radiotherapy for gynecological diseases (cervical and endometrial cancer).

Methods: Twenty-six patients educated at the use of daily Santes® vaginal suppositories during radiotherapy were evaluated in comparison with a matched group of 26 control subjects. Santes® were administered 1 suppository/die in the evening starting from day one of treatment to 12 months after the end of RT, for 2 weeks each month. All 52 patients received neoadjuvant (n=20) or adjuvant (n=32) treatment with Helical Tomotherapy in 25-28 fractions with a prescribed dose of 45-50.4 Gy. Late vaginal toxicity, as vaginal dryness, vaginal obstruction and dyspareunia was investigated with portec-3, quality of life questionnaire, during treatment and 12 months from the end of radiation therapy. Adverse events were scaled using CTCAE v5 criteria. Chi-square test were conducted to evaluate any potential difference between the treatment arms, assuming a

p≤0.05 for statistically significative.

Results: Median age was 53 (range, 28-67). Late vaginal toxicity rates were: G0 in 9, G1 in 15, G2 in 2 in the control sample, and G0 in 19, G1 in 6, G2 in 1 in the Santes® arm; no G3 observed. Most common adverse event was vaginal dryness in both groups (12 and 5, respectively). A statistical difference between the two groups was detected for G≥1 toxicity (p=0.015), however no statistically significant difference was found in terms of G≥2 toxicity.

Conclusion: Despite the small sample size, in our series the daily assumption of Santes® vaginal suppositories during and after treatment shows a beneficial impact on the onset of late vaginal toxicity in patients treated with radiotherapy for gynecological cancer. Specifically, younger patients with G0 toxicity reported absence of dyspareunia, a potential cause of vaginal obstruction, in the months following radiotherapy, particularly on days of Santes® use.

**PO068**

## REPORT OF TOXICITY AND CLINICAL OUTCOMES OF MODERATE HYPOFRACTIONATED HELICAL TOMOTHERAPY FOR LOCALIZED PROSTATE CANCER: A MONO-INSTITUTIONAL ANALYSIS

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Aims: To evaluate toxicity and clinical outcomes of moderate hypofractionated Helical Tomotherapy (HT) for the curative treatment of a series of 170 patients with localized prostate cancer (PC).

Methods: From December 2012 to May 2018 170 patients with median age 75 years (range, 56-88) were treated with definitive intent for PC. 34% were low risk (LR), 30% intermediate risk (IR), 36% high risk (HR). Median iPSA was 8.79 ng/ml (1.3-170). Androgen deprivation therapy was prescribed according to NCCN recommendations for IR and HR groups. All patients received 70 Gy in 28 fractions to the prostate; 61.6 Gy were delivered to the seminal vesicles for IR; pelvic lymph-nodes irradiation for a total dose of 50.4 Gy was added in the HR subgroup. Toxicity was evaluated basing on CTCAE V4.0 scales, biochemical failure was defined following Phoenix criteria. Time-to-event data were analysed using Kaplan-Meier method and log-rank test.

Results: Median follow-up was 36 months (range, 12-65); acute toxicity was as follows: G1 and G2 in 27.6% and 19.4% of cases for GI; 53% and 24% for GU. No G≥3 event observed. At 1 year (n=170), GI late rates were G1=5.8%, G2=4.1%, G3=1.1%, GU rates were G1=24% and G2=4.7% At 2 years (n=153), GI and GU G≥2 adverse events were 7.1% and 4.6%, including respectively 4 and 3 cases of G3 toxicity. At 3 years (n=93) GI G2 toxicity was 12.9%, no G3 events observed. For GU G≥2 was seen in 8.5% including one case of G3 urethral stenosis. No statistical correlation between late G3 incidence and clinical or dosimetric parameter was found. At the time of final assessment, twelve patients experienced a biochemical relapse, including 3 nodal recurrences, successfully treated with stereotactic body radiotherapy, and 2 bone metastases who underwent palliative RT, resulting in 2- and 3- biochemical relapse free survival rates of 90% and 87.5%, respectively. 2- and 3-yrs OS were 96.4% and 90%. The log-rank test revealed no difference between the risk groups in terms of biochemical control (p=0.16).

Conclusions: Moderate hypofractionated RT with HT for localized prostate cancer reported excellent outcomes with mild acute and late toxicity incidence, with biochemical control rates comparable to other experiences of hypofractionation available in literature.

**PO069**

## LATE TOXICITY EVALUATION IN PATIENTS SUBMITTED TO VOLUMETRIC MODULATED ARC THERAPY(VMAT) RADIATION TECHNIQUES FOR HEAD END NECK DISTRICT MALIGNANT NEOPLASMS

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Aims: To evaluate effectiveness of radiotherapeutic techniques implementation in the treatment of head and neck tumors. No changes had been recently observed in survival and prognosis for this malignant tumors, but increasing interest is now pointed on the treatment side effects reduction. In particular patients(pts.) report more psycological and physical distress in case of late effects, such as xerostomia and disphagia, causing an important detrimental impact on quality of live. Moreover we have neither effective medical therapies nor physiotherapeutic exercises that could reduce such toxicity. Among our department cases we analized the most important late effects in these subset of pts. in order to introduce improvements in radiotherapeutic techniques.

Methods: We collected data of pts. treated for head and neck tumors from January 2012 and December 2016. We considered all anatomical sites treated in this site as: tongue, oral cavity, parotid gland, oropharynx, hypopharynx, nasopharynx, paranasal sinuses, pharinx, thyroid. We also considered cervical lymph nodes localization even in case of unknown primary tumor. We analized 78 pts. of whom 19 pts.(24%) were treated with 3D conformal Radiotherapy (3DRT), 1 pts.(2%) died before starting 3DRT, 1 pts.(2%) died soon after the beginning of 3DRT for disease progression, 2 pts.(3%) didn't start RT for personal decision, 1 pts.(2%) didn't start 3DRT for adverse event before radiotherapy beginning, 1 pts.(2%) stopped 3DRT after

only one day for cognitive impairment. The remaining 53 pts. were treated with Volumetric Modulated Arc Therapy (VMAT) techniques. Histology was: 1 (2%) polymorphic adenocarcinoma, 1 (2%) adenoid cystic carcinoma, 1 (2%) carcinoma wiyh squamous and papillary aspects, 1 (2%) solid-papillary adenocarcinoma, 49 (92%) squamous carcinoma. Fifteen pts underwent different type of surgery (28%) and 38 pts.(71%) not received primary surgery. Standard VMAT radiotherapy schedule consisted in 54 Gy (1.80 Gy x 30 fractions) for prophylactic irradiation of neck lymph nodes with simultaneous integrated boost(S.I.B.) of 60 Gy (2 Gy x 30 fractions) for pathological nodal localization or positive margins and further S.I.B. of 66 Gy (2.20 Gy x fractions) on primary tumor. In 32 pts. (60%) concomitant chemotherapy was combined, usually with cisplatin administered one or three times a week.

Results: Median follow-up was 24(1-56) months. Median age was 67 years. 34 pts.were males and 19 pts. females. All pts. developed a G1 mucosal and skin toxicity a month after radiotherapy completion. Only 1 pts. developed G2 mucosal toxicity. Three pts. developed toxicity of subcutaneous tissues lasting undetermined time. G1 salivary glands toxicity was developed in 12 (22%) pts. after six months and in 2 of them this salivary glands toxicity lasted during follow-up. Only 1 pts developed severe dysphagia despite no mucosal reaction. Unfortunately 10 pts. (18%) pts were lost at follow-up. In 30 pts.(56%) no evidence of neoplasia, both on primary tumor and on latero-cervical neck lymph nodes was observed. 10 pts.(18%)developed tumor recurrence on primary site, 3 pts.(6%) had disease persistence both on primary tumor and nodes and 1 pts.(2%) relapesed only on neck nodes. No G3 - G4 toxicity were observed and only in the two pts who developed salivary glands toxicity we noticed a significant impact on quality of life.

Conclusions: Radiotherapy techniques improvement has significantly changed late toxicity incidence and severity for these kind of pts and has improved their quality of life. The use of intensity modulated RT or VMAT should be mandatory and further improvement could be achieved introducing better immobilisation systems and breath control systems. Two aims should be researched: realize a higher dose escalation for tumor treatment and minimize dose at organs at risk. Morover clinical benefits for pts. could be obtained by the introduction of new better tolerated drugs.

**PO070**

## MILD-HYPOFRACTIONATED VMAT IN PROSTATE CANCER: THE TOXICITY PROFILES AND SURVIVAL IN OUR CASISTIC

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Aims: To evaluate acute and long-time toxicity profiles and survival data among patients (pts) with prostate cancer, treated with radical mild-hypofractionated radiotherapy.

Methods: The clinical series included 85 pts with prostate cancer, treated with radical radiotherapy at our Institute, between 2012 and 2017. During follow up, we collected genito-urinary, rectal and sexual impairment toxicity data according to CTCAE scale v5.0. Statistical analysis was performed using SPSS® software.

Results: The median age was 73 years (range 56-85). Fourty-six pts (54%) were included in a favorable intermediate risk category of disease; 21 pts (25%), 11 (13%), 4 (5%) and 3 (4%) were in high risk, unfavorable intermediate, very high and low category, respectively. Seventy-six pts (89%) underwent also concomitant ormonotherapy. Radiotherapy was performed with mild-hypofractioned simoultaneous integrated boost and the prescribed dose to the PTV (prostate + seminal vescicles) was 56 Gy/2 Gy per fraction and to the prostate (boost) was 70 Gy/2.5 Gy per fraction. The treatment was delivered with imaged guide support (Cone-Beam-CT). During treatment an adequate rectum-bladder preparation was strongly suggested. Regarding acute toxicity, 25 pts (29%) did not show any degree of dysuria, while 50 (59%) and 10 (12%) pts reported grade 1 and 2, respectively. Fifty-four pts (63%) developed an increase of urinary frequency of grade 1, while 22 (26%) and 9 (10%) showed G0 and G2 events, respectively. Only 4 pts (5%) developed acute G1 diarrhea. Seventy-two pts (85%) had no grade of acute proctitis. The remaining 13 (15%) showed only G1 events. Regarding long time toxicity, no pts developed chronic fecal incontinence, while only 5 pts (6%) showed G1 urinary incontinence. Only 2 pts (2%) developed G1 proctitis and no one rectal stenosis and/or bleeding. Seventy-eight pts (92%) did not show any degree of sexual disfunction, only 5 (6%) and 2 (2%) showed grade 1 and 2, respectively. After a median follow up of 37 months, only 2 pts (2%) developed biochemical relapse and also metastasis. At Chi-square analysis, there was no significant correlation with initial risk category of disease or concomitant ormonotherapy. The 2 and 5 years overall survival was of 97% and 94% respectively.

Conclusions: The analysis confirmed low toxicity and good survival data. These data underline the importance of an adequate pts selection, an adequate treatment delivery and optimal rectum-bladder conditions.

**Table 1.**

| Acute toxicity (CTCAE v5.0) | Dysuria | Increase urinary frequency | Diarrhea | Proctitis |
|---|---|---|---|---|
| G0 | 25 (29%) | 22 (26%) | 81 (95%) | 72 (85%) |
| G1 | 50 (59%) | 54 (63%) | 4 (5%) | 13 (15%) |
| G2 | 10 (12%) | 9 (11%) | 0 (0%) | 0 (0%) |
| **Chronic toxicity (CTCAE v5.0)** | **Faecal incontinence** | **Urinary incontinence** | **Proctitis** | **Sexual impairment** |
| G0 | 85 (100%) | 80 (94%) | 83 (98%) | 78 (92%) |
| G1 | 0 (0%) | 5 (6%) | 2 (2%) | 5 (6%) |
| G2 | 0 (0%) | 0 (0%) | 0 (0%) | 2 (2%) |

PO071

## ROLE OF POSTOPERATIVE RADIOTHERAPY (PORT) AFTER COMPARTMENTAL SURGERY FOR LOCALLY ADVANCED ORAL CAVITY TUMORS: A RETROSPECTIVE ANALYSIS ON 185 PATIENTS

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Aim: Literature data on the role of postoperative radiotherapy (PORT) in locally advanced oral cavity tumors derived mainly form patients (pts) treated with a non-compartmental surgical approach. Therefore the role of PORT after Compartmental Sugery (CS) has not been yet fully investigated. In order to quantify the benefit of PORT in such cohort of patients, we performed a retrospective analysis on 185 consecutive pts treated with CS +/- PORT at our Institute between 2000 and 2016. Incidence and site of locoregional recurrence (LRR) was assessed and analyzed according to the adjuvant treatment.

Patients and Methods: Inclusion criteria were: 1) locally advanced (stage III and IV, TNM 7th ed) oral cavity tumors 2) no previous tumor and/or oncologic treatments in head and neck region 3) CS performed for oral cavity tumors 4) minimum follow-up of 6 months from surgery. One hundred and eighty-five pts (127 male, median age 54 years, range 17-81 years) were eligible. Most of pts (90%) had a pathologic stage IV. PORT was administered to 158 (85%) pts. Eighty-three (50%) were treated with adjuvant concurrent chemoradiation.

Results: After a median follow-up of 51 months (range 6-221 months), 107 (58%) pts were alive without disease, 36 (19.5%) were alive with local and/or distant metastases, 32 (17%) died for tumor progression, 10 (5.5%) died for other causes. Tumor, lymph nodes and both tumor and lymph node recurrences were found in 26 (14%), 24 (13%), and 3 (1.5%) pts, respectively. Median time between surgery and LLR was 9.83 months (range 2-145 months). LLR occurred in 42 (26.5%) and 14 (52%) pts treated with or without PORT, respectively. Median interval between CS and LRR was 61 and 10.2 months for pts treated with and without PORT, respectively. Statistical analysis is ongoing.

Conclusion: Preliminary results showed that PORT seems to maintain its role in reducing LLR also in pts treated with CS. Further ongoing analysis should help to optimize pts stratification in order to better tailor adjuvant treatments.

PO072

## ANALYSIS OF DOSIMETRIC PARAMETERS IN PATIENTS TREATED WITH VOLUMETRIC ARC THERAPY (VMAT) RADIOTHERAPY METHOD. MONO-INSTITUTIONAL EXPERIENCE

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Purpose: Future challenges in oncology include 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 Volumetric Arc therapy (VMAT) radiotherapy method.

Methods: Between the end of 2018 and May 2019, 30 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 30 patients were collected for analisys. in the subset of patients with late bladder toxicity grade $\geq 2$ (in terms of haematuria, cystitis and dysuria), we observed a correlation with a Vd equal to 55 Gy (p.value 0.019). Relating to patients with late rectal toxicity grade $\geq 2$ (in terms of proctitis, tenesmus) we observed a correlation with a Vd equal to 48 Gy (p.value 0.022). Local control was 99.5% (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: The development of toxicity prediction models, which increasingly favor the use of a more personalized treatments is the desirable goal of modern radiotherapy. Our preliminary 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. Our analysis, as already mentioned, is to be considered preliminary because they are still considered a relatively poor number of patients and as regards the considerations of late toxicity the follow-up times are still short.

PO073

## INTENSITY MODULATED ADJUVANT HYPOFRACTIONATED BREAST/CHEST WALL AND REGIONAL NODAL RADIOTHERAPY: TOXICITIES AND CLINICAL OUTCOMES

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Aims: To evaluate retrospectively treatment-related toxicity , loco-regional and distant control in patients with breast cancer and nodal involvement, treated with intensity modulated Hypofractionated Radiation Therapy (IMHyRT) of the whole breast or chest wall and ipsilaterals regional nodes.

Methods: From September 2016 to Dicember 2018, 65 patients with breast cancer and nodal involvement were treated with surgery (quadrantectomy -67% or mastectomy- 33%, Stage pT3 and/or ≥4 positive lymphnodes) followed by adjuvant IMHyRT. Twenty-one patients were treated on chest-wall and ipsilateral regional lymph nodes and 44 patients on whole breast and ipsilaterals regional lymph nodes. Total dose was 42.4 Gy in 16 fractions and patients treated on whole breast received concomitantly a dose of 48 Gy in 16 fractions on tumor bed (with IMRT-SIB technique). Common Terminology Criteria for Adverse Events v 4.0 (CTCAE) was utilized to quantify acute and late side effects at a maximum follow up of 31 months (range 3-31 months).

Results: Median age was 58 years ( range 34-84 years). Median actuarial follow up was 19 months (range, 3-31 months, 95% CI 15.7-22.3); 26% of all patients developed Grade 2 skin toxicity during radiotherapy, 3% reported Grade 1 dysphagia and Grade 2 lymphedema was observed in 4.6% of cases. No Grade ≥ 2 skin toxicity at 1, 6 and 12 months were collected. At median follow up no Grade 2 lymphedema and late toxicity were recorded. Six out of 65 patients (9.2%) had distant metastases, three of these had a cancer related death. Two patients presented local relapse and one a lymph-nodal relapse. Two-year OS , local relapse free survival (LRFS), local nodal relapse-free survival (LNRFS) and distant metastasis free survival were 89.7%, 96.9%, 93.8% and 82.9%, respectively.

Conclusions: IMHyRT seems to be associated with a minimal acute and late toxicity and with a great disease control. Prospective studies with a larger sample and with a longer follow-up are necessary to confirm this result.

PO074

## OUTCOMES IN INTERMEDIATE RISK PROSTATE CANCER PATIENTS TREATED WITH HYPOFRACTIONATED RADIOTHERAPY

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Aims: To evaluate clinical efficacy and outcomes of hypofractionated radiotherapy (HyRT) in intermediate risk prostate cancer patients (IRPCp).

Methods: Between January 2005 and February 2017, 176 patients affected by intermediate risk prostate cancer (cT2 or Gleason 7 or pre-treatment PSA value ranging from 10 to 20 ng/mL) were treated with HyRT. The median age at diagnosis was 74 years (range 53-88 years). Multiparametric-MRI was performed for local staging and for better outline the Clinical Target Volume (CTV) in the majority of patients. Fourty one patients were scheduled to 3D conformal radiotherapy delivering 43.8 Gy in 12 fractions to seminal vesicles and 54.75 Gy in 15 fractions to the prostate, three times weekly. One hundred thirty five patients were scheduled to IMRT-IGRT radiotherapy delivering 54.75 Gy to the prostate plus the first cranial centimeter of seminal vescicles and 49,5 Gy to the seminal vescicles, in 15 fractions, 3.65Gy/fraction three times weekly. All patients underwent neoadjuvant, concomitant and adjuvant hormonal therapy for a total duration of 9 months. Acute and late toxicities were evaluated according to RTOG scale. Biochemical relapse was defined using PSA nadir + 2 ng/mL.

Results: Median actuarial follow-up was 84 months (95% I.C.= 76.7-92.1). Minimum follow-up was 7 months and maximum follow-up was 108 months. Thirty-six patients (13.23%) presented biochemical failure and subsequently developed loco-regional and/or distant failures. Twenty-eight (15.6%) died from causes not related to prostate cancer, whereas 8 (4.5%) patients died from progression of disease. Median OS, CSS, BFFS and MFS were not reached. Seven-year OS, CSS, BFFS and MFS were 88,4%, 97.7%, 85,7% and 96.2%, respectively. Patients with PSA ≤0.7 ng/ml at first follow-up presented a statistically better OS, CSS, BFFS and MFS (p=0.024, p=0.004, p=0.03 and p=0.037, respectively). Acute toxicities were as follow: Grade 1-2 Genitourinary (GU) toxicities were 42.5%, while 1,2% presented Grade 3 toxicities; Grade 1 Gastrointestinal (GI) toxicities were 13,7%, Grade 2 GI toxicities were 5.8%. Late GU and GI toxicities ≥ Grade 2 recorded at the last follow-up were 1.0% and 0.5% respectively.

Conclusions: HyRT in IRPCp is a feasible treatment schedule with low rates of both acute and late GI and GU toxicities, and it's a good option to gain high rate of tumor control in terms of OS, CSS, BFFS and MFS.

PSA ≤0.7 ng/ml at first follow-up is a prognostic factor of better outcomes.

## PO075

### CLINICAL OUTCOMES AND TOXICITY PROFILE OF HEAD AND NECK CANCER PATIENTS TREATED WITH IMRT/VMAT: A SINGLE INSTITUTE ANALYSIS

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Aims. Nowadays, Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) are standard irradiation technique for head and neck cancers (HNC) treatment. In this context, asimultaneous integrated boost (SIB) may offer an additional radiobiological advantage allowing lower fractional dose to normal tissues whereas higher dose per fraction to the target volume, leading to an improved outcome while toxicity is potentially reduced. The aim of our study is to analyze survival and toxicity outcomes of patients affected by HNC treated with IMRT or VMAT.

Methods. Between July 2015 and December 2018, 40 consecutive HNC patients were treated with IMRT (N=20) and VMAT (N=20). Data concerning patients and disease parameters, treatment characteristics, acute and long-term radiation induced toxicity according to CTCAE v. 4.03 scale were collected. Statistical analysis to compare outcomes was performed.

Results. Patients and treatment characteristics were reported in Table 1. On a total of 40 HNC: twenty-six (65%) patients had postoperative treatment, while fourteen (34%) received a primary treatment. Ten (25%) patients received concurrent chemotherapy, thirty (75%) patients radiotherapy alone. The doses were 70 Gy to the gross tumor, 66 Gy to the high-risk postoperative sites and 54 Gy to the subclinical disease. Twenty-six (65%) patients received a SIB. All patients completed treatment. Mean follow-up was 13.27 months (range 3-44.78 months). There were 11 disease progressions: 4 (10%) were loco-regional recurrence and 7 (17.5%) distant metastases. The 24-months PFS and OS were 60.1% and 84.9%, respectively. There was a statistically significant correlation between PFS and stage III-IV (p=0.039) and Karnofsky performance status ≤70 (p=0.002). Considering acute toxicity (<3 months), 3 (7.5%) cases of G3 mucositis and 4 (10%) G3 dysphagia were observed, while late toxicity-wise (>3 months), no xerostomia ≥G2 and only 1 (2.5%) patient with G3 dysphagia were observed. No statistically significant difference in toxicity rates between IMRT and VMAT was observed.

Conclusions.The most important outcome for patients treated for HNC is overall survival and loco-regional control, with increasing concerns about quality of life due to treatment sequels. Our results seem to show that IMRT and VMAT for HNC can reduce toxicities without compromising local control and overall survival, in agreement with literature data.

**Table 1.**

**a. Patients characteristics**

| Parameter | N (%) |
|---|---|
| **Gender** | |
| male | 31 (77,5) |
| female | 9 (22,5) |
| **Age** | |
| mean | 63,925 |
| range | 40-89 |
| **Smoking** | |
| yes | 20 (50) |
| no | 20 (50) |
| **KPS** | |
| 100 | 8 (20) |
| 80-90 | 24 (80) |
| ≤70 | 8 (20) |
| **Tumor site** | |
| oral cavity | 8 (20) |
| oropharynx | 12 (30) |
| hypopharynx-larynx | 10 (25) |
| nasopharynx | 2 (5) |
| parotid | 3 (7,5) |
| skin ear | 3 (7,5) |
| other | 2 (5) |
| **Tumor histology** | |
| squamous | 36 (90) |
| other | 4 (10) |
| **Tumor stage** | |
| I | 4 (10) |
| II | 9 (22,5) |
| III | 5 (12,5) |
| IV | 22 (55) |

**b. Treatment characteristics**

| Parameter | N (%) |
|---|---|
| **RT intent** | |
| esclusive | 14 (35) |
| postoperative | 26 (65) |
| **Dose (cGy)** | |
| 7000 | 12 (30) |
| 6000 | 24 (60) |
| 5400 | 1 (2,5) |
| **Dose/fraction (cGy)** | |
| 200 | 20 (50) |
| 220 | 14 (35) |
| 233 | 6 (15) |
| **BOOST** | |
| SIB | 26 (65) |
| Sequential | 8 (35) |
| **RT Technique** | |
| IMRT | 20 (50) |
| VMAT | 20 (50) |
| **Concomitant Therapy** | |
| No | 24 (60) |
| Yes | 16 (40) |
| **Cisplatin** | 10 (25) |
| 100 mg 3 weekly | 9 (22,5) |
| 40 mg weekly | 1 (2,5) |
| **Cetuximab** | 6 (15) |

## PO076

### ROLE OF BONE DOSIMETRY ON HAEMATOLOGICAL TOXICITY IN LOCALLY ADVANCED RECTAL CANCER PATIENTS UNDERGOING NEOADJUVANT CHEMORADIATION

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Aim: to assess the relationship between dosimetric distribution in pelvic bones haematological toxicity in neoadjuvant chemoradiotherapy for locally advanced rectal cancer.

Methods: We performed a retrospective analysis of patients treated at our Radiation Oncology Unit between January 2017 and December 2018. The pelvic bone consisted of the whole hip bone, the lumbosacral spine, and the heads of the femurs. In each patient, the entire pelvic bone was recontoured on the planning CT and divided in subsets, as follows: BM1 (L5 and sacrum), BM2 (ilium from iliac crests to upper side of

femur head), BM3 (lower pelvis: pubis, ischium, acetabular fossa, proximal third of femur, to the ischiatic tuberosity), BM4 (pelvis: BM2 + BM3), BM5 (whole pelvis: BM1 + BM4). Haematological toxicity was scored with the CTCAE of the EORTC for anaemia, neutropenia and thrombocytopenia. The association between haematological toxicity of any grade (≥G1) and the dosimetric parameters (V10, V20, V30, and V40 and mean doses) of each BM volume were studied using univariate correlate analyses (ChiSquare method). The significant variables in the univariate correlate analyses were then simultaneously entered into the multivariate linear regression models in a stepwise manner and a ROC curve was generated for each haematological toxicity. A p-value < 0.05 was defined as statistically significant.

Results: A total of 24 patients were enrolled in the present study, 14 males and 10 females, with a median age of 71 yr (mean age 70.5 yr, 9.4 ds, range 54-85 yr). The BM volumes that were correlated with anaemia are BM1-V20 (p: 0,025), BM3-V40 (p:0,036), BM4-Mean (p:0,015), BM4-V10 (p:0,036), BM4-V20 (p:0,048), BM4-V30 (p:0,021), BM4-V40 (p:0,039), BM5-Mean (p:0,022), BM5-V10 (p:0,035), BM5-V20 (p:0,029), BM5-V30 (p:0,022). Conversely, we did not find any correlation with the development of either leucopenia or thrombocytopenia. At multivariate analysis, taking into consideration BM4-mean and the clinical variables (staging, sex, age), the parameters that remained significant was only BM4-mean (p:0,033, OR 1,05, 95% CI:1,03-1,10), with an R2 of 0,322. The ROC curve for the prediction of anaemia showed an AUC of 0,781 (95% CI 0,59-0,96),

Conclusions: Our work has the limits of a single-institutional case studies, retrospective work and a small number of cases. At the same time the correlation between bone dosimetry and hematological toxicity needs to be further studied.

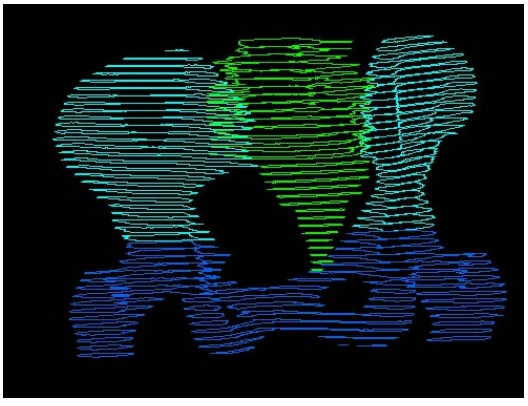

**Figure 1.**

**PO077**

## FOLLOW UP IN RECTAL ADENOCARCINOMA PATIENTS TREATED WITH NEOADJUVANT IMRT AND CHEMOTHERAPY: OUR EXPERIENCE

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Aims: Nowadays neoadjuvant radio-chemotherapy (RT/CT) is a firm point in patients' (pts) management with locally advance rectal tumor. In this study we analyze our experience with 20 pts who had undergone surgery after RT/CT PET/CT-based.

Methods: We collected datas of 20 pts with a mean age of 69 (range 45-88 y.o.) treated in our structure between 2016 and 2019. The pts (11F, 9M), were all diagnosed with advanced adenocarcinoma of the rectum: 12 had been classified as stage 2 (T3-4, N0) and 8 as stage 3 (N+); moreover, 60% of the tumors were localized in the low rectum, 20% in the mid rectum and 20% in the proximal one.The treatment included folfox or capecitabine - based CT and IMRT with 45 Gy (1,8 Gy per fraction) on the pelvis, followed by a boost of 5,4 Gy (1,8 per fraction) on the rectum, for a Total Fractionated Dose (TFD) of 50,4 Gy. FDG-PET, performed to all pts, showed uptake in the place of disease with a mean SUV max value of 25,13(range 6,5-49,5), and was integrated with the centering on CT to optimize the dose on the target. Weekly visits to evaluate local toxicity (as classified by RTOG scale) and follow-up were carried out as prescribed by AIOM guidelines. After 4-10 weeks pts underwent surgical excision (SE).

Results: Following the RT/CT in 90% of the pts has been observed a clinical downstaging and downsizing of the diseased, and in 78% could be observed a downstaging of the lymphonodal compromission. This led all of the pts to have radical surgical excision of the disease, all but for one who showed complete tumor remission right after CT/RT. According to RTOG toxicity evaluation scale, during CT/RT were observed: acute grastrointestinal (GI) toxicity (none in 10% of pts, first degree in 15% and second degree in 75%), acute genito-urinary toxicity (none in 80% of pts, first degree in 10% and second dregree in 10%); only 2 pts showed a persistence of G1 gastrointestinal toxicity following the end of CT/RT and none of the GU kind. Following the SE, at a mean follow up of 18 months (range 3-38 months) 90% of pts showed no evidence of disease, 5% died because of tumoral progression and 5% died of unrelated causes.

Conclusions: Our study has confirmed IMRT's importance PET/CT - based, in the neoadjuvant management of rectal tumors. It has shown to improve overall survival (OS) and local control of the disease.

Furthermore, its downsizing and downstaging effect on the tumor has led to a larger number of pts elegible for radical surgical treatment.

## PO078

### EVALUATION OF THE RESPONSE AND SURVIVAL IN PATIENTS WITH 1 BRAIN METASTASES TREATED WITH FRACTIONATED STEREOTACTIC RADIOTHERAPY (FSRT): THE EXPERIENCE OF OUR INSTITUTION

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Aims: Evaluation of the response and survival in patients with 1 brain metastases (BM) treated with fractionated stereotactic radiotherapy (FSRT).

Methods: We prospectively observed 10 patients with BM from different primary tumors (breast, lung, colorectal), treated with FSRT from 2018 to 2019. Patients presenting 1 BM, age <70 years and Karnofsky Performance Status > 70%. Patients were treated with VMAT (Volumetric Modulated Arc Therapy) radiotherapy technique, using schedules: 24 Gy in 3 fractions (8 Gy/day). For all patients a baseline MRI performed before starting FSRT was co-register with planning-TC using a rigid algorithm; to evaluate treatment response MRI was acquired 3 months after the end of FSRT, every 3 months during first year of follow up than every 6 months. Response to treatment was evaluated considering changes both in the larger tumor diameter according to RECIST criteria and 2 larger diameters according to WHO criteria, measured at each MRI control on T1 sequences.

Results: To date 7/10 patients were evaluable for tumor response at least at 3 months after the end of FSRT; evaluation of response to treatment showed an agree between WHO and RECIST criteria for all patients evaluated at 3 months; this correlation appears to remain in subsequent MRI. Treatment response observed at 3 months consisted in: 1 complete responses (CR); 3 partial responses (PR); 1 stable disease (SD); 2 progressions (PD). At a follow-up of 6 months, 6 patients could be evaluated: 1 CR; 1 PR; 2 SD; 2 PD. At 9 months, on 4 evaluable patients, we observed: 1 CR; 1 SD; 2 PD. Only 4 patients were evaluable at 12 months: 3 SD and 1 PD. 3 patients died between 3 and 6 months of follow-up, no patients died between the 6 and 12 months; one patient died after 12 months follow-up.

Conclusions: Although the sample size is still small, FSRT seems efficacy in terms of local control and survival. The obtained results correlate to prognostic factors as reported by literature data and used for our analysis; a longer follow-up will confirm this trend.

## PO079

### 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.

Materials and 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.

## PO080

### DOSIMETRIC CONSTRAINTS IN TERMS OF GEUD FOR PULMONARY TOXICITY IN LEFT BREAST RADIOTHERAPY WITH VMAT AND FIMRT TECHNIQUE

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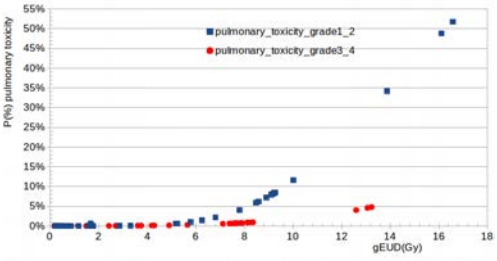
Aims: The purpose of this work is to find dose volume constraints for lungs toxicity, due to left breast

radiotherapy treatment, in terms of generalized Equivalent Uniform Dose (gEUD) proposed by Niemierko (1997, 1999). The Dose Volume (DV) effect incorporated by a EUD-based model is of paramount importance: in fact, the assumption that a normal tissue responds in serial manner leads to lack of control over the low- and mid-dose range, as the risk of complications is predominantly determined by the high doses.[1]




| Pulmonary toxicity Grade 1-2 | |
|---|---|
| Constraint (Gy) | NTCP |
| gEUD < 6 | < 1% |
| gEUD < 8 | < 5% |
| gEUD < 10 | < 10% |
| gEUD < 12 | < 20% |

| Pulmonary toxicity Grade 3-4 | |
|---|---|
| Constraint (Gy) | NTCP |
| gEUD < 8 | < 1% |
| gEUD < 13 | < 5% |

**Figure 1.**

Materials: 10 female patients undergoing left breast radiotherapy were evaluated: for them, the estimate of pulmonary toxicity, with the relative serial model, had a range from 0.0% to 61%. Two treatment plans were optimized for every patient, one with fIMRT technique (fractionation: 2Gy/fr x 25fr, boost 2Gy/fr x 5fr) and one with VMAT (SIB: 1.8Gy/fr x 28 fr, boost 2.1Gy/fr). EQD2 was calculated from the dose absorbed by the lungs (both ipsilateral and contralateral) and then the Relative Seriality model for radiation pneumonitis was used as method to evaluate the probability of pulmonary toxicity for both lungs. (Grade1-2: $\alpha/\beta$=3Gy, s=0.15, D50=16.3Gy, g=1.08; Grade 3-4: $\alpha/\beta$=3Gy, s=0.01, D50=30.1Gy, g=0.97). The concept of gEUD was used to equalize the probability of lung toxicity calculated once using the physical dose distribution (heterogeneous) and another using the gEUD (homogeneous). The radiobiological parameter "a" was determined (a = 0.9 for Grade1-2 toxicities, and, a=0.62 for Grade 3-4 toxicities) and a correlation was determined between the probability of pulmonary toxicity and gEUD.

Results: Significant correlations have been found between pulmonary toxicity (Grade 1-2 and Grade 3-4) and gEUD and some common threshold levels, in terms of NTCP, have been considered for a convenient clinical use.

Conclusions: Optimization criteria based on biologically related models are potentially more versatile and directly associated with treatment outcome than those based on DV criteria. The gEUD has found considerable support among proponents of biologically based optimization because it offers a compromise between purely biological indices, such as TCP and NTCP, and traditional DV metrics.

**Reference**

Report of AAPM "The Use and QA of Biologically Related Models for Treatment Planning" (2012) TG 166 of the Therapy Physics Committee

## PO081

## IMRT TREATMENTS OF INTERNAL MAMMARY CHAIN IN ADJUVANT RADIOTHERAPY: WHY NOT?. PRELIMINARY DATA

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Aims: To date the role of adjuvant radiotherapy (ART) in the treatment of internal mammary chain (IMC) remains still controversial. Lung and cardiac toxicities and dosimetrical matters are the main reasons limiting its use in high risk node positive breast cancer patients with conventional techniques. Herein we report our retrospective experience on adjuvant radiotherapy including IMC with several IMRT modalities.

Materials and Methods: From 2015-2019 45 consecutive patients (pts) with high risk node positive breast cancer were treated with extended nodal ART. ART-IMC was prescribed in pts with pN2 and pN3 breast cancer trated simoultaneously to the supraclavicular fossa (SVC) and the residual breast or postmastectomy chest wall with or without breast prosthesis implants. SIB-IMRT delivery techniques consisted of 6 -10 MV photon beams dual-arc VMAT (d-VMAT plan, 15 pts), hybrid-VMAT (h-VMAT plan 13 pts), IMRT 7-8 beams sliding-window (sw-IMRT plan , 17 pts). According to ICRU 83, the prescribed dose was 2 Gy/50 Gy to the breast or post-mastectomy chest wall and IMC; for SVC the PD was 1.92 cGy/48 Gy . Plans were optimized on Monaco ® TPS with a grid size of 3 mm, the same dose constraints and LINAC (Elekta Precise). Dosimetry respected for each PTVs, the V95% ≥ 95%, V105 < 3%,and V107< 1%. Constraints of OAR's were as follows : heart V17 (Gy) < 10% and mean heart dose < 6 Gy for left side and < 3 Gy for right side, ipsilateral lung V17 Gy < 35%, V5 Gy < 70% V20 Gy < 35% and MLD < 20 Gy respectively; controlateral lung V5 < 40%; mean controlateral breast dose < 5 Gy. Planning techniques were evaluated in each patients and compared on the basis of DVHs .

Results: The mean dose coverage on PTV IMC was 97.5±1.5% ( 96.4-99.8±1.1%); the mean heart dose was 4.8 Gy (4-6.5 Gy ) for left PTvs and 3.5 Gy (2.2-5 Gy) for right PTVs. The mean ipsilateral V5 was. 60% (56.4-65%), the controlateral lung mean V5 was 25.5% (20-45%). Both, h-VMAT and sw IMRT showed the best IMC coverage with a mean V95%= 97.5% (96-99.8%) and a better OAR's sparing for ipsilateral V5 and heart V17 than d-VMAT( p= 0.03) . At median fol-

low-up time of 2.5 years (2-5 yrs), no cardiac or lung acute and late toxicities have been recorded.

Conclusions: IMRT delivery modalities as h-VMAT and sw-IMRT resulted a feasible solution to obtain an optoimal coverage of the IMC minimizing OAR's exposure to low doses.

**PO082**

## INTENSITY MODULATED RADIOTHERAPY (IMRT) IN THE TREATMENT OF SQUAMOUS CELL ANAL CANAL CANCER: ACUTE AND EARLY LATE TOXICITY, OUTCOME AND EFFICACY

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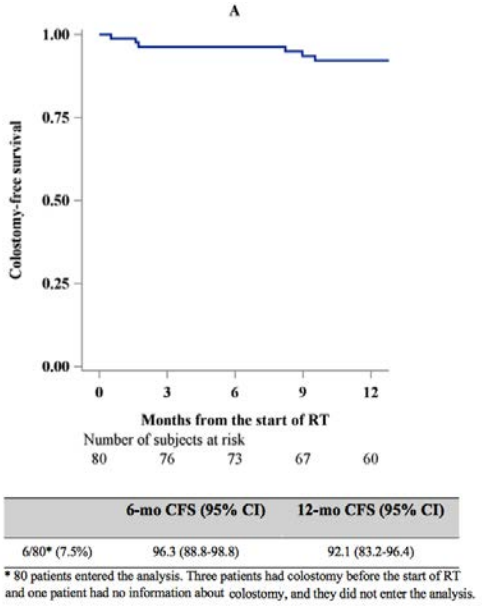
Aims: To retrospectively review our experience on 84 patients with squamous cell anal canal cancer (SCAC) within 12 months after combined treatment with intensity modulated RT (IMRT), in terms of acute (from the end of RT, to 6 months) and early late toxicity (after 6-12 months post RT completion) toxicity, compliance, overall treatment time and interruptions, colostomy free survival (CFS) and tumor response.

Methods: All the patients were treated with IMRT, using either RapidArc® technique with Trilogy linac or Tomotherapy®, and underwent oncologic evaluation to assess concurrent ChT administration. Acute gastrointestinal (GI), genitourinary (GU) and cutaneous (CU) toxicities were assessed according to Common Toxicity Criteria for Adverse Events (CTCAE) version 4.03. Early late toxicity was scored using the Radiation Therapy Oncology Group (RTOG) late radiation morbidity scoring system. The reported toxicity represents both any grade and specifically severe (≥G3) acute and early late toxicity. Tumor response was evaluated with response evaluation criteria in solid tumors (RECIST) v1.1.

Results: Of the entire cohort, 62 patients (74%) were treated with RapidArc® and 22 patients (26%) with Tomotherapy®. The elective low-risk PTV received a median dose of 41.4 Gy (range 32.4 Gy-48.6 Gy), high-risk PTV received a median dose of 46 Gy (range 40 Gy-56 Gy), while tumor and positive nodes received boost dose up to a total median dose of 56 Gy (range 36 Gy-60 Gy). Acute toxicity was collected for 84 subjects (100%): severe GI and skin toxicity was observed in 4 (5%) and 19 patients (23%), respectively . Early late toxicity was collected for 73 subjects (87%): severe GI and vulvo-vaginal toxicity was observed in 2 (3%) and 2 (3%) patients, respectively. No acute or early late GU toxicity was reported. A treatment interruption, due mainly for skin toxicity, occurred in 65 patients (77%) with a median interruption of 7 days (range 1-21 days). CFS was 96% (95% CI 89-99) at 6 months and 92% (95% CI 83-96) at 12 months. At 6 months after the end of RT complete response (CR), partial response (PR) and progressive disease (PD) was observed in in 70 (83%), 3 (4%) and 7 patients (8%), respectively. At 12 months CR was observed in 60 patients (81%); 11 patients (15%) experienced PD .

Conclusion: Our study showed an excellent clinical result and very low acute toxicity rates, confirming the use of IMRT as standard of care for curative treatment of anal cancer patients.




| | 6-mo CFS (95% CI) | 12-mo CFS (95% CI) |
|---|---|---|
| 6/80* (7.5%) | 96.3 (88.8-98.8) | 92.1 (83.2-96.4) |

* 80 patients entered the analysis. Three patients had colostomy before the start of RT and one patient had no information about colostomy, and they did not enter the analysis.

**Figure 1. Colostomy-free survival (CFS) during the first year after the start of RT.**

## PO083

### POSTOPERATIVE RADIATION THERAPY FOR PROSTATE CANCER WITH MODERATE HYPOFRACTIONATION AND SIMULTANEOUS INTEGRATED BOOST (SIB): ACUTE AND LATE TOXICITY

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Aims: Radiotherapy (RT) is being used with increased frequency in the management of prostate cancer (PC) following radical prostatectomy. However there is some concern that its use in the form of a hypofractionated regimen may lead to tissue injury when carried out in the postoperative setting. In the present study we retrospectively reported on acute and late gastrointestinal (GI) and genitourinary (GU) toxicities in a series of patients who received a course of moderately hypofractionated RT post-prostatectomy.

Methods: Thirty patients with adverse pathologic features or early biochemical failure following radical prostatectomy were included. All were treated with Volumetric Modulated Arc Therapy (VMAT), and Simultaneous integrated boost (SIB) in 28 fractions for a total dose of 66,64 Gy to the prostate bed and 53,2 Gy to the pelvic drainages, respectively. Androgen deprivation therapy (ADT) was administered to 66% of patients. After completion of RT, follow up was scheduled at 3 months and every 6-12 months thereafter. Acute and Late toxicities were assessed using Common Terminology Criteria for Adverse Events v4. 3-year biochemical disease-free survival (bDFS) was also evaluated.

Results: With a median follow-up of 36 months (range: 6.5 to 59.9 months), no ≥G3 late GI or GU toxicities were encountered. Two patients experienced a G3 acute and a G2 late GU toxicity, respectively. Two (6%) G2 acute GI toxicities were documented. 3-year bDFS was 70%. No treatment interruptions > 5 days occurred.

Conclusion: Moderately hypofractionated RT for PC by means of VMAT and SIB technique resulted in a excellent toxicity profile when applied postoperatively, either in the adjuvant or salvage setting. A larger cohort of patients with long term follow-up is warranted to confirm these findings.

## PO084

### INDUCTION CHEMOTHERAPY FOLLOWED BY RADIOCHEMOTHERAPY IN LOCALLY ADVANCED OR RECURRENT HEAD AND NECK CANCER: EFFICACY AND TOXICITY ANALYSIS

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Aims: To assess the feasibility and toxicity profile of treatment with induction chemotherapy (iCT) followed by moderately accelerated intensity-modulated radiation therapy (IMRT/VMAT) and weekly cisplatin in patients (pts) with locally advanced or recurrent head and neck cancer (LAHNC).

Methods: Two or three cycles of docetaxel, cisplatin and 5-fluorouracil (DCF) or with cisplatin and 5-fluorouracil (CF) were prescribed. Thereafter, radiotherapy was delivered with a simultaneous integrated boost IMRT/VMAT technique according to the following doses: 67.5 Gy or 70.5 Gy in 30 fractions to primary tumor and involved nodes, 60 Gy to high-risk nodal areas, and 55.5 Gy to low-risk nodal areas. Concomitant weekly cisplatin was associated. Toxicity was evaluated according to WHO and RTOG scales.

Results: Fifty-seven patients (median age: 58 years, range 32-76; male/female ratio: 52/5) were retrospectively analyzed. The most represented primary sites were oropharynx (35%), larynx/hypopharynx (23%), nasopharynx (19%) and oral cavity (17.5%). The majority of pts had clinical IV stage (46 pts, 81%), nodal involvement was present in 38 cases (67%). Before Radio-Chemotherapy (RCT), 32 (56%) pts received CF and 25 (44%) pts received DCF. Asthenia was the most frequent symptom reported by pts. Four (7%) pts showed a Grade ≥3 hematologic toxicity. Concerning RCT, 70.5 Gy and 67.5 Gy were delivered in 28 (49%) and 27 (47%) pts, respectively. VMAT strategy was preferred in 58% of cases, while IMRT in the remaining 42%. Fifty-five pts (96%) completed the overall treatment as prescribed. Twenty-six (46%) required at least one day CRT rest (mean: 2.7 days, range 0-24). Two pts (3%) failed to complete CRT due to severe toxicities

(mucositis and arrhythmia), while 13 patients (23%) reported Grade 3 mucositis and 1 pt (2%) Grade 3 dysphagia. Within one-month after the end of treatment, 3 pts (5%) died because of heart failure. Twenty-eight (49%) pts had clinical response after iCT, with an overall response rate of 79% after RCT (complete response rate: 52%). Two-year local control was 72.4%, the 2-year progression free survival and overall survival were 68% and 73%, respectively.

Conclusion: A moderately accelerated IMRT/VMAT CRT was feasible after iCT. An overall early death rate of 5% highlights the need for suitable predictive criteria to better select those patients who are most likely to benefit from this treatment modality and less likely to experience severe toxicity.

**PO085**

## EVALUATION OF THE RELATIONSHIP BETWEEN MINOR RISK FACTORS AND RELAPSE FREE SURVIVAL IN HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC) TREATED WITH ADJUVANT RADIOTHERAPY

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Aims: Surgery followed by adjuvant radiotherapy is often the treatment of choice in locally advanced HNSCC. When major risk factors are present (positive margins and extracapsular node extension) surgery is followed by concomitant CHT-RT. If minor risk factors are present, the use of combined CHT-RT is controversial. This study evaluates the presence of a correlation between minor risk factors (histological grading, lympho-vascular invasion, perineural invasion, involved nodes and pT4) and disease free survival (DFS) and overall survival (OS) in patients with HNSCC treated with surgery and adjuvant radiotherapy without chemotherapy.

Methods: We conducted a retrospective cohort study in a group of 42 patients treated with surgery and adjuvant RT from January 1, 2010 to December 31, 2015. 55% of patients have been treated with VMAT technique, and 45% with 3D-CRT. We included HNSCC of oral cavity, oropharynx, hypopharynx and larynx and escluded patient with extracapsular extension and positive margin. The correlation between minor risk factors and DFS and OS was evaluated with Kaplan Meier analysis and Log Rank Test.

Results: Recurrence occurred in 30% of patients after an average of 29 months. Lymphovascular invasion, perineural invasion, grading and especially involved cervical nodes seem to have an impact on DFS and OS; even if we did not reach a statistical significance. In our cohort, patients with pT4 tumors had a better DFS and OS. This result is apparently in contrast with literature, but in our group of pT4 patients we noticed a lower prevalence of pN0, supporting the importance of involved nodes.

Conclusion: This study showed a negative impact of lymphovascular invasion, perineural invasion, grading and especially involved cervical nodes on DFS and OS. Further analysis can include other risk factors such as close margin and depth of invasion. The impact of minor risk factor on OS can be analized in different sub sites of tumors and we can also evaluate the correlation between risk factors and the site of recurrence. A larger number of patients may allow us to obtain statistically significant results.

**PO086**

## VOLUMETRIC INTENSITY MODULATED RADIOTHERAPY IN THE ANAL CANCER: MONO-CENTRIC RETROSPECTIVE ANALYSIS

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Aims: To report the acute toxicity and clinical results in patients with anal cancer treated with volumetric modulated arc therapy (VMAT) concomitant with chemotherapy.

Methods: Retrospective monocentric analysis of a cohort of 21 patients, with histologically confirmed squamous cell carcinoma of the anal canal, treated with modulated volumetric intensity radiotherapy and concurrent chemotherapy at the SC of Radiotherapy of the A.S.O.SS. Antonio Biagio. Dose prescription was 39.6 Gy, 1.8 Gy/ fraction for the elective nodal PTV, the macroscopic (tumor and involved lymph nodes) PTV doses were 19.8 Gy up to a total dose of 59.4 Gy in 11 patients. Two patients were treated with 41.4 Gy for elective nodal and boost of 18 Gy up to a total dose of 59.4 Gy and another with boost of 21.6 Gy up to a total dose of 63 Gy. One patient received a boost dose of 9 Gy after 45 Gy for elective nodal PTV; One patient received a dose of 60 Gy for elective nodal PTV and SIB dose of 64.5 Gy. One patient received a boost dose of 10 Gy after 50 Gy for elective nodal PTV; Chemotherapy with MMC and 5-FU/Capecitabine was administered concomitantly according Nigro's scheme. End points were local control (LC), disease-free survival (DFS) and overall survival (OS) and acute and late toxicity.

Results: Median follow-up time was 24 months. Two year OS was 93%, DFS was 87.5% and LRC was 87.5%. Acute and late toxicities were analyzed using the CTCAE scales.4 .Acute dermatological toxicity G3 was recorded in two patients, ten patients (62.5%) experienced a G2 skin toxicity, while G1 toxicity was regi-

stered in four patients (25%). No patient developed Grade 3 acute gastrointestinal (GI) toxicity, 7 patients (43.7%) experienced grade 2 acute GI toxicity and 8 patients (50%) G1 toxicity. Acute genitourinary toxicity G2 was recorded in two patients (12.5%). 8 patient experienced grade 1 acute GU toxicity (50%). Acute hematology toxicity G4 was recorded in one patient, two patient experienced a G3 toxicity. Maximum late toxicities were: anaemia G3 6.25%- proctitis G2 18.75%-diarrhea G2 6,25% now being treated with Questrant.

Conclusions: Our retrospective data support VMAT as standard radiotherapy technique in the combined modality treatment of anal cancer, with mild toxicity and promising sphincter preservation and survival rates. VMAT treatment of Anal cancer patients to be equally effective than Conformal Radiotherapy but it was associated with reduction toxicity.

## PO087

## MODULATED IRRADIATION TECHNIQUES-SIMULTANEOUS INTEGRATED BOOST (IMRT-SIB)AND CONCOMITANT CHEMO/BIOTHERAPY IN UNRESECTABLE STAGE IV (M0) HEAD AND NECK CANCER PATIENTS. IS IT FEASIBLE IN A DAILY CLINICAL PRACTICE?

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Aims: To evaluate feasibility of intensity modulated radiotherapy-simultaneous integrated boost (IMRT-SIB) concurrent with chemo/biotherapy in unselected unresectable stage IV (M0) head and neck cancer (HNC) patients in daily clinical practice.

**Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n=41).**

| | |
|---|---|
| Sex | |
| Male | 32 |
| Female | 9 |
| Age (years) | |
| Median | 74 |
| Range | 55-93 |
| Tumor Site | |
| Hypopharinx | 3 |
| Oral cavity | 15 |
| Oropharinx | 11 |
| Larinx | 12 |
| Tumor Grading | |
| G1 | 5 |
| G2 | 22 |
| G3 | 14 |
| Tumor Stage | |
| T2 | 6 |
| T3 | 11 |
| T4 | 24 |
| Nodal Stage | |
| N0 | 4 |
| N1 | 3 |
| N2a-c | 30 |
| N3 | 4 |

**Table 2. Courses of chemotherapy delivered in 22 patients.**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Total |
|---|---|---|---|---|---|---|---|---|
| Concurrent Chemotherapy (CDDP 1-22) | 2 | 6 | | | | | | 14 |
| Concurrent Chemotherapy (CDDP weekly) | 1 | | 2 | 3 | | 1 | | 25 |
| Concurrent Cetuximab | | | 3 | 3 | | | 1 | 28 |

**Table 3. Organs-at-risk and dose-constraints.**

| Organ | 0.1cc < (Gy) | Maximum Dose (Gy) | Mean Dose < (Gy) | Priority |
|---|---|---|---|---|
| Spinal cord | 45 | 46 | | High |
| Brain stem | 54 | 60 | | High |
| Optical chiasm | 54 | 60 | | High |
| Optical nerve/s | 54 | 60 | | High |
| Brachial plexus | 60-66 | | | |
| Eyes | | | 35 | High |
| Glottis | 30 | 40 | 25-30% | High |
| Oral cavity (outside PTV) | 1cc <30 Gy-36Gy | | | Medium |
| "Body" | 80 | 81 | | Medium |
| Temporal lobe/s | 1cc <60 | 65 | | Medium |
| Parotid/s | V30 <50-60% | V40 <33% (contr.) | 26 | Medium |
| Internal ear/s | | 52.5 | 50 | Medium |
| Pituitary gland | 40 | 50 | | Low |
| Temporomandibular J | 70 | | | Low |
| Len/s | | <4-6 | | Low |
| Larynx (supraglottic) | | 66 | | Low |
| Larynx (whole) | | 50 | 40-45 | Low |
| Mandible | V55 <20% | 70 | | Low |
| Constrictor muscles | | | 50 | |
| Oesophagus | 1cc <45-55 | | | |
| Tyroid gland | V45<50% | | | |

**Table 4. Cumulative acute toxicities in 41 patients. The table reports the number of patients and (%) that experienced acute toxicities.**

| | G1 | G2 | G3 | G4 |
|---|---|---|---|---|
| Skin | 4 (9.75) | 3 (7.31) | 4 (9.75) | |
| Neutropenia | | 3 (7.31) | 1 (2.43) | 1 (2.43) |
| Mucositis | 5 (12.19) | 3 (7.31) | 8 (19.51) | |
| Oral candidiasis | | 4 (9.75) | 4 (9.75) | |
| Dysphagia | 11 (26.83) | 7 (17.07) | 2 (4.87) | |
| Xerostomia | | 2 (4.87) | | |
| Dysphonia | | 3 (7.31) | | |
| Stomatitis | 1 (2.43) | 1 (2.43) | | |
| Dysgeusia | | 2 (4.87) | | |
| Edema | | 3 (7.31) | | |
| Nausea/Vomiting | 3 (7.31) | 1 (2.43) | 2 (4.87) | |
| Anemia | | 2 (4.87) | 2 (4.87) | |
| Piastrinopenia | | 2 (4.87) | | |
| Peripheral Neuropathy | 1 (2.43) | 1 (2.43) | | |

**Table 5. Cumulative late sequelae. The table reports the number of patients and (%) that experienced acute toxicities.**

| | G1 | G2 | G3 | G4 |
|---|---|---|---|---|
| Mucositis | 1 (2.43) | 1 (2.43) | 1 (2.43) | |
| Dysphagia | 3 (7.31) | 3 (7.31) | 2 (4.87) | |
| Xerostomia | | 2 (4.87) | 1 (2.43) | |
| Dysgeusia | | 1 (2.43) | | |
| Mandibular toxicity | | | | 1 (2.43) |

**Table 6. Overall response to treatments (n=38).**

| Response | n (%) |
|---|---|
| Complete | 21 (55.3) |
| Partial | 11 (28.9) |
| Stable | 5 (13.2) |
| Progression Disease | 1 (2.7) |

Methods: We retrospectively reviewed record data of stage IV HNC patients treated in two Messina

radiotherapy centers. We evaluated: toxicities, local control rates and overall survival. Patients with unknown primary site tumor, nasopharnx cancer and sinonasal primitives were excluded as well as patients with earlier or active concurrent malignancy.

Results: 22 patients were retrieved; 21/22 received the planned doses of radiotherapy and 1 patient interrupted radiotherapy for unacceptable decline of performance status at 55Gy due to toxicity. Main acute regional toxicities were radiodermatitis and mucositis. We also reported one case of mandibular osteoradionecrosis as late toxicity (Tables). At completion of treatment, objective responses were evaluated: 16/22 patients had complete (72%) and partial 6/22 (28%) response. The 1- and 5- year LC rates were 70.83% and 64.39% respectively. The 1-, 3-, and 5-year OS rates were 84.78%, 60.56% and 40.88% respectively.

Conclusion: Intensity modulated irradiation with SIB is feasible and can be used with concomitant chemotherapy/biotherapy in daily clinical practice out of protocol studies.

**PO088**

## INTENSITY MODULATED/IMAGE-GUIDED RADIOTHERAPY FOR ELDERLY PATIENTS WITH ANAL CANCER

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Aims: Chemoradiotherapy (CRT) is accepted as standard initial treatment for anal cancer. Elderly patients (pts) not always can tolerate full- dose CRT or the RT volumes and doses. This study aims to assess the efficacy and tolerability of IMRT/IGRT for elderly , not frail, pts ( 70 years or older).

Methods: We performed a retrospective review of 44 consecutive pts with histologically confirmed anal cancer, stage II- IIIB, treated in our department since December 2012 till February 2018 with IMRT/IGRT in all but 4 pts combined with concurrent CT. 12 pts were 70 yrs old or older (range 70- 92), while 32 were younger (range 47- 69). 5 pts in the younger group were HIV positive. Dose prescription were: 42- 46.2 Gy for inguinal/external iliac lymph nodes, 45-50.4 Gy for internal iliac, perirectal and obturator lymph nodes, 50-54 Gy for involved lymph nodes and 54- 60 Gy for the gross tumor volume. CT with MMC and 5-FU/Capecitabine was administered concomitantly. No gap for radiotherapy treatment was planned. 1/3 pts in the elderly group did not receive chemotherapy concomitantly, due to associated diseases.

Results: All pts completed treatment as planned. Median follow-up is 35.5 months (range 2- 77 months). 22% of patients in the younger group presented G3+ acute skin toxicity while only 16% of the elderly group experienced the same toxicity (probably due to the lower doses and/or exclusion of concurrent chemotherapy). Diarrhea G3+ occurred in the 15% of the younger group and in the 12% of the elderly group. Grade 3-4 hematologic toxicities occurred in 7.6% and 0% respectively. Soiling occurred in 15.2% and 5%, of elderly and younger patients. Overall survival (OS) at three years is 96,8% in the younger group, and 100% in the elderly Group. One pt in the younger group developed liver metastasis and died after 3 months. Local control at 3 and 5 yrs is 91.6% and 91.6% in the elderly, and 96% and 93.75% in the younger respectively. There was no statistically significant difference in acute and late toxicities as well as survival between the two groups (although the number of the treated patients is small).

Conclusions: Elderly but not frail pts with anal cancer may tolerate radiation with IMRT/IGRT as well as younger patients. The current series confirm the feasibility of sphincter conserving treatment in such a population. Rates of acute and late complications appeared like ones recorded in younger pts, with oncologic results at least as favorable as those.

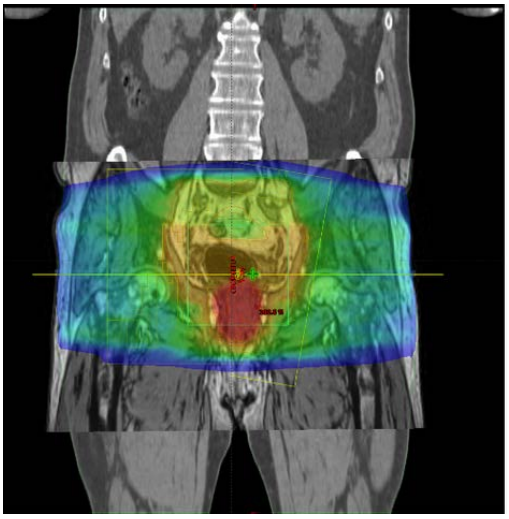

**Figure 1.**

PO089

## TOSSICITÀ A LUNGO TERMINE NELLE PAZIENTI GINECOLOGICHE TRATTATE CON IMRT TOMOTERAPIA

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Aims: We evaluated long-term toxicity of Intensity Modulated Radiation Therapy (IMRT) with Tomotherapy in gynecologic patients, treated in our institution, with almst three months follow-up.

Methods: 44 gynecologic patients were treated from March 2015 to May 2018 with IMRT (Tomotherapy) in our institution with different purposes: 5 received neoadjuvant radiation therapy for cervical cancer with concomitantweekly cisplatin chemotherapy; 6 patients were treated with definitive chemo-radiation therapy for cervical cancer and endometrial recurrence; 27 received adjuvant radiation therapy after surgery for endometrial, cervical, vaginal and vulvar cancer. Only 8 patients of adjuvant group received concomitant cisplatin chemotherapy, all with cervical cancer. Median doses delivered with IMRT were: 50.4 Gy in 28 fractions with boost to 60.2 Gy in adjuvant subgroup; 46 Gy in 23 fractions with concomitant boost to 48,76 Gy in neoadjuvant subgroup; definitive chemo-RT group received several doses based on the different istologic types. Lomboaortic lymphonodes were irradiated with 45 Gy only in 6 patients.

Results: Median age during treatment was 62 years. Median PTV treatment volume was 760cc. Median bladder mean dose was 40 Gy, while median rectal mean dose was 37 Gy. With 19 months median follow-up, only 2 patients experienced long-term G1 toxicity (diarreha); 3 patients showed G2 anemia, all treated for cervical cancer; 3 patients experienced G2 pelvic pain, all treated for cervical cancer. As regard GU late toxicities, 2 patients experienced recurrent G2 bladder infection and 3 patients needed percutaneous nephrostomia because of G3 urinary retention.

Conclusions: Pelvic IMRT with Tomotherapy for gynecologic malignancies demonstrated safety and efficacy with limited G2-3 long-term toxicities.

PO090

## TOXICITY EFFECTS AFTER INTENSITY MODULATED RADIATION THERAPY COMPARED TO 3D CONFORMAL RADIATION THERAPY IN BLADDER CANCER PATIENTS

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Aims: To evaluate acute gastrointestinal and genitourinary toxicity in patients treated for bladder cancer with IMRT versus 3D-CRT techniques

Patients and Methods: Were reviewed clinical records of bladder cancer patients treated in two Radiotherapy Centres of Sicily (Papardo Hospital and Policlinico G. Martino in Messina) from March 2013 to May 2019. The toxicity was evaluated with RTOG acute and late morbidity scoring. Thirty patients (3 female and 27 male) treated with curative radiotherapy were evaluable. The median age was 82 years (range 74-90). All patients were submitted to TURB (trans uretra bladder resection) both to define the histological type and to perform an adequate tumor debulking. 2/30 had local chemotherapy instillation; 4/30 had concomitant radiochemotherapy; 24/30 had only radiotherapy. The radiotherapy techniques used were: IMRT in 4/30 patients, IMRT-IGRT in 12/30 patients, , 3DCRT in 4/30 patients and 3DCRT-IGRT 10/30 patients. The median delivered dose was 60,05 Gy (range 29,10-69,60 Gy). Dose-volume histograms of anorectal, small/large intestine and bladder were calculated; all constraints have been respected.

Results: In Patients treated with 3DCRT (14/30), genitourinary acute toxicities was observed in 12/14 patients; n=6 G1, n=4 G2, n=2 G3. The remaining patients (n=2) showed no genitourinary toxicities. 2/14 patients reported gatrointestinal toxicity G1. Using IMRT technique 3/16 patients showed genitourinary toxicity; n=5 G1, n=3 G2, n=1 G3, while gastrointestinal toxicity G1 was observed in 3/16 patients. Data were analyzed using a parametric test (indipendent simple T-test) and a non parametric test ( Mann- Whitney U-test); they showed that in the two different groups of patients treated with 3D-CRT versus IMRT techniques there are no statistically significant differences on acute genitourinary and gastrointestinal toxicity.

Conclusions: According to our experience, 3D-CRT radiotherapy can be a valid alternative for the treatment of bladder cancer in small centers not equipped with IMRT techniques.

**PO091**

## TOXICITY EVALUATION IN VERY ELDERLY PATIENTS WITH HNSCC TREATED WITH CURATIVE RADIOTHERAPY

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Aims: To evaluate toxicity in very elderly patients with HNSCC treated with curative radiotherapy using 3D-CRT and IMRT techniques.

Methods and Materials: We analyzed a group of patients affected by Head and Neck cancer with squamous histological typetreated in two radiotherapy centers of Sicily (Papardo Hospital and Policlinico G. Martino in Messina) from January 2007 to March 2019. We evaluated toxicities in very elderly patients >/ 75aa who were treated with curative radiotherapy, using RTOG acute morbidity scoring.

Results: We evaluated 45 HNSCC patient s>/75 years old with a median age of 79,68 (range 75-93); 34 patients were male and 11 were female. Primitive tumor sites were: oral cavity (12/45), larynx (21/45), oropharynx (4/45), parotid gland (5/45), nasopharynx (4/45) paranasal sinus (2/45).We found comorbidities in 33/47 patients and were distributed as follow: cardiovascular diseases (15/45), metabolic diseases such as diabetes mellitus, hypercholesterolemia and dysthyroidism (15/45); 20/45 patients were affected by hypertension; 2/45 benign prostatic hyperplasia and 1/45 positive history of EBV; 5/45 patients had a positive cancer clinical history (1/45 prostate cancer, 1/45 kidney cancer, 2/45 bladder cancer, 1/45 colon cancer 1/45 esophagus and 1/45chronic lymphatic leukemia). We offered curative treatment with 3D-CRT (2/45), VMAT (4/45), IMRT (19/45) and IMRT-IGRT (20/45) with prescribed median dose of 64,97Gy (60-70Gy) and median daily dose of 2.11 Gy (range 2-2.3Gy).Of these patients 8/45 received systemic therapy; 5/45 concomitant Cetuximab, 3/45 concomitant Chemotherapy. Only one patient not completed the planned RT treatment for important dysphagia (G3.) We found toxicity in all patients, in particular 16 patients dysphagia G1-2, and 1/45 G3; 9/45 skin erythema G1-G2 and 3/45 G3; 9/45 mucositis G1-G2; xerostomia 7/45 G1-G2; we observed others symptoms like dysgeusia 2/45 patients, arytenoid edema 1/45, odynophagia 3/45, anemia 2/45 and hoarseness 2/45.

Conclusions: The results reported in this study confirm the feasibility, in term of toxicities, of curative radiotherapy in very elderly patients.

**PO092**

## INTENSITY MODULATED RADIOTHERAPY (IMRT) VERSUS 3D CONFORMAL RADIOTHERAPY (3D-CRT) IN GLIOBLASTOMA PATIENTS: DO THEY HAVE AN IMPACT OVER ACUTE TOXICITIES?

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Aims: To evaluate acute toxicities in Glioblastoma patients treated with radiotherapy and temozolamide (TMZ) with IMRT versus 3D-CRT.

Methods: From January 2017 to May 2019 we retrospectively analysed 51 Glioblastoma patients treated with radiotherapy (RT) and TMZ in our centre.

Results: All patient underwent to concomitant TMZ and irradiation followed by adjuvant TMZ (fractionated focal irradiation in daily fractions of 2 Gy given 5 days per week for 6 weeks, for a total of 60 Gy), plus daily TMZ administration (75 mg per square meter of body-surface area per day, 7 days per week from the first to the last day of radiotherapy), followed by at least six cycles of adjuvant TMZ (150 to 200 mg per square meter for 5 days during each 28-day cycle). 29 patients were treated with IMRT and 22 with 3D-CRT. Asthenia and nausea were observed in almost all of them; thrombocytopenia was observed in 30 patients. Coordination deficit of the upper limbs and visus reduction were observed in one patient submitted to IMRT, hemianopsie was observed in one patient treated with 3D-Conformational radiotherapy and walking deficit in one patient treated, instead, with IMRT.

Conclusions: IMRT has not impact on the onset of acute toxicity during concomitant treatment.

**PO093**

## RADICAL RADIO-CHEMOTHERAPY IN H&N CANCER: RETROSPECTIVE COMPARISON BETWEEN WEEKLY AND 3-WEEKLY CDDP

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Aim: Even if three weekly (3w) CDDP is considered the standard chemotherapy given concurrently with radiotherapy in the treatment of head and neck cancer,

the alternative use of weekly (w) CDDP is widely adopted, because is thought to be less toxic and more manageable. This retrospective analysis aims to compare toxicity and survival of these two schedules.

Methods: All patients were treated with radical radio-chemotherapy for meso/hypo-pharyngeal or laryngeal locally advanced disease. Patient, disease and treatment characteristics were analyzed and related with toxicity and survival, using $\chi^2$-test, log-rank test and propensity score (1:2) (matching on age, sex, performance status and stage disease) analysis.

Results: Between Jan 2010 and Jan 2017 166 patients were treated in two large reference Italian Centres, 52 pts with 3w (100 mg/m$^2$) and 114 pts with w-CDDP (40 mg/m$^2$). Patients treated with w-CDDP had a significant older age (p=0.005), worse Karnofsky performance (p=0.000); higher smoking and alcohol consumption (p=0.000). Moreover, in this group there were less meso-pharyngeal (p=0.001) and N2-3 disease (p=0.02) and more T3-4 disease (p=0.05). All patients were treated with equivalent RT doses and CDDP doses were equivalent in both groups. Clinical response was similar in the two group. Local relapse rate is higher in w-group while metastases occurrence is worse in 3w-group (p=0.01). Anaemia, leukopenia, renal toxicity, mucositis and dysphagia rates were similar in the two groups. Thrombocytopenia, nausea and vomiting were more frequent in the w-group (p=0.01 and 0,007 respectively). Overall survival (OS) was influenced by tumor site (better for mesopharynx p=0.04), nodal stage (p=0.01), and nodal response to treatment (p=0.004) but not by the CDDP schedule (p=0.433). Relapse free survival (RFS) was influenced only by the nodal response to treatment (p=0.015). The results of Propensity Score Analysis, on 89 patients, confirmed no differences in terms of RFS and OS.

Conclusion: With the limits of a retrospective analysis the study showed the equivalence of the two CDDP schedules in terms of survival outcomes. The higher rates of some toxicities and the higher rates of treatment interruptions in the w group could be explained by the worse patients and disease characteristics at baseline. A prospective randomized study comparing these two schedules is desirable to define the optimal chemotherapy association for patients treated with radical intent.

**PO094**

## STUDY PROPOSAL FOR LONGITUDINAL ASSESSMENT OF NEUROCOGNITIVE FUNCTIONS IN PATIENTS RECEIVING VOLUMETRIC MODULATED ARC THERAPY (VMAT) FOR HIGH GRADE GLIOMAS (HGG): A MONO-INSTITUTIONAL EXPERIENCE

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Aims: There is still a lack of data about cognitive outcome in patients with high-grade gliomas (HGG) treated by radiation therapy. However, owing to the fact that more and more patients with HGG now survive for longer periods, neurocognitive evaluation became significantly relevant among neuro-oncologic community. In the present study, we aim to assess long-term cognitive outcome in this set of patients, and to evaluate feasibility and adequacy of the proposed test battery for this purpose.

Patients and Methods: From December 2017 to March 2019 the evaluation of neurocognitive functions has been performed in 14 patients treated for HGG using VMAT at Federico II University, Naples. Histology was glioblastoma multiforme (GBM) in 61.54% of patients and HGG in 38.46% with a median age of 54 years (range 38-73). All patients have been treated by maximal feasible tumour resection (biopsy, partial resection, gross total resection), followed by VMAT with median dose of 58Gy (range 40-60Gy) plus concomitant and adjuvant chemotherapy. Radiotherapy treatment was well tolerated by all patients. None of the patients with a follow-up greater than - or equal to - 6 months developed severe acute toxicity (≥G3, graded according to CTCAE v4). The assessment of neurocognitive functions was performed pre and post-radiation therapy, every 4 months. A test battery consisting of Mini Mental State Examination, Montreal Cognitive Assessment, Frontal Assessment Battery, Phonological and Semantic Verbal Fluencies, Stroop Test, Rey's 15 words learning test, Rey-Osterrieth complex figure (direct copy and delayed recall) and Frontal Behavioural Inventory has been used.

Results: Despite a small set of patients and an insufficient number of neurocognitive check-ups, those few who have a follow-up seem to show substantial stability from a cognitive point of view, at least after the first 4 months.

Conclusion: This battery of neuropsychological tests seems suitable for a long-term assessment of cognitive functions in patients undergoing VMAT for HGG. A longer follow-up is required to better evaluate long-term neurocognitive outcome, despite our preliminary promising results.

**PO095**

## IMPACT ON EFFICACY AND LATE TOXICITY IN HEAD AND NECK CANCER PATIENTS TREATED WITH POST-OPERATIVE INTENSITY-MODULATED RADIOTHERAPY (IMRT): A 5-YEAR MONO-ISTITUTIONAL EXPERIENCE

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Aims: To report efficacy and late toxicity of intensity modulated radiotherapy (IMRT) in patients with head and neck (H&N) cancer in postoperative setting.

Methods: Head and neck cancer patients with high risk of recurrence after radical surgery and treated with adjuvant radiotherapy were included in this retrospective analysis. All patients were treated with IMRT technique with conventional fractionation or moderate hypofractionation. A median total dose of 60.0 Gy (range: 58.8-66) in 30 daily fractions (range: 28-33) was delivered to surgical bed. Clinical revaluation with endoscopy was performed every 3-4 months after the treatment, instrumental revaluation (18F FDG-PET/CT and MRI) every 6 months. Metabolic response was assessed with PERCIST criteria, late toxicities with EORTC-RTOG scale.

Results: From January 2013 to December 2018 a total of 37 patients were treated [M/F=22/15; median age: 68 years; tumor site: oral cavity (37.8%), larynx (32.4%), salivary glands (16.2%), metastatic cervical carcinoma from unknown primary (5.4%), ear canal (2.7%), nasal fossa (2.7%), and oropharynx (2.7%); histology: squamous cell carcinoma (83.5%), other (16.5%); stage: I (5.4%), II (16.2%), III (18.9%), IV (59.5%); concomitant RT-CT (46.0%), RT alone (54.0%)]. With a median follow-up time of 14 months (range: 6-54 months), 85.2% of patients showed CR, 3.7% PR, and 11.1 PD. Only 1 patients (3.7%) presented ≥G3 late xerostomia.

Conclusions: Adjuvant IMRT treatment showed a favorable late toxicity profile and promising results in terms of long-term efficacy in head and neck cancer patients.

**PO096**

## HYPOFRACTIONATED RADIOTHERAPY WITH CONCOMITANT IMRT BOOST FOR BREAST CANCER: PIACENZA HOSPITAL CLINICAL EXPERIENCE

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Aims: Hypofractionated for whole-breast radiotherapy (WBRT) is considered a standard therapeutic option for early breast cancer (EBC) in postoperative setting after breast conservation (BCS). A boost to the tumor bed may further increase local control. Our aim is to evaluate skin toxicity and cosmetic results in 133 patients treated with hypofractionated WBRT with concomitant boost.

Methods: from January 2014 to December 2016, 133 patients affected by breast cancer undergoing conservative surgery were underwent hypofractionated WBRT with concomitant boost. All patients were treated with a basic course of radiotherapy consisting of 40.05 Gy to the whole breast in 15 fractions (2.67 Gy daily) with 3 dimensional conformal radiotherapy and with an additional boost dose of 0.30 Gy delivered concomitantly to the tumor bed with intensity modulated radiation therapy (IMRT). The tumor bed was delineated with the guidance of surgical clips. We have retrospectively evaluated skin toxicity and dosimetric aspects related to PTV whole breast (CC), PTV boost (CC) , mean heart dose (Gy) and ipsilateral mean lung dose (Gy). A clinical evaluation of the patients was carried out at the end of radiotherapy and at 6 and 12 months after the end of RT. Toxicity was scored according to CTCAE (Common Terminology Criteria for Adverse Events) v. 3.0 scale.

**Table 1. Patients characteristics.**

| Parameter | N° | % |
|---|---|---|
| **Age, years** | | |
| Median | 67 | |
| Range | 42-88 | |
| **T-stage** | | |
| pT1 | 113 | 85 |
| pT2 | 20 | 15 |
| **N-stage** | | |
| pN0 | 97 | 73 |
| pN1 | 30 | 23 |
| pNx | 6 | 4 |
| **Histology** | | |
| IDC | 106 | 80 |
| ILC | 15 | 11 |
| Mixed IDC/ILC | 2 | 2 |
| Papillary | 1 | 1 |
| Mucinous | 5 | 4 |
| **Grading** | | |
| 1 | 25 | 19 |
| 2 | 80 | 60 |
| 3 | 28 | 21 |
| **ER/PgR** | | |
| Negative | 16 | 12 |
| Positive | 117 | 88 |
| **Chemotherapy** | | |
| Yes | 29 | 22 |
| No | 104 | 78 |
| **Hormonal therapy** | | |
| Yes | 110 | 83 |
| No | 23 | 17 |

Results: Baseline characteristics of all 133 patients are reported in Table 1. All patients completed the planned radiotherapy program, without interruptions. The maximum toxicity collected at the end of RT was G2 erythema in 12 (9%) patients. Most patients (62%) presented G1 erythema at the end of treatment. The toxicity did not occur in the boost region. We did not collect any G2 toxicity at 3 and 12 months. During the last follow up, five patients presented G1 telangiectasia and two patients G2 fibrosis (Table 2). At median follow up of 48 months (range: 12–60 months) no G2 late toxicity was recorded, we detected only one axillary node relapse and one metastatic localization. In Table 3, dosimetric aspects of PTV and boost volumes together with doses to ipsilateral lung and heart (for left-sided tumors) are reported.

Conclusions: Hypofractionated WBRT with concomitant boost to the tumor bed after BCS in EBC led to good clinical results. However, more follow-up is needed to confirm these initial results.

**Table 2. Skin Toxicity (%).**

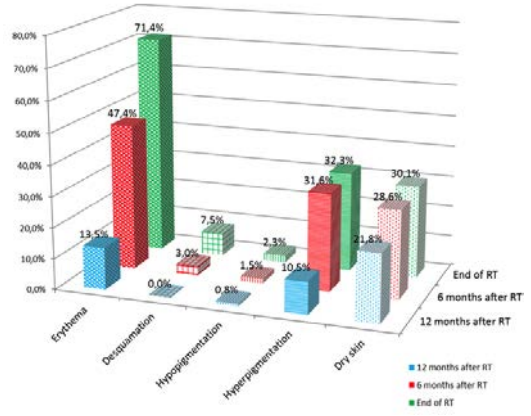


**Table 3. Statistics of data. Parameters are grouped in right breast and left breast treatments. Minimum, 1st quartile, median, mean, 3rd quartile, maximum, IQR ans standard deviation are reported.**

| Treatment Site | Parameter | Min | 1st Quartile | Median | Mean | 3rd Quartile | Max | IQR | St Dv |
|---|---|---|---|---|---|---|---|---|---|
| Right Breast | PTV (cc) | 335.5 | 814.6 | 1038.4 | 1060.5 | 1300.6 | 2164.2 | 486.0 | 371.2 |
| | PTV Boost (cc) | 9.9 | 26.3 | 36.4 | 38.1 | 46.2 | 92.8 | 19.9 | 17.5 |
| | Mean Dose Ipsilateral Lung (Gy) | 0.3 | 3.9 | 4.9 | 5.1 | 6.2 | 13 | 2.4 | 2.1 |
| Left Breast | PTV (cc) | 114.6 | 724.4 | 982.0 | 1033.8 | 1302.9 | 2243.9 | 578.5 | 433.4 |
| | PTV Boost (cc) | 5.7 | 24.5 | 32.5 | 38.0 | 48.1 | 120.9 | 23.6 | 19.9 |
| | Mean Dose Heart (Gy) | 0.2 | 1.34 | 1.9 | 2.3 | 3.02 | 5.7 | 1.7 | 1.2 |
| | Mean Dose Ipsilateral Lung (Gy) | 0.1 | 3.0 | 3.9 | 3.9 | 5.2 | 7.8 | 2.2 | 1.7 |

**PO097**

## CHRONIC TOXICITIES IN ENDOMETRIAL AND UTERINE CERVICAL CANCER PATIENTS TREATED WITH PELVIC INTENSITY-MODULATED RADIATION THERAPY (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) for endometrial cancer and uterine cervical cancer.

Methods: Of the 270 patients treated from March 2016 to October 2018, we retrospectively analyzed 29 of them who underwent IMRT. The median age at the time of treatment was 66 years (range 35-88 years). In 22 patients the primary tumor site was endometrium, while 7 of them were affected by uterine cervical cancer. Toxicities were assessed through a phone questionnaire at a median time of 25 months from the date of treatment. Pain was evaluated with the Numerical Rating Scale (NRS), while late toxicities were assessed using the Radiation Therapy Oncology Group (RTOG) scale.

Results: The median total dose delivered was 45 Gy (range 44-53.75 Gy), with a median number of fractions of 25 (range 20-28). In addition, in 14 patients a radiation boost on vaginal vault was delivered using brachytherapy; in particular 12 of them received a total dose of 15 Gy in 3 Fx and 2 of them 12 Gy in 3 Fx. Furthermore, a simultaneous integrated boost (SIB) with a median dose of 2.1 Gy/day has been delivered in 4 patients, whereas one patient received a sequential boost (total dose 6 Gy in 2 Fx). The median V40 of the bladder was 37.21%, while the median V30 was 76.01%. 15 patients developed GU toxicities: G1 10 patients (34.5%); G2 2 patients (6.9%); G3 3 patients (10.3%). A volume of 230 cc of the intestine absorbed a median dose of 33.765 Gy. GI toxicities were reported by 14 patients: G1 9 patients (31%) and G2 5 patients (17.2%). Six patients referred a pain of grade 2 of the NRS, nine a grade 3, two a grade 4. Only two patients reported a pain grade higher than 4 (one 6 and one 7).

Conclusions: Our data confirm the excellent tolerability and low profile of late toxicity of IMRT treatments on pelvis in gynecological patients. To better evaluate late toxicity in this type of treatment it would be preferable to promote prospective studies.

**PO098**

## BONE FRACTURES AS A LATE COMPLICATION OF MULTIMODALITY TREATMENT OF EXTREMITY SOFT-TISSUE SARCOMA: A MATCHED COHORT ANALYSIS

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Aim: Purpose of this matched cohort analysis is to define potential risk factors for long-bone radiation-induced fractures in patients with extremity soft-tissue sarcoma (STS).

Methods: Data of patients with extremity STS, treated between May 1992 and March 2012 with primary surgery +/- perioperative radiotherapy (RT) and/or chemotherapy (CT), were retrospectively reviewed. For each patient who experienced bone fracture was selected a patient that has not, matched for age, T stage and localization.

Results: A total of 40 patients were selected. Median age at diagnosis was 53.4 years (range 12-80). Among the tumors, 5 (12.5%) measured <5 cm in greatest dimension, 27 (67.5%) measured between 5 and 10 cm and 8 (20%) >10 cm. The most common histologic subtype was myxoid liposarcoma (14 patients [35%]), followed by fibrosarcoma (7 patients [17.5%]) and myxofibrosarcoma (7 patients [17.5%]). All patients underwent surgery of the primary tumor. Neoadjuvant and adjuvant chemotherapy was administered in 20 patients (50%). 4 patients (15%) underwent preoperative radiotherapy, 35 patients (87.5%) post-operative radiotherapy (PORT) and 2 (5%) pre and post-operative radiotherapy. Radiation technique consisted in 28.2% of cases in exclusive external beam radiotherapy (EBRT) and in 35.8% in a combination of EBRT and brachytherapy (BT). 14 patients (35%) underwent surgery twice, for re-excision in case of close or positive margins or for local relapse before bone fracture occurrence. Among the group of patients who experienced bone fracture, 6 (30%) underwent preoperative radiotherapy (141,1 to 191,9; 95% CI; p=0.22) and 15 (75%) underwent PORT (141,1 to 191,9; 95% CI; p=0.0048). Most of the bone fractures occurred in patients with STS of the thigh (12 patients [60%]) (p<0.0001). No correlations with sex (p=0.25), age (p=0.41), lesion size (p=0.99) and second surgery (p=0.97) were found.

Conclusion: In our analysis PORT and tumor location appear to be potential risk factors for long-bone fractures in STS patients treated with primary surgery and perioperative CT and RT. Further clinical studies are needed to better define the clinical profile and dose-volume relationship with higher risk of this late debilitating toxicity.

**PO099**

## LATE TOXICITY PRELIMINARY RESULTS IN PROSTATE CANCER PATIENTS TREATED WITH VOLUMETRIC MODULATED ARC THERAPY (VMAT) RADIATION TECHNIQUE

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Aim: The aim of this work is to retrospectively analyze the incidence of late gastrointestinal (GI) and genitourinary (GU) toxicity of Volumetric modulated arc therapy (VMAT) radiotherapy for prostate cancer at our institution.

Methods:From July 2011 to March 2019 a total of 410 patients (pts) were treated for prostate cancer with VMAT technique . This work represents a retrospective analysis of 283 pts (median age at diagnosis: 72 years) treated until December 2016 in order to evaluate late toxicity. Media and median follow up are 48 and 54 months respectively (ranging from 28 to 91 months). Treatments included local or local plus pelvic radiotherapy for prostate cancer with radical, adjuvant or salvage purpose. All patients were treated using VMAT technique with prescribed dose to PTV ranging from 66 to 76 Gy (1.8 or 2 Gy/fr). The target volume was contoured according to ICRU-report 62. Clinical target volume (CTV) included prostate or surgical prostate bed for prostate only RT and in case of pelvic RT lymph nodes up to the aortic bifurcation were included. Bladder, rectum , anal canal, intestinal cavity, penis bulb and femora were consider as organ at risk (OAR). Patients were clinically examined every 3 months after the end of RT. During each follow up they answered a questionnaire about GI and GU side effect (EORTC/RTOG criteria for classification).

Results: All results are summarized in Table 1. 6% of pts experienced late G2 GI side effects and 14% of pts had late grade ≥ 2 GU adverse events, 11 pts (4%) had incomplete urinary obstruction. No patients reported GI or GU side effects > G3.

Conclusion: The treatment was in general well tolerated resulting also in the maintenance of patients' quality of life. The acute effects (not mentioned in this work) never caused treatment interruptions and no acute > grade 2 toxicities were recorded. This data should be confirmed by statistical studies that take into account for dosimetric variables, pharmacological/hormonal treatments and patient comorbidities.

**Table 1.**

| | Late GU toxicities | | Late GI toxicities | |
|---|---|---|---|---|
| G0 | 148 | (52%) | 184 | (65%) |
| G1 | 96 | (34%) | 82 | (29%) |
| G2 | 28 | (10%) | 17 | (6%) |
| G3 | 11 | (4%) | 0 | (0%) |
| G4 | 0 | (0 %) | 0 | (0%) |

## PO100

### TUMOR CONTROL AND TOXICITY IN VOLUMETRIC MODULATED ARC THERAPY WITH SIMULTANEOUS INTEGRATED BOOST (VMAT-SIB) COMPARED TO 3D CONFORMAL RADIOTHERAPY (3D-CRT) IN THE TREATMENT OF ANAL CARCINOMA

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Aims: To retrospectively evaluate the preliminary toxicity profile and tumor control of a modulated intensity radiation treatment with simultaneous integrated boost (VMAT-SIB) compared to a three-dimensional conformational treatment (3DCRT) in a cohort of patients who were treated with chemoradiotherapy for anal carcinoma.

Methods: Twenty eight patients with locally advanced anal carcinoma, 9 of whom treated with 3D-CRT and 19 with VMAT-SIB, were included in the study. PTV1 was defined as the anorectal lesion and the positive lymph nodes identified at both CT and/or Fdg PET CT, and PTV2 as the negative inguino-pelvic nodes. The VMAT-SIB group were prescribed 27 fractions for a total dose of 54 Gy to the PTV1 and 49.95 Gy to the PTV2, respectively. The 3DCRT group received a total dose of 54 Gy in 30 fractions to both the PTV1 and PTV2. Concomitant chemotherapy with Mitomycin + 5-FU (Nigro regimen) and continuous infusion 5-FU was administered in 22 and 3 patients, respectively. Three patients were not eligible because of cardiovascular comorbidities. Assessment of treatment related acute toxicity was performed according to CTCAE v 4.0 scale. Tumor regression rate was assessed according to RECIST criteria. Data were analyzed according to the Fisher's exact test.

Results: With a median follow up of 17 months (range 6 to 105) ≥G2 acute skin toxicity was 52% in the VMAT-SIB group and 55% in the 3D-CRT group (p=0.604). Fifty-two patients in the VMAT-SIB group and 66% in the 3D-CRT group, respectively, experienced a ≥G2 acute gastro-intestinal toxicity (p=0.388). The same features for ≥G2 acute urinary toxicity were 15.69% and 33.3%, respectively (p=0.280). Major late side effects occurred only in the VMAT group, with 2 patients (22%) who suffered from a ≥G2 late gastro-intestinal toxicity. Complete pathological response at 6 months was obtained in 16 patients (84%) in the VMAT-SIB group and in 6 patients (66.%) in the 3D-CRT group, respectively (p=0.280).

Conclusions: VMAT-SIB technique in association with concomitant chemotherapy resulted in better - although not statistically significant - tumor control and low toxicity profile compared to 3D-CRT for locally advanced anal carcinoma. Prospective studies are needed to further establish the role of VMAT-SIB for anal carcinoma in daily clinical use.

## PO101

### RECONSTRUCTION FAILURE RISK AFTER POST-MASTECTOMY RADIOTHERAPY WITH HYPO-FRACTIONATION IN PATIENTS WITH IMPLANT-BASED IMMEDIATE BREAST RECONSTRUCTION

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Aims: To evaluate the reconstruction failure (RF) in a series of patients (pts) with immediate breast reconstruction (IBR) receiving hypofractionated postmastectomy radiotherapy (PMRT) matched with a comparable group of pts without PMRT.

Methods: Stage II–III breast cancer pts, treated with PMRT using helical IMRT (Tomotherapy®), were stratified in two groups according to IBR type: one stage with permanent implants (PI group) and two-stage with temporary expander (TE replaced with PI, TE -> PI group). The irradiated pts were matched one- to- one with non-irradiated pts according to the type of IBR. The clinical target volumes comprised the chest wall and the infra/supraclavicular nodal region. Dose of prescription was 40.05 Gy in 15 fractions. Primary endpoint was the rate of RF defined as major revisional surgery (MaRS): removal of PI or conversion to autologous reconstruction. Secondary endpoints included minor revisional surgery (MiRS): substitution of the PI with another PI.

Results: Ninety-nine pts were treated from May 2012 to May 2015. Fifty-four pts belonged to the TE-group and 45 to the PI-group and they were compared to a non-irradiated TE group of 54 pts and a non-irradiated PI group of 45 pts. Median age was 46 years (25-73 years). Median follow: 51.1 months (7.5-73.1). MaRS was performed in 3/45 pts (6.7%) of the irradiated PI subgroup (1 removal for exposed prosthesis and 2 conversion to autologous reconstruction, and in 1/54 pts (2.2%) of the non-irradiated PI subgroup (1 removal for infection), which did not hold statistical significance. No major events were registered in the TE -> PI group. Median time to RF in irradiated patients was 17.6 months (range: 11.8-21.5 months) and 15 months (range: 5.6-24.4 months) in non-irradiated patients. MiRS was performed in 16/45 (35.6%) pts of the irradiated PI subgroup (PI-substitution in 14 cases and PI

repositioning in 2 patients), and in 14/45 (31.1%) pts of the non-irradiated PI subgroup (PI repositioning in 1 and PI substitution in 13 cases). MiRS was carried out in 8/54 TEs (14.8%) in the irradiated subgroup, and in 5/54 TEs (9.3%) of the non-irradiated subgroup, without any statistically significant difference.

Conclusions: In patients receiving mastectomy and IBR, hypofractionated PMRT is feasible and safe. These data showed an acceptable rate of RF in pts treated with helical IMRT when compared with unirradiated pts, regardless of the use of PI or TE.

## PO102

### EFFICACY AND SAFETY OF VOLUMETRIC MODULATED ARC THERAPY (VMAT) COMPARED TO 3D CONFORMAL TECHNIQUE (3D-CRT) IN THE NEOADJUVANT CHEMORADIOTHERAPY OF LOCALLY ADVANCED RECTAL CANCER (LARC)

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Aims: To retrospectively evaluate the safety and efficacy of Volumetric modulated arc therapy (VMAT) compared to 3D conformal technique (3D-CRT) in a cohort of patients who underwent neoadjuvant chemoradiotherapy for locally advanced rectal cancer.

Methods: 144 consecutive patients with LARC underwent a course of chemoradiotherapy with neoadjuvant intent at a single institution (HSG Monza): 131 patients were treated with 3DCRT and 13 with VMAT. The majority of them received a total dose of 50.4 Gy in 28 fractions. The dose was escalated to 54 Gy in 14 and 7 patients in the 3D-CRT and VMAT group, respectively. All patients were administered concomitant chemotherapy with oral Capecitabine or 5-FU. CTCAE 5.0 scale along with definitive and/or RT interruptions ≥5 consecutive days were used to assess treatment-related side effects. Tumor regression was measured by Mandard grade and% of recanalizations after rectal anterior resection (RAR) . The Fisher's exact test was used for statistical analysis.

Results: The median follow up was 55 months (range 5 to 195). No G4 events were registered in both groups. 54 patients (41%) in the 3D-CRT group and 7 (53%) in the VMAT group, respectively, experienced a ≥G2 proctitis (p=0,277); the same features for ≥G2 diarrhoea were 24% and 23%, respectively (p=0,609); ≥G2 acute genitourinary toxicity occurred in 19 patients (14,5%) in the 3D-CRT group and 3 patients (23%) in the VMAT group, respectively (p=0,316); 3 patients in the 3D-CRT group and one in the VMAT group, respectively, definitively interrupted RT (p=0,318); while 6 patients in the former and none in the latter group had temporary RT interruptions (p=0,561). Sixty-six patients (50%) in the 3D-CRT group and 6 patients (46%) in the VMAT group, respectively, obtained a complete pathologic response (TRG=1,2) (p=0,5); recanalization after RAR was possible in 98 patients (74%) in the former and 9 patients (76%) in the latter group, respectively (p=0,44).

Conclusions: Our findings show that VMAT compared favourably with 3D-CRT in terms of both efficacy and of safety in the neoadjuvant treatment of LARC, although no statistically significant difference was found due to the small sample size. A prospective validation of a larger patients population is mandatory to confirm these results.

## PO103

### LONG TERM IMRT TOXICITY AND OUTCOMES IN YOUNG PATIENTS WITH LOCALLY ADVANCED HEAD AND NECK CANCER

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Aim: Head and neck tumors are generally characterized by high aggressiveness, particularly evident in younger patients, where local and/or distant relapse rates are still reported to be high. The development of intensity-modulated radiation therapy has played a major role in improving outcomes and decreasing morbidity in head and neck cancer patients. Dermatitis, mucositis, dyshagia, xerostomia, are the main sequelae of radiotherapy for head and neck cancer, and the main factors in reducing long-term patient quality of life, expecially in younger patients.The aim of this retrospective analysis was to assess the feasibility and efficacy of intensity-modulated for head and neck cancer in young patients (<60 years) in terms of acute and late toxicity and long term outcomes.

Methods: Between November 2012 and May 2018, 30 patients younger than 60 years were treated with curative intent. The median age was 53 years (41-60), 18 pz (60%) undergoing definitive and 12 pz (40%) postoperative radiotherapy. Used techniques was IMRT, in coplanar or non-coplanar modality based on the site, critical structures and patient's anatomy. Used Treatment Planning was Pinnacle 9.10. A daily cone-beam computed tomography was performed during the first week and twice a week for the next time. The induction chemotherapy was used in 6 patients (20%) and a combination schedule was used in 21 patients (70%): 17 of them were treated with Cisplatin (CDDP) regimen (80%) and 4 with Cetuximab regimen (19%). Primary tumor sites were oral cavity (35%), nasopharynx (15%) oropharynx (15%), hypopharynx (5%), larynx (15%), maxillary sinus (5%). To evaluate the treatment planning were used normal tissue Quantec Dose Constraints. The mean radiotherapy dose was 60 Gy (range 70-50). The CTCAE 4.03 toxicity scale was used. All patients underwent infusion supportive therapy with intravenous ascorbate and elettrolitic infusion during the treatment. The median treatment break was 2 days.

Results: Median follow-up was 32 months (range 7-79). The median Local Control was 30 months , Overall Survival was 32 months, Disease Free Survival was 30 months, Metastases Free Survival was 32 months. Four patients had locoregional recurrences, one of these presented lung metastases too and died of disease progression. The recurrences were treated with surgery.The incidence of acute Grade 3 toxicity was limited: mucositis(5%), dyshagia (5%), xerostomia (3%) dermatitis (15%). Late Grade 3 toxicities were fibrosis (3%), dyshagia (3%), permanent xerostomia (0%).

Conclusions: In our experience with head and neck cancer patients the intensity modulated radiation therapy achieved respectable locoregional control and overall survival, with acceptable toxicity, so it would be used expecially in younger patients. Recommendations for dose limits to these organs, based on measurements of dermatitis, mucositis, xerostomia, disfagia, following radiotherapy are needed.

## PO104

### VOLUMETRIC MODULATED RADIOTHERAPY IN HEAD & NECK CANCER. RESULTS REVIEWED ACCORDING TO 2018 STAGING SYSTEM

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Aims: To evaluate if the 8th edition of AJCC/UICC TNM staging system, as compared with 7th, precisely differentiates between stages and reflects overall survival (OS) in patients (pts) with diagnosis of 'Head & Neck' (HN) tumor treated with radical radiotherapy in our Centre.

Methods: From September 2013 to May 2019, we retrospectively analyzed 77 pts who were diagnosed with HN tumor (namely 65 oropharynx, 9 hypopharynx and 3 oral cavity), we reviewed all diagnosis with both TNM staging system (7th and 8th edition). The 8th edition provides some changes, the most important being a new classification for p16 positive oropharyngeal cancers, tumors that have p16 immunohistochemistry overexpression.

Results: The median age was of 62.6 (range 44.7 – 92.5) years. 63/77 (81.8%) pts were males, 14/77 (18.2%) were females, 32/77 (41.6%) were strong smokers. 60/77 (80%) were classificated in IV old stage. In 46/65 (70.8%) oropharynx cancers, p16 positivity was found. For all pts, the treatment was completed without interruptions longer than three consecutive days and SNG/PEG were needed, during treatment, in 29/77 pts (37.7%). All pts were treated in our Centre using IG-IMRT with daily kV-CBCT setup verification. A radical dose of 68 – 72 Gy in 1.8 – 2.0 Gy/fraction (5/w) was prescribed according to NCCN guidelines. Concomitant chemotherapy (CT) was prescribed in 59/77 pts (76.6%); CT with CDDP-CBDCA/W was prescribed in 45/77 pts (58.4%), CT with CDDP/3W in 11/77 pts (14.3%), CT with cetuximab in 3/77 pts (3.9%) respectively. Neoadjuvant chemotherapy with TPF in 3/77 pts (3.9%). 15/77 pts (19.5%) received RT alone because of age and/or performance status. Kaplan Meier method and Log rank test were used to evaluate the influence of OS according to 7th and 8th edition. Median OS was 41.7 (35.4-48.1) months. The 8th edition of TNM classification resulted to be predictive of OS (p = 0.0197) unlike the 7th edition (p = 0.9416).

Conclusion: Our findings confirm that in unselected patients, the 7th edition of UICC shows an invalid discrimination between different stages in HN tumors. The 8th edition of AJCC/UICC TNM staging system provides better OS stratification and can be used as prognostic factor.

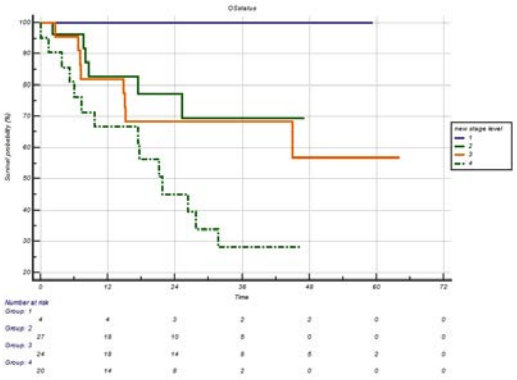

Figure 1.

## PO105

### VMAT AND 3DCRT IN THYMOMA: A DOSIMETRIC COMPARISON AND ANALYSIS OF ACUTE AND LATE TOXICITY

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Aims: Thymoma is the most common malignant tumor of anterior mediastinum. Total thymectomy is the treatment of choice while postoperative radiotherapy is defined by stage and extent of resection.Literature doesn't show a clear position about benefits of IMRT vs 3DCRT Also recent NCCN guidelines suggest both use of 3DCRT or IMRT to reduce surrounding normal tissue damage.In order to clarify this question, a dosimetric comparison between 3DCRT and VMAT plans have been done for a group of patients, treated in U.O.C of Radiotherapy of Lucca, with adjuvant RT.Conformity

index(CI), homogenity index(HI), dose to OAR were evaluated. Analysis of toxicities are ongoing.

Methods: Between May10 and April 18, 9 patients with a proven diagnosis of thymoma have been treated with adjuvant radiotherapy in Lucca's Radiotherapy. Staging was defined by Masaoka (7 stage IIB and 2 stage IIA) and WHO classification (1 stage A,3 stage AB,1 stage B1,3 stage B2 and 1stage B3).Mean age was 64(range 33-80),3 men, 6 woman;5 pts are treated with 3DCRT, 4 withVMAT. For each patient a 3DCRT and a VMAT plan for a PTV dose of 50 Gy(25 fractions) were calculated. Median PTV was 202,5 cc. The two plans were analyzed in terms of target volume coverage (V95%), CI, HI and OAR dosimetric parameters (V20, V5, mean dose for both lungs; mean dose,V5 and V20 for total lung; V40 and mean dose for heart, V35 and mean dose for esophagus).Treatment related-toxicity was graded according to CTCAE v4.0.

Results: Both techniques provide adeguate target dose coverage, but VMAT shows higher percentage of V95% than 3DCRT (99,75% vs 92,0%) better CI(0,99 vs 0,92) and HI(0,098 vs 0,16)Moreover,in VMAT plans, OAR sparing is better than in 3DCRT ones (Table 1). No toxicity treatment-related were observed: only one patient treated with VMAT developed subacute cardiac pericarditis G2; no late toxicity have been reported for all pts.

Conclusions: In the present study, VMAT technique shows superior normal tissue sparing with a better CI to the target. Even if this OAR-sparing could suggest reduction of toxicity rates, no differences in term of side effects incidence was observed in comparison to 3DCRT pts. Finally, thanks to the absence of lung pneumonia(acute/late) summed with data precedently showed, we could affirm that VMAT is an optimal technique for this kind of pts. These characteristics, added to a simple and fast delivery, has made IMRT the treatment of choice in our istitute for mediastinal thymoma.

| | VMAT | 3D |
|---|---|---|
| | MEAN±SD | MEAN±SD |
| IPSILATERAL LUNG | $V_{20Gy}$=24,3±1,5 | $V_{20Gy}$=27,0±2,1 |
| | $V_{50y}$=74,7±3,1 | $V_{50y}$=69,0±5,4 |
| | $D_{mean}$=(11,4±0,9) Gy | $D_{mean}$=(15,4±1,5) Gy |
| CONTROLATERAL LUNG | $V_{20Gy}$=0,37±0,05 | $V_{20Gy}$=1,02±0,01 |
| | $V_{50y}$=8,5±2,2 | $V_{50y}$=50,0±0,2 |
| | $D_{mean}$=(2,19±0,07) Gy | $D_{mean}$=(7,9±0,1) Gy |
| TOTAL LUNG | $V_{20Gy}$=9,0±1,9 | $V_{20Gy}$=16,2±3,5 |
| | $V_{50y}$=44,8±2,5 | $V_{50y}$=64,0±5,1 |
| HEART | $V_{40Gy}$ =13,9±0,5 | $V_{40Gy}$ =19,0±0,9 |
| | $D_{mean}$=(15,1±0,9) Gy | $D_{mean}$=(21,7±1,1) Gy |
| ESOPHAGUS | $V_{35Gy}$=0 | $V_{50y}$=0 |
| | $D_{mean}$=(11,0±0,3) Gy | $D_{mean}$=(16,1±0,4) Gy |

**Table 1.**

**PO106**

## IMPACT ON EFFICACY AND LATE TOXICITY IN HEAD AND NECK CANCER PATIENTS TREATED WITH DEFINITIVE INTENSITY-MODULATED RADIOTHERAPY (IMRT): A 5-YEAR SINGLE ISTITUTIONAL EXPERIENCE

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Aims: To report efficacy and late toxicity of intensity modulated radiotherapy (IMRT) in patients with head and neck (H&N) cancer in the definitive setting.

Methods: Inoperable head and neck cancer patients or patients who had refused surgery treated with radical radiotherapy were included in this retrospective analysis. All patients were treated with IMRT technique with either sequential boost or simultaneous integrated boost (SIB). IMRT was delivered with moderate hypofractionation. A median total dose of 66.0 Gy (range: 59.2 - 66.0) in 30 daily fractions (range: 27-33) was delivered to the primitive tumor and nodal involvement. Clinical revaluation with endoscopy was performed every 3-4 months after the treatment, instrumental revaluation (18F FDG-PET/CT and MRI) every 6 months. Metabolic response was assessed with PERCIST criteria, late toxicities with EORTC-RTOG scale. Progression-free survival (PFS) was analysed with Kaplan-Meier method.

Results: From January 2013 to December 2018 a total of 42 patients were treated [M/F=36/6; median age: 67 years (range: 38-82); tumor site: oropharynx (47.6%), larynx (16.7%), nasopharynx (12.0%), oral cavity (12.0%), metastatic cervical carcinoma from unknown primary (9.5%), and ear canal (2.2%); histology: squamous cell carcinoma (85.7%), indifferentiared (10.0%), adenocarcinoma (4.3%); stage: I (16.7%), II (11.9%), III (19.0%), IV (52.4%); concomitant RT-CT (76.0%), RT alone (24.0%)]. With a median follow-up time of 14 months (range: 6-60 months), 71.4% of patients showed CR, 14.3% PR, and 14.3 PD. Only 1 patients (2.4%) presented ≥G3 late xerostomia.

Conclusions: Definitive moderate hypofractionated IMRT showed a favorable late toxicity profile and promising results in terms of long-term efficacy in head and neck cancer patients.

## PO107

### RADICAL IMRT-SIB IN BREAST LOCALLY ADVANCED AFTER MASTECTOMY UNFIT TO CHEMOTHERAPY: A CASE REPORT

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Aims: Radiotherapy is a gold standard treatment for locally advanced- nodes positive- breast cancer after mastectomy. RT reduce recurrence in up to 10% and the 20-year mortality rate in up to 8% of locally advanced breast cancer. We describe a case report of IMRT-SIB in locally advanced breast cancer, pT2N2M0, patient unfit to systemic therapies. We reported CL, PFS and toxicity (cosmetic and functional sequelae).

Methods: A 68-years-old female patient- PS ECOG 0, comorbidity hypertension in medical therapy was affected by multicentric and multifocal ductal carcinoma right breast. Total right mastectomy and ascellar dissection was performed in December 2017 for CDI- pT2 N2 (5/22)- ER and PgR negative, HER2:3+, Ki67: 50%, G3. Staging with CT and bone scintigraphy releaved no distant metastases. The patient was enrolled to chemotherapy but she's judged unfit for acute myocardial infarction and edema pulmonary occurred in February 2018, then radiation therapy was exclusive treatment. 18-FDG PET/CT in April 2018 detected radiotracer uptake on right pectoral nodes, on pectoral muscle. In may 2018 she started the radiation therapy. Prescription dose was 60 Gy/25 fx to PET positive nodes, 50 Gy/25 fx to chest wall and in sovraclavear region 45 Gy/25 fx in IMRT-SIB. All plans were normalized to 95% of doses. DVH are according QUANTEC.Image-guided radiotherapy (IGRT) was performed. Setup deviations no described. The toxicities was evaluated according RTOG scale.

Results: Patient completed the treatment without break. Follow-up time was 12 months. After 40 days to the end IMRT-SIB was performed CT body, that detectated no metastases distant. At 50 days to the end EBRT was performed a 18-FDG CT/PET: partial response on treated lesions. 18-FDG CT/PET in April 2019 demonstrated stable disease. We recorded acute skin toxicities G1-2, treated with oxide-zinco; late skin toxicity G0. No functional sequelae is recorded.

Conclusions: To improve dosimetry and decrease normal structure doses complex techniques have been adopted for radiation treatment for breast cancer. In this case report IMRT-SIB improved control local and progression-free survival and reduced acute and late skin toxicities.

## PO108

### IMPACT ON EFFICACY AND LATE TOXICITY IN PROSTATE CANCER PATIENTS TREATED WITH RADICAL INTENSITY-MODULATED RADIOTHERAPY (IMRT): A 5-YEAR MONO-ISTITUTIONAL EXPERIENCE

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Aims: To report the outcome of radical intensity modulated radiotherapy (IMRT) with conventional fractionation in patients with prostate cancer.

Methods: Patients with histologically proven prostate cancer diagnosed by biopsy and not undergone to radical prostatectomy were included in this retrospective study. All patients were treated at Maria Cecilia Hospital in Cotignola and received a total dose of 76-78 Gy to prostate and seminal vescicles if involved, 60-62 Gy if uninvolved (2 Gy/fraction). Patients with pelvic lymph nodes irradiation were not included in this analysis. PSA assessment was performed every 6 months after treatment and evaluated according to Phoenix criteria. Late toxicity was recorded and evaluated according to RTOG-EORTC scale.

Results: From January 2013 to December 2018 a total of 252 patients were treated [median age: 76 years (range 53-87); GS: 6 (25.3%), 7 (58.6), 8 (15.1%), 9 (1.0%); risk: low (17.2%), intermediate (55.5%), high (27.3%)]. With a median follow-up time of 6 months (range: 6-24), G3 late gastointestinal and genitourinary toxicity was recorded in 1.2% and 4.8% of patients, respectively. 95% of total dose was delivered in 17.9% and 23.8% of rectum and bladder, respectively. Overall 1-year biochemical relapse-free survival (bRFS) was 96.7%.

Conclusions: Radical IMRT treatment with conventional fractionation showed a favorable late toxicity profile and satisfying results in terms of long-term efficacy in prostate cancer patients not undergone to surgery.

## PO109

### A CASE OF COMPLETE PATHOLOGICAL RESPONSE AFTER NEOADJUVANT RADIOTHERAPY USING HELICAL TOMOTHERAPY IN INFLAMMATORY BREAST CANCER

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Aims: Inflammatory breast cancer (IBC) is a rare syndrome of aggressive invasive breast cancer. We report a case of complete pathological response (CPR)

in a patient with IBC treated with neoadjuvant radiotherapy (RT) using helical tomotherapy.

Methods: A 46 years old woman with a history of bilateral nipple sparing mastectomy for intraductal carcinoma experienced a disease relapse presenting an IBC involving the reconstructed right breast. Bioptic pathological examination reported neoplastic lymphatic involvement of the dermis and immunohistochemical pattern was: ER 0%, PgR 0%, Ki-67 50% and HER-2/neu 3+. A total body CT revealed multiple locally advanced disease with lymphadenopathies located at the axilla and internal mammary chain but no evidence of distant metastases. The patient underwent 4 cycles of chemotherapy with doxorubicin and cyclophosphamide followed by weekly paclitaxel plus trastuzumab. At the post-chemo evaluation surgery was excluded due to the extension of the disease, therefore RT was proposed. Clinical examination displayed edema and erythema of the reconstructed right breast. A post-chemotherapy simulation PET-CT was performed for treatment planning purpose and no longer evidence of lymphadenopathy was found. CTV A was defined as right thoracic wall including breast implant and CTV B encompassed right sovraclavear, infraclavear and internal mammary nodal regions. PTV A and PTV B were generated adding an isotropic margin of 5 mm to respective CTVs. Prescription doses were 5880 cGy (210 cGy/fraction) to PTV A and 5040 cGy (180 cGy/fraction) to PTV B for an overall treatment time of 28 fractions. IMRT plan was generated with simultaneous integrated boost (SIB) technique. Treatment was delivered with tomotherapy and an image guided RT (IGRT) protocol with daily MVCT was carried out.

Results: The patient well tolerated the treatment, showing CTCAE skin and esophageal G1 toxicity. A reduction of the presenting symptoms was observed 1 month after RT course. The patient underwent mastectomy with implant removal one year after RT and pathological review reported a complete response with no evidence of residual disease both at the thoracic wall and axillary nodes.

Conclusions: The role of radiotherapy in IBC is ill defined. The use of tomotherapy allowed to treat an extended volume including the skin with a homogeneous dose distribution obtaining CPR and no relevant toxicity.

## PO110

### EVALUATION OF QUALITY OF LIFE (QOL) USING EORTC QUESTIONNAIRES (QLQ-C30/QLQ-EN24/QLQ-CX 24) IN WOMEN TREATED FOR GYNECOLOGIC MALIGNANCIES WITH ADJUVANT RADIATION THERAPY

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Aims: The purpose of this study was to assess self-reported overall QoL and QoL related to urinary, bowel symptoms and sexual functioning and correlate them with dose-volume parameters of organ at risks (OARs) in patients affected by cervical and endometrial cancer after adjuvant radiation therapy.

Methods: The anonymous EORTC QLQ-C30 questionnaire was administrated to 173 patients, 139 with endometrial cancer and 34 with cervical cancer, selected among the patients treated with pelvic radiotherapy and vaginal brachytherapy from 2003 to 2017 in regular follow-up in our center. This questionnaire was combined with EORT QLQ-EN24, in case of endometrial cancer, or with EORT QLQ-CX 24, in case of cervical cancer. There were no limitations with regard to age or performance status. We analyzed overall health and overall quality of life, bladder symptoms, dysuria, bladder incontinence and fecal incontinence and correlated them with dose-volume parameters of OARs (whole bladder, bladder trigone, rectum and lumbosacral plexus).

Results: All patients accepted to compile the questionnaire. The patients found that the questions were clear and easy to understand. All the items exhibited good compliance with no missing values, except for values about sexuality (100/173, 57.8%). More than half of women judged their overall health and quality of life good and only 20 judged their QoL poor. Nobody had faecal incontinence, but 60/173 (34.7%) had bladder incontinence or dysuria. Only 5/100 (5%) reported dyspareunia. According to the multiple linear regression analysis performed, bladder V53 was related to urinary incontinence with a regression value of 0.27, and to the onset of abdominal pain with a regression value of 0.02.

Conclusions: Patients exhibited good compliance to questionnaires. From our analysis, it emerged that treated women had quite good QoL after treatment with slight limitations of daily activities. Moreover, there is a correlation between bladder dose-volume parameters and the onset of bladder incontinence and abdominal pain.

## PO111

### ADJUVANT RADIOTHERAPY IN VULVAR CANCER: A SYSTEMATIC REVIEW

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Aims: Aim of this paper is to assess the role of radiotherapy in postoperative adjuvant setting for

patients affected by vulvar cancer.

Methods: A systematic review of the literature was performed using the bibliographic databases PubMed, according to the PRISMA statement, from January 1998 to January 2019, to answer the question ''what is the role of adjuvant radiotherapy in vulvar cancer?'' and to assess the impact of Intensity-modulated radiotherapy (IMRT). The exclusion criteria were: 1) review articles or correspondence to the editor; 2) studies not focused on squamous cell vulvar cancer; 3) papers not reporting radiotherapy details in terms of doses and treatment volumes; 4) papers published earlier than 20 years ago; 5) papers not studying radiotherapy, or studying radiotherapy not in adjuvant setting; 6) single case report; 7) papers not in English, Italian, French, Spanish, or German.

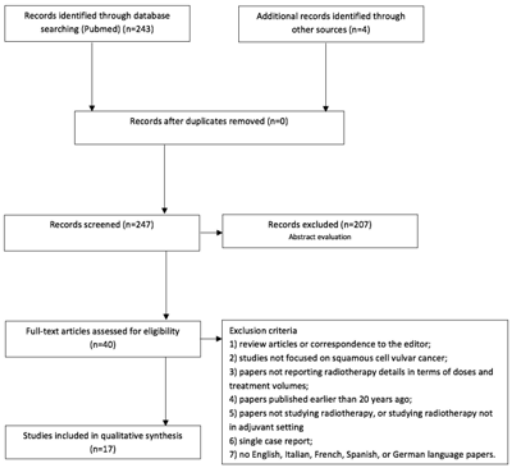


**Figure 1. Flowchart of the systematic literature search process.**

Results: According to the search strategy, 17 full-text articles, published from 2000 to 2018, fulfilled inclusion criteria and were included in the final review (Figure 1). 16 papers were retrospective analyses and 1 was a randomized controlled trial. 5255 patients were treated by adjuvant radiotherapy in the previous papers. The main indications for an adjuvant radiotherapy were: findings of more than 1 positive nodes in the histological examination; findings of 1 positive lymph node eventually with other risk factors as extracapsular extension, major dimension of nodal disease >5mm; positive or close (<8mm) resection margins; large tumor (>4cm). The dose in adjuvant setting were from 6 to 70 Gy. Several outcomes were used as endpoint, according to the aim of each study; the most used was the 5-years overall survival (5yOS, proposed in 5 studies for a total amount of 1926 patients). Where available 5yOS was between 29.4%-73%. Only in 1 study IMRT was systematically performed, in 3 papers IMRT was performed but not for the whole patient's cohort, in 11 studies IMRT was not used and 2 studies radiotherapy technique was not declared.

Conclusion: Our work confirms the role of adjuvant radiotherapy in vulvar cancer to prevent the local relapse and improve the overall survival, with a low level of evidence. The impact of IMRT could not be assessed according to the low number of patients treated by IMRT in the studies included in this systematic review.

## PO112

## COMPARISON OF A 3D-CRT VS IMRT RT TREATMENT FOR LOCALLY ADVANCED CERVICAL CANCER: LONG-TERM IMPACT ON TOXICITY AND EFFICACY

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Aims: The endpoints were acute/late rectal and bladder toxicity, overall survival (OS), locoregional failure-free survival (LFFS) and disease-free survival (DFS), outcomes of delivering concurrent cisplatin and external beam radiotherapy (EBRT)+ high-dose-rate (HDR) brachytherapy (BT), using intensity-modulated radiotherapy technique (IMRT) or 3D-CRT for locally advanced cervical cancer.

Methods: Between 2008 and 2019, 56 women with International Federation of Gynecology and Obstetrics stage IIA to IVA cervical carcinoma treated with definitive concurrent cisplatin-based chemotherapy and EBRT 45 Gy/50.4 Gy (25 /28 fractions) with a consecutive boost 9/14.4 Gy (5/8 fractions) to involved nodes/Parametria, followed by planned prescription dose of 21 Gy (3 fractions) of BT HDR boost was retrospectively reviewed. All patients (pts) receiving definitive treatment for cervical cancer were treated with EBRT using 3D-CRT/IMRT technique and concurrent cisplatin (or other schedule for 4 pts).

Results: All pts completed the prescribed course of EBRT+BRT. Median age was 54 years, median treatment length was 70 days (range 60-80). The median follow-up was 23 months. A comparison of 3-year OS and 3-year DFS revealed no significant difference between IMRT (24 pts) and 3D-CRT (32 pts). 3D-CRT:The estimated 3-year LFFS, DFS, and OS were 32%, 50%, and 74%, respectively. IMRT: The estimated LFFS, DFS, and OS rates were 19%, 61%, and 88%, respectively. The incidence of acute gastrointestinal (GI) toxicity and genitourinary (GU) toxicity in patients who received IMRT was significantly lower. No patient suffered acute or subacute grade 4 GI or GU toxicity.

Conclusions: In this study, 3D-CRT/IMRT technique was used to successfully deliver EBRT with concurrent chemotherapy + HDR BT for cervical cancer. IMRT and conventional radiotherapy demonstrated equivalent efficacy in terms of 3-year OS and DFS. Additionally, IMRT significantly reduced acute GI and GU toxicities as well as chronic GU toxicity in patients with cervical cancer. This role for IMRT merits further

evaluation with larger patient numbers and longer follow-up.

**Table 1.**

| Patient characteristics | | N. 56 OF PATIENTS |
|---|---|---|
| AGE (range 37-84)<br>MEDIAN AGE (54) | < =54 y<br>> 54 y | 28<br>28 |
| HISTOLOGY | Adenocarcinoma<br>Squamous cell carcinoma<br>neuroendocrino | 4<br>51<br>1 |
| GRADE | 3<br>1 and 2 | 27<br>29 |
| CLINICAL<br>LYMPH NODE<br>METASTASIS | <br>Pelvic node only<br>Para-aortic and/or Pelvic node | <br>8<br>1 |
| FIGO STAGE | <br>IIA<br>IIB<br>III<br>IVA | <br>2<br>39<br>5<br>10 |
| RADIOTHERAPY<br>3D-CRT<br>IMRT | Pelvis | 56<br>32<br>24 |
| BRT-HDR<br>7 Gy/FRZ | 3 frz<br>2 frz<br>1 frz | 52<br>3<br>1 |
| CHEMOTHERAPY<br>CDDP | Monthly/Weekly | 54 |

**IMRT**

| tox GU | acuta | cronica | tox GI | acuta | cronica |
|---|---|---|---|---|---|
| G0 | 52% | 68% | G0 | 32% | 68% |
| G1 | 28% | 32% | G1 | 52% | 32% |
| G2 | 8% | 0% | G2 | 16% | 0% |
| G3 | 12% | 0% | G3 | 0% | 0% |

**3D-CRT**

| tox GU | acuta | cronica | tox GI | acuta | cronica |
|---|---|---|---|---|---|
| G0 | 40,0% | 48% | G0 | 4% | 64% |
| G1 | 48,0% | 32% | G1 | 56% | 16% |
| G2 | 12,0% | 8% | G2 | 16% | 0% |
| G3 | 20,0% | 12% | G3 | 24% | 20% |

## PO113

## EXPLORING THE ROLE OF RADIOTHERAPY IN PARANASAL SINUS CANCER: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Radiation therapy (RT) in paranasal sinus cancer (PSC) plays several roles depending on the different clinical scenarios. Since the rarity and the heterogeneity of the disease, prospective clinical trials are difficult to perform and large retrospective studies are lacking. The aim of this study is to investigate possible factors related to survival outcomes in this specific population.

Materials and Methods: From April 2008 to November 2019, 86 patients treated for PSC at our Institution were retrospectively identified. Most of them were male with good KPS; 22% were workers considered at risk for developing PSC. Median age was 62 years (range 30-86). Patients usually presented with locally advanced disease (clinical T4a/T4b 60.5%) and histological subtypes and anatomical subsites were pretty well balanced in the series (melanoma were excluded from the series). 30% of the patients underwent neoadjuvant chemotherapy (NCT) (mainly docetaxel-cisplatin-5FU based); 75% underwent curative or debulking surgery and all patients received radiotherapy (either with curative or post operative intent).

Results: In the whole series 2 years and 5 years local control (LC) were 61 and 54% respectively while 2 years and 5 years overall survival (OS) were 59 and 48%; at univariate analysis locally advanced diseases (T4a/b vs others; N+ vs N0) and poorer Karnofsky Index (IK) caused a negative impact on survival. Complete (CR) or partial response (PR) to NCT showed significant impact on OS (1 y OS 64% vs 24% in patients with CR/PR vs no change/progression, p .013); analogously better outcomes were seen in patients treated with surgery plus RT compared to NCT + surgery + RT or NCT + RT. Moreover, RT dose below 66 Gy and good clinical response at 3-4 months after treatment were also strongly associated with better survival outcomes. At multivariate analysis, including in the model clinical and treatment characteristics, the only characteristics impacting negatively on OS were KI and locally advanced disease (univariate and multivariate analysis in Table 1).

Conclusions: These results showed that in PSC the main prognostic factor is the stage of the disease; robust prospective trials are needed to define better therapeutic strategies for locally advanced diseases.

**Table 1.**

| | 2 y OS | 5 y OS | p | RR (IC 95%) on OS | p |
|---|---|---|---|---|---|
| cT1-T3 vs cT4a/b | 78% vs 65% | 69% vs 34% | .010 | 3.3 (1.4-7.9) | .008 |
| cN0 vs cN+ | 63% vs 36% | 52% vs 24% | .035 | 3.8 (1.6-8.8) | .002 |
| IK≥80 vs <80 | 67% vs 36% | 62% vs 12% | .000 | 2.2 (1.1-4.5) | .023 |
| CR/PR vs NC/PRO to NCT | 64% vs 0% | 51% vs 0% | .013 | / | / |

## PO114

### DOSE INTENSIFIED (70 GY) VERSUS STANDARD DOSE (66 GY) IN SALVAGE POST-PROSTATECTOMY IMAGE-GUIDED VMAT: PRELIMINARY ASSESSMENT OF GENITOURINARY AND GASTROINTESTINAL TOXICITY

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Aims: To study acute and late tolerance of men receiving dose-escalated radiotherapy (39 ptz) (70 Gy) versus standard dose (57 ptz) (66 Gy) in a salvage post-prostatectomy (SRT) setting.

Methods: The records of 96 men treated with prostatectomy and subsequent SRT to the prostate bed were analyzed. Men included required to have a pre-RT PSA <2 ng/mL. Men were treated with image-guided VMAT. Tolerance to treatment was determined from the chart and graded according to RTOG scale. Differences in toxicities were compared using Fisher exact test. Significance was defined as two tailed p-value <0.05.

Results: *Acute toxicity*. The acute toxicity was assessed 15 days after SRT. Fifteen days after RT, 7 men (18%) in the group treated with dose-intensified SRT and 10 patient (17,5%) in the group treated with standard dose suffered from G1-2 acute GI toxicity (p=1.0). Of these, 3 (7,7%) in the group treated with dose-intensified SRT and 3 (5,2%) in the group treated with standard dose suffered from G2 acute GI toxicity. Men treated with dose-intensified and standard SRT experienced higher incidence of acute GU than GI toxicity. Ten men (25,6%) in the group treated with dose-intensified SRT and 19 patient (33,3%) in the group treated with standard dose suffered from G1-2 GU toxicity (p=0.4). Two men (3,5%) in the group treated with standard dose and 5 patient (12,8%) in the group treated with dose-intensified SRT suffered from G2 acute GU toxicity. No acute grade 3 or higher GU and GI toxicity was detected. *Late toxicity*. The late toxicity was assessed six months after the end of postoperative RT in 76 men. Only 5 out 37 patients (13.5%) in the group treated with dose-intensified SRT and 4 out of 39 patients (10.2%) in the group treated with standard dose suffered from G1-2 late GU toxicity (p=0.7). Three men (8.1%) in the group treated with dose-intensified SRT and 2 men (5.4%) in the group treated with standard dose suffered from G2 late GU toxicity. No grade 3 or higher GU toxicity was detected. No late G2 or higher GI toxicity in the group treated with standard dose was observed while 2 men in (5.4%) in the group treated with dose-intensified SRT suffered from G2 late GI toxicity.

Conclusions: With a low rate of relevant acute and late GI and GU toxicity no significant difference of symptoms burden in the SRT with a dose-intensified protocol was found with respect to standard SRT dose in short-term period. However our results should be verified in a large prospective trials.

## PO115

### TREATMENT APPROACHES IN THE MANAGEMENT OF ELDERLY LARYNGEAL CANCER PATIENTS

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Aim: To describe the elderly population of laryngeal cancer patients (pts) treated with combined modalities at a tertiary cancer center in Italy.

Methods: We retrospectively analyzed 104 pts aged ≥ 65 treated at our Institution from 2002 to 2017. Survivals were estimated using Kaplan-Meier method and median follow-up was measured through reverse Kaplan-Meier method. Contingency tables were analyzed with chi-squared or Fisher tests and survival curves were compared with log-rank test. Statistical significance was set at $p < 0.05$.

Results: At our Institution, 104 laryngeal cancer pts were treated with curative intent. Median age was 73 years (range 65-92) and the majority of them were men (91%). Median follow-up was 69.9 months. More than half of tumors (59) were glottic and in most cases (90%) it was a primary tumor. Stage was I in 30% of the cases, II in 15%, III in 36% and IV in the remaining 19%. Generally, radiotherapy (RT) was delivered with Intesity Modulated Radiation Therapy (IMRT) technique, in particular 70 Gy in 33 fractions as radical intent and 66-70 Gy for post-operative pts. According to the stage of the disease, pts underwent different types of treatments. Exclusive IMRT was delivered in the 45% of cases, total laryngectomy in 31%, conservative surgery in 7%, chemo-RT in 17%. Median disease-free survival (DFS) and overall survival (OS) of the whole study population were not reached (NR) (95% CI 56.2-NR) and 77.1 (95% CI 51.6-NR). At univariate analysis, clinical factors associated with statistically different OS were age (p=0.043), site (p=0.03 considering glottic vs non-glottic cancer), TNM (p<0.0001 7th and 8th editions), and comorbidity (p=0.035). At multivariable analysis, the only covariates maintaining an indepen-

dent statistical significant association with OS were age (HR 1.06, p=0.03) and TNM (HR 2.15 for the seventh edition, p=0.004). Severe (G≥3 according to CTCAE) late sequelae were observed in three subjects: two cases of chronic aspiration for which a permanent percutaneous gastrostomy was placed; one cancer recurrence-free patient with persistent radiation-induced laryngeal edema treated with total laryngectomy.

Discussion: Taking into consideration that in this retrospective study we did not have control arms for comparison or validation cohorts, age and TNM (both 7th and 8th editions) showed to be independent prognostic factors in this study population.

## PO116

### PATTERN OF LOCOREGIONAL FAILURE IN BREAST CANCER PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY AFTER MODIFIED RADICAL MASTECTOMY AND BREAST RECONSTRUCTION: A SINGLE INSTITUTION EXPERIENCE

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Aim: Our study analyzes the occurrence of recurrent breast cancer in patients treated with mastectomy, reconstruction and post mastectomy radiotherapy (PMRT).

Methods: We retrospectively reviewed 140 patients with Stage I-II-III breast cancer treated with modified radical mastectomy, axillary lymph node dissection and systemic therapy between 1992 and 2016 at our Department. We defined "in field" locoregional recurrence (LR) when breast cancer recurrence occurred within the radiotherapy field, and/or the chest wall; "marginal recurrence" when breast cancer recurrence was located up to 1 cm from treatment field; and "out-field recurrence" when site of LR was located at distance larger than 2 cm from the radiotherapy field.

Results: The median age was 48,7 years. Hundred-eleven (82%) women were T1-T2 stage and twenty five (18%) women were T3-T4 stage. Most of patients showed (94%) pN1-3 disease. Sixtyeight (49%) tumors were grade 3; 114 (81%) patients were estrogen receptor positive. Lymphovascular invasion (LVI) was present in 82 (58%) of the cases. The median dose of radiotherapy was 50,9Gy (range 50-70 Gy). With a minimum follow up of 36 months, 10 (7,1%) patients experienced a LR. Mean PFS was 75,7 month. All relapses on the chest wall were observed above the breast tissue expander or mammary prosthesis. Three (30%) LR was observed in-field of radiotherapy treatment volume; two (20%) LR was observed out-field of radiotherapy treatment volume, two patients relapsed either in field and out-field. Three patients had a marginal LC. Six patients relapsed over the expander and two patients relapsed both over the expander and in the axillary lymph nodes. At the Univariate analysis for PFS patients who did not recive NCT have better PFS (p=0.0006); grading, T and the presence of LVI had impact negative impact on PFS. All the variables of the univariate analysis maintain their significance at univariate analysis. Univariate analysis for OS show's that patients who did't recieve NCT have better survival. The presence of LVI and high T impact significantly on OS.

Conclusions: This study suggests that chest wall LR are rare after PMRT and are related to biologic aggressiveness of the disease rather then to inadequate irradiation of target volumes. All relapses on the chest wall were observed above the breast tissue expander or mammary prosthesis, These findings corroborate the new ESTRO guidelines recently published.

## PO117

### SURVIVAL AND PROGNOSTIC FACTORS OF A LARGE DATASET OF NASOPHARYNGEAL CANCER PATIENTS IN NON-ENDEMIC SETTINGS

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Background: Nasopharyngeal carcinoma (NPC) is a rare cancer in most areas including Europe. Data regarding natural history, prognostic factors and treatment strategies in NPC patients (pts) are derived from studie conducted in endemic region.

Methods: We retrospectively collected clinical data on 75 consecutive NPC pts treated in non-endemic setting from 2005 to 2016. Main objective of the study was to collect clinical and biological parameters to describe characteristics in non-endemic settings and to correlate them with the outcome.

Results: The dataset included 75 pts from our Institution, mainly male (80%), all with ECOG PS 0 and median Charlson Comorbidity Index 3.24, advanced stage (stage III 20%, IV 52%), with a median age of 51.13 years. Epstein-Barr encoded RNA was assessed in 30.7% (95% positive). All patients had radiotherapy as radical treatment. Induction and concurrent chemotherapy (CT), were administered to 25.3% and 73.3% of the pts, respectively. Main RT techniques employed were IMRT (56%) and 3DRT (44%). With a median follow up of 4.75 years, OS at 3- and 5-year was 75% and 70%, respectively. Among the 29 pts who relapsed, distant metastases were the main localization (41.37%). No toxicity >; 3 was recorded. At univariate and multivariate analysis, using the Cox regression model, the following variables showed to favorably correlate with OS: T (1 vs 2 vs 3 vs 4, p=0,0417); global stage (I-II vs III-IV, p=0,0487), concomitant chemotherapy (p=0,0370).

Conclusions: In non-endemic areas, NPC showed survival figures comparable to endemic areas. Concomitant chemotherapy, global stage, T stage turned out to be prognostic factors.

## PO118

### RETROSPECTIVE ANALYSIS OF NASOPHARYNGEAL CANCER PATIENTS TREATED BY HELICAL TOMOTHERAPY: OUTCOME AND TOXICITY

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Aims: To evaluate overall survivall (OS) , acute and late toxicity in 56 patients with nasopharyngeal cancer treated by Helical Tomotherapy.

Methods: We retrospectively analyzed 56 patients with non metastatic nasopharyngeal carcinoma treated from March 2009 to March 2018. All patients but 3 were treated with platinum based concurrent chemoradiotherapy and 27 patients received also neo-adjuvant chemotherapy. Before treatment a magnetic resonance imaging ( MRI) and/or a contrast enhanced computer tomography and a positron emission tomography (PET) were performed. Prescription dose was 66 Gy for high-risk CTV at 2.2 Gy/fraction, 60 Gy for intermediate CTV at 2 Gy/fraction and 54 Gy for low CTV at 1.8 Gy/fraction with simultaneous integrated boost (SIB). Treatment was delivered every day, five fractions/week for a total of 30 fractions. Acute toxicity was evaluated thought a weekly visit according to CTCAE v 4.0 while late toxicity was according to RTOG/EORTC.

Results: The median age was 53 years ( range 11-77); 47 (84%) patients were males and 9 (16%) were females. 14 (25%) and 42 pts (75%) presented stage I-II and stage III-IV disease, respectively. As regards grade 3 acute toxicity: 3 (5%) patients, 6 patients (11%) and 4 patients (7%) developed mucositis, dysgeusia and dysphagia respectively. Five patients needed parenteral nutrition. All patients completed treatment without interruption. We observed 47 CR and 7 PD, 2 pts were not evaluable (deceased before re-evaluation). With a median follow-up of 52 months (range 2-114), 51 patients were alive and 5 pts died, two due to toxicity (sepsi) at 2-3 months from the end of radiotherapy and three for PD. Grade 2 late toxicity was respectively dysgeusia in 9%, xerostomia in 32% and hearing loss in 2%. No patients reported late grade 3 toxicity. 5 yy OS was 89.3%.

Conclusions: Patients suffering from nasopharyngeal cancer can be treated by Helical Tomotherapy with a good coverage of the target and a good sparing of the organs at risk (OARs) , obtaining good response rate and toxicity profile that leads to an excellent quality of life.

## PO119

### CAN NEUTROPHIL-TO-LYMPHOCYTE RATIO HAVE A CORRELATION WITH ACUTE TOXICITY IN ADJUVANT RADIOTHERAPY FOR BREAST CANCER?

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Aims: A high neutrophil-to-lymphocyte ratio (NLR) is a marker of systemic inflammation and has been proposed as prognostic marker in several tumors. The aim of this study is to evaluate the effect of adjuvant radiotherapy on lymphocyte, neutrophilic and relative ratios in breast cancer patients. We also explored correlation between NLR, skin toxicity and different radiotherapy regimes.

Methods: We retrospectively reviewed patients who received adjuvant radiotherapy for breast cancer and performed a complete blood cell count before and after two weeks from the end of radiotherapy course. Neutrophil-to-lymphocyte ratio was defined as the absolute neutrophil count divided by the absolute lymphocyte count. Differences (Δ, delta values) between values at different time points were calculated. Radiotherapy was performed with 3D-conformational technique or in irregular surface compensator technique. Patients underwent periodic controls during treatment and toxicity was assessed using the Common Terminology Criteria for Adverse Events version 4.02.

**Table 1.**

| | Before RT (mean) | After RT (mean) | p |
|---|---|---|---|
| **Lymphocytes** (x10*3/uL) | 2.2 | 1.5 | **<0.001** |
| **Neutrophils** (x10*3/uL) | 4.4 | 4.2 | 0.375 |
| **NLR** | 2.3 | 3.0 | **<0.001** |

**Table 2 Delta values.**

| | Hypofractionated RT (mean) | Standard RT (mean) | p |
|---|---|---|---|
| **Lymphocytes** (x10*3/uL) | -0.48 | -0.73 | 0.196 |
| **Neutrophils** (x10*3/uL) | -0.71 | -0.41 | 0.393 |
| **NLR** | 1.24 | 2.07 | **0.028** |

Results: We identified 78 breast cancer patients treated at our institution. Radiotherapy was performed with conformational technique and in with irregular surface compensator technique in 67 (86%) and 11 (14%) patients, respectively. 31 patients (40%) received hypofractionated treatment. Recorded skin toxicity at the end of treatment was as follows: G1 in 35 pts (45%) and G2 in 16 pts (20%). No patient experienced G3 toxicity. Due to toxicity, only 3 patients needed suspension and 3 early interrupted radiotherapy course. Data

on changes in blood cell counts values and ratio were summarized in Table 1. At the end of radiotherapy a lymphocyte count reduction as well as a NLR increase was observed in the entire patients population (p=<0.001). Among patients treated with hypofractionated regimen, delta NLR was lower than in patients treated with standard RT dose (see Table 2). No differences were observed in NLR changes between patients experiencing grade 2 skin toxicity and patients with grade < 2 skin toxicity.

Conclusions: Our data suggest that adjuvant radiotherapy in breast cancer induces lymphopenia and a delta NLR increase. Different fractionations seem to have different impact on immunity. Therefore, additional studies are needed to further explore the relationship with toxicity and prognosis in breast cancer patients undergoing radiotherapy.

## PO120

### CHEERING RESULTS IN TERMS OF ACUTE AND LATE TOXICITY OF SIB IMRT TREATMENT OF SQUAMOUS CELL ANAL CANCER

I. Chiola[1], E. Tornari[1], L. Carmisciano[3], E. Olivetta[1], A. Bacigalupo[2], L. Belgioia[1,2], S. Vagge[2], R. Corvò[1,2]

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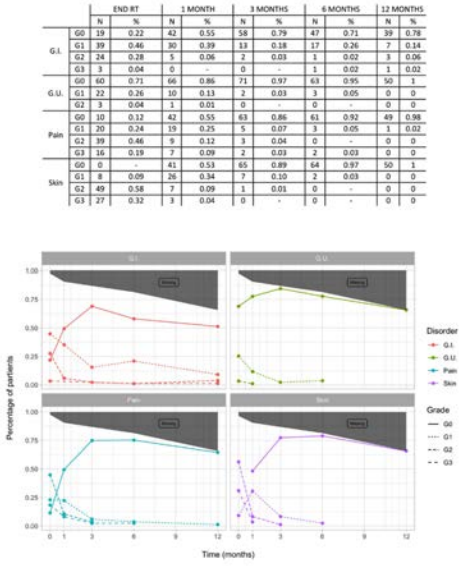
Aims: Treatment strategy of anal cancer is based on a conservative approach. Aim of treatment is definite cure possibly without mutilating surgery. Treatment is mainly based on concurrent chemoradiotherapy (CTRT).The majority of patients (pts) treated with CTRT with anal cancer has an excellent outcome. However, particular problems related to early side effects as well as late toxicity are present and can negatively affect the quality of life. Our primary end point is to evaluate clinical acute and late toxicity, secondary endpoint is overall survival.

Methods: From March 2009 to May 2018 we retrospectively analyzed a total of 87 patients with squamous anal cancer 2 pts were excluded due to unreported FU. Patients were treated with intensity-modulated radiotherapy (IMRT) and concurrent chemotherapy. Radiotherapy was delivered with simultaneous integrated boost (SIB) technique by helical tomotherapy, and doses were adapted to two clinical target volumes according to the tumor-node-metastasis (TNM) stage. Toxicity were scored according to CTCAE scaleat the end of treatment, one month later, and subsequently every 3 -6-12 months after EBRT.

Results: Pts treatments schedule were the following: concomitant chemotherapy (only 5 pts didn't receive CT because of comorbidity or early stage) and external beam radiotherapy (EBRT) with IMRT or Tomotherapy, with a median dose 55 Gy (range 43,2-58,05) on CTV1 and median dose 45 Gy (range 39,6-52,8) on CTV2with a median of 25 total fraction (range 22-30). Median follow up is 39,3 months (IQR 20,2-62,6 months), and OS is 86% (95% CI 78-95) at 39,3 months.Here we report results of toxicity, the grey area of the plot shows the percentage of missing data (pts lost at follow up, pts death…).

Conclusions: In our experience symptoms score registered have a decreasing grade trend: skin and pain toxicities are very common in at the end of RT (respectively 58% of pts G2 and 46% of G2) but in long term FU the total of follow up have a complete response. Gastrointestinal toxicity has a decreasing grade trend, but at 1 year after end of RT 11 pts (22%) presented grade other than G0.



| | | END RT | | 1 MONTH | | 3 MONTHS | | 6 MONTHS | | 12 MONTHS | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % | N | % |
| G.I. | G0 | 19 | 0.22 | 42 | 0.55 | 58 | 0.79 | 47 | 0.71 | 39 | 0.78 |
| | G1 | 39 | 0.46 | 30 | 0.39 | 13 | 0.18 | 17 | 0.26 | 7 | 0.14 |
| | G2 | 24 | 0.28 | 5 | 0.06 | 2 | 0.03 | 1 | 0.02 | 3 | 0.06 |
| | G3 | 3 | 0.04 | 0 | - | 0 | - | 1 | 0.02 | 1 | 0.02 |
| G.U. | G0 | 60 | 0.71 | 66 | 0.86 | 71 | 0.97 | 63 | 0.95 | 50 | 1 |
| | G1 | 22 | 0.26 | 10 | 0.13 | 2 | 0.03 | 3 | 0.05 | 0 | 0 |
| | G2 | 3 | 0.04 | 1 | 0.01 | 0 | - | 0 | - | 0 | 0 |
| Pain | G0 | 10 | 0.12 | 42 | 0.55 | 63 | 0.86 | 61 | 0.92 | 49 | 0.98 |
| | G1 | 20 | 0.24 | 19 | 0.25 | 5 | 0.07 | 3 | 0.05 | 1 | 0.02 |
| | G2 | 39 | 0.46 | 9 | 0.12 | 3 | 0.04 | 0 | - | 0 | 0 |
| | G3 | 16 | 0.19 | 7 | 0.09 | 2 | 0.03 | 2 | 0.03 | 0 | 0 |
| Skin | G0 | 0 | - | 41 | 0.53 | 65 | 0.89 | 64 | 0.97 | 50 | 1 |
| | G1 | 8 | 0.09 | 26 | 0.34 | 7 | 0.10 | 2 | 0.03 | 0 | 0 |
| | G2 | 49 | 0.58 | 7 | 0.09 | 1 | 0.01 | 0 | - | 0 | 0 |
| | G3 | 27 | 0.32 | 3 | 0.04 | 0 | - | 0 | - | 0 | 0 |



Figure 1.

## PO121

### CAROTID-SPARING APPROACH IN EARLY GLOTTIC CARCINOMA RADIOTHERAPY: A RETROSPECTIVE FEASIBILITY ANALYSIS

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Aims: The most serious side effect of early glottic cancer radiotherapy is cerebrovascular accident (CVA), as demonstrated by a recent SEER analysis (cumulative incidence of fatal CVA at 15 years 2.8% versus 1.5% in patients receiving EBRT relative to surgery, p.024). Aim of this work is the feasibility of carotid sparing VMAT in early glottic cancer undergoing exclusive RT.

Methods: In our department, all the patients with early stage glottic cancer underwent carotid Doppler ultrasound before treatment and we selected patients with severe carotid stenosis >70% (NASCET criteria). Three patients with T1-T2 N0 glottic cancer were included in this protocol. Target volumes included larynx (false and true VC, ant + post commissure, arytenoids and ariepiglottic folds and subglottic region). A 2-mm planning target volume was uniformly added to each CTV as per our institution's standard when daily IGRT was applied. Organs at risk (OARs) included the bilateral carotid arteries, constrictor muscles, thyroid gland, spinal cord, and submandibular glands. We contoured left and right carotid artery separately (from the aortic arch on the left and brachiocephalic trunk on the right and extended superiorly to at least 2.5 cm superior to the hyoid bone). A VMAT plan was generated using 2 partial arcs with with 2 full 360° arcs, using 6-MV photons prescribed to the PTV mean . We tried to push down the dose to carotids as low as possible with no specific constraints due to the lack of well-defined dose thresholds associated with carotid toxicity.

Results: In all the patients, 100% of the PTV received >95%prescription dose (63Gy at 2.25 Gy per treatment). The median PTV mean dose was below 107%. A mean dose of 22 and 23 Gy was achieved to the left and right carotid, respectively.Left carotid Median V40 dose was 26 Gy; Right carotid Median V40 dose was 30 Gy. Left carotid Median V50 dose was 11.6 Gy; Right carotid Median V50 dose was 11.6 Gy. In the follow up visits, the carotid stenosis was stable in all the treated patients.

Conclusions: Carotid Doppler ultrasound evaluation seems to be useful in patients with HNSCC undergoing radiation therapy. Carotid sparing VMAT is technically and dosimetrically feasible to implement CS-IMRT approaches into clinical practice. At the same time there's a lack of consensus in target volume definition, dose constraints and prescribed dose. Ultimately, long-term prospective data are required to show the benefit of CS-IMRT.

**PO122**

## SIMULTANEOUS INTEGRATED BOOST (SIB) AND THE IMPACT ON FECAL INCONTINENCE IN ANAL CANAL CANCER

I. Chiola[1], E. Tornari[1], L. Carmisciano[3], E. Olivetta[1], A. Bacigalupo[2], L. Belgioia[1,2], S. Vagge[2], R. Corvò[1,2]

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Aims: The main function of the anal canal is to maintain continence and to allow passage of stools at an appropriate time and place. Damage to any of the structures carries a risk of fecal incontinence or defecatory disturbances. Treatment strategy of anal cancer is based on a conservative approach without mutilating surgery. The majority of patients (pts) treated with CTRT after being diagnosed with anal cancer has an excellent outcome. Unfortunately, long-term survivors often suffer from severe anorectal symptoms. The aim of the study is investigating acute and late incontinence in anal canal cancer patients treated with CTRT.

Methods: From March 200 9 to May 2018we retrospectively analyzed a total of 87 patients with squamous anal cancer 3 pts were excluded due to unreported FU, 2 pts were excluded due to colostomy pretreatment. Pts were treated with intensity-modulated radiotherapy (IMRT) and concurrent CT. RT was delivered with simultaneous integrated boost (SIB) technique by helical tomotherapy, and doses were adapted to 2 clinical target volumes according to the tumor-node metastasis (TNM) stage. Fecal incontinence was scored according to Wexner score (WS) at start and end of treatment, 1 month later, and subsequently 3 and 12 months after EBRT.

Results: Pts treatments schedule were concomitant CT (only 5pts didn't receive CTbecause of comorbidity or early stage) and external beam radiotherapy (EBRT) with IMRT or Tomotherapy, with a median dose 55Gy (range 43, 2-58, 05) on CTV1 and median dose 45 Gy (range 39, 6-52, 8) on CTV2 with a median of25total fraction (range22-30). Median time between RT start and RT end is 37 days (IQR 35-40). We divided incontinence's score in 4 categories, based on total score (TS) (Group 1pts with TS of 0, group 2pts with a TS between1-10, group 3 pts with a TS between 11-16TS and group 4 pts with a TS between17-20). Median follow up is 41,2 months (IQR 21, 5-65, 6 months), and OS is 83% (95% CI 74-92) at 41,2 months with 13pts died. CFS is78% (95% CI 69-88) at 41, 2 months with 7 pts who underwent a colostomy. In table results.

Conclusions: WS has become a widely used for the assessment of severity of fecal incontinence. It is simple and easily to use. Main limitations of this study are being retrospective and the difficulty in finding information:where there is no reportedinformation about incontinence, we considered no incontinence. On our data we found: a decreasing grade trend in that pts who developed incontinence after treatment, and a high per-

cent of pts (41 pts 50%) is stable to 0 score at every reported time.

The Wexner score[4]

| Type of incontinence | Frequency: Never | Rarely | Sometimes | Usually | Always |
|---|---|---|---|---|---|
| Solid | 0 | 1 | 2 | 3 | 4 |
| Liquid | 0 | 1 | 2 | 3 | 4 |
| Gas | 0 | 1 | 2 | 3 | 4 |
| Wears pad | 0 | 1 | 2 | 3 | 4 |
| Lifestyle alteration | 0 | 1 | 2 | 3 | 4 |

Never, 0; rarely, <1/month; sometimes, <1/week, ⩾1/month; usually, <1/day, ⩾ 1/week; always, ⩾1/day. 0, perfect; 20, complete incontinence.

| score | START RT | | END RT | | 1 MONTH | | 3 MONTHS | | 12 MONTH | |
|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 78 | 0.95 | 63 | 0.77 | 60 | 0.73 | 59 | 0.76 | 52 | 0.83 |
| > 1 and < 1 | 3 | 0.04 | 14 | 0.17 | 14 | 0.17 | 15 | 0.19 | 9 | 0.14 |
| >10 and < | 1 | 0.01 | 5 | 0.06 | 6 | 0.07 | 4 | 0.05 | 2 | 0.03 |
| >16 | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |

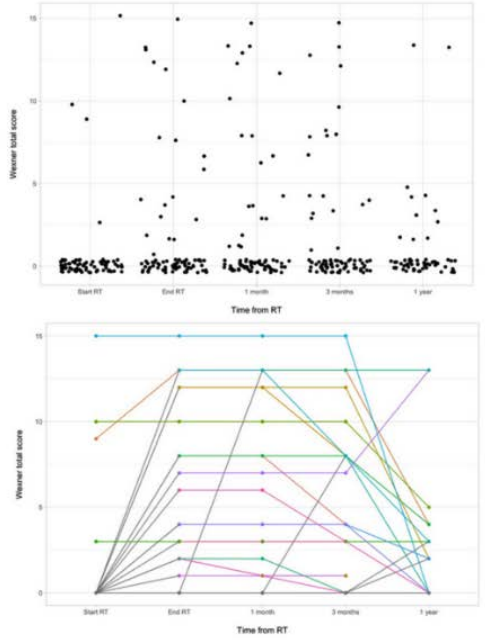


**Figure 1.**

**PO123**

## PREOPERATIVE RADIO-CHEMOTHERAPY (RT-CT) IN LOCALLY ADVANCED RECTAL CANCER (LARC) USING TWO DIFFERENT DOSES; PRELIMINARY FINDINGS OF A MONOISTITUTIONAL EXPERIENCE

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Aims: The aim of this study was to evaluate pathological response and toxicities in patients (pts) affected by LARC underwent neoadjuvant RT-CT using two different doses.

Methods: From January 2014 to May 2018, 33 pts affected by LARC underwent neoadjuvant RT-CT followed by surgery. Twenty-one pts were male (55,3%) and 17 were female (44,7%). The median age was 68 years old (42 to 81 years old). Twenty-seven pts (Group 1) received 55 Gy in 25 FF (45 Gy to the pelvis, 55 Gy to the T, N+ and mesorectum in SIB technique) and 11 pts (Group 2) received 50.4 Gy to the pelvis in 28 daily FF. In association with RT treatment Capecitabina 1650 mg/mq/day was given to all pts. We evaluated clinico-pathological characteristics, acute and late toxicity according to CTCAE vs 5 scale.

Results: After a median follow-up of 28 months (range 3-56 months) 4 year PFS was 88% in group 1 and 82% in group two, respectively. At histological examination 8 pts (26,7%) had a T- complete response (CR), 26 pts (68.5%) had N-CR and 4 pts (15.8%) had both T and N-CR. There was no statistically differences between two groups; however there was a trend in favor of group 1 regarding N-CR (p-value 0,13). Tumour down-staging was observed in 27 (79%) pts; 70% Group 1 and 63.5% Group 20. Nodal down-staging was found in 86.8% of pts; 88,8% in Group 1 and 77% in Group 2. Sphincter preserving was reached in 71% (74% Group 1 and 55% Group 2). Only 4 pts had disease progression and underwent systemic treatment. (2 pts in Group 1 and 2 in Group 2). Of them 3 pts reported distant metastases and one pts had locally and distant metastases. GI and GU G2/3 acute toxicity was observed in 9 pts (23,5%): 6/27 (22%) Group 1 and 3/11 (27,2%) Group 2. Late G2/G3 toxicity was observed in two patients (5,3%): one patient reported wound dehiscence and one pt recto vesical fistula.

Conclusions: Neoadjuvant RT-CT with a TD of 55 Gy/25ff (45 Gy to the pelvis and 55 Gy to mesorectum, T and N+ with SIB technique) improved tumor response, nodal response and sphincter preserving. Acute and late toxicity was acceptable with no statistically differences between two groups. Randomized trials with

higher number of pts and longer follow-up are necessary to confirm our results.

## P0124

### VMAT VERSUS 3D-CRT FOR THE IRRADIATION OF LEFT BREAST OR CHEST WALL PLUS SUPRA/INFRACLAVICULAR NODES: A DOSIMETRIC COMPARISON AND ANALYSIS OF TOXICITY

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Aims: To compare a dual arc VMAT technique and half beam block 3D-CRT for the irradiation of left breast or postmastectomy chest wall plus supra/infraclavicular lymphnodes in terms of target coverage and doses to OAR. An evaluation of acute e late toxicity was also carried on.

Materials: 26 planning CT were segmented. For every CT two plans were generated: a 3D-CRT with two tangential half beam block for the breast/chest wall and two nearly opposed half beam block for the lymphnodes, using the same isocenter for all the beams (6MV, 10MV or 15MV - Philips Pinnacle3 TPS) and a dual arc VMAT of 240°± 20° starting from gantry at 180° (6MV - Elekta Monaco TPS). Both plans were optimised in order to obtain the best compromise between target coverage of the two PTVs (in terms of V95, CI and HI) and OAR sparing (in terms of V20, V5 and mean dose for lungs; V30, V5 and mean dose for heart; right breast V5 and mean dose). 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. Acute and late radiation toxicities were detected and scored by RTOG/CTCAE scales.

Results: Due to the better conformity of the technique, VMAT, compared to 3D, shows: -highly significant better coverage for both the PTVs; -heart V30 significantly lower (p=0.002); -V20 of ipsilateral and total lung lower, although not significant; -OAR low doses higher. No significative acute toxicities were observed except of rare cases of skin reaction (usually GR 1-2, max GR.3) and dysphagia (max. GR.2); evaluation of late toxicity is still ongoing but, from preliminary data, we can affirm that no substantial late side effects affected women treated by VMAT.

Conclusions: Results obtained from the present study show that VMAT for the irradiation of left breast/chest wall plus nodes offers: -better target coverage, CI and HI than 3D; -better V30 for heart and V20 for lung; -higher low dose parameters for all OAR. This little group of patients, at last, had also a low incidence of acute and late toxicity. It follows from the above that VMAT has become the favourite technique applied in Lucca's Radiotherapy Unit considering that, furthermore, as reported in recent literature, low dose bath observed in this technique doesn't seem to determine higher detriment to healthy tissues, which is instead frequently reported in the medium-high dose region usually larger in 3D.

## P0125

### RETROSPECTIVE COMPARISON BETWEEN IMRT VS 3D-CONFORMAL RADIOTHERAPY IN GASTRIC CANCER: MONO-INSTITUTIONAL EXPERIENCE AT UNIVERSITY OF CATANIA ON SAFETY, TOLERANCE AND EFFICACY

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Aims: To report our clinical experience in radiation treatment (RT) for patients (pts) with gastric cancer: to compare intensity modulated (IMRT) versus conformal radiotherapy (3D-CRT) and to report efficacy, safety and tolerance.

Methods: From January 2013 to December 2018, 52 pts (M:40; F:12), with histologically proven gastric adenocarcinoma were treated. Median age was 66 years (range: 54-74), median KPS: 80 (range: 70-90). Forty-three pts underwent surgery and were treated in adjuvant setting, 28 of whom in combination with chemotherapy (concomitant 5FU/Cape in 21 pts, 5FU-CDDP or Docetaxel-CDDP-5FU before RT in 7 pts). Six patients were treated with radical or palliative intent, three treated in neoadjuvant setting in combination with DCF chemoterapy. Stage distribution was as follow: clinical or pathological T2N1 3 pts, T3-4 N0-x 9 pts, T3-4 N1-2 26 pts, any T N3 14 pts. Positive R1-2 margins were detected in 5 cases. 3D-CRT technique was used in 25 cases with dose of 45-50,4 Gy and in 3 pts to a dose of 30 Gy, static IMRT technique was administered in 21 pts to a dose of 45-50,4 Gy, 3 pts underwent Simultaneus Integrated Boost (SIB) to 60,2 Gy.

Results: 49 pts (95%) completed RT, three suspended for GI grade III toxicity. Median follow-up was 39.1 months (5 – 77). According to CTCAE scoring criteria 8 pts in 3D-CRT group experienced GI toxicity (2 grade III, 6 grade II), while in IMRT group only 1 pt had grade III and 2 grade II GI toxicity. No haematological toxicity was seen in IMRT group, while 3 pts in 3D-CRT group had grade II-III anemia. Local failure, mainly in regional lymphnodes, was detected in 15% pts in IMRT group vs 26% in 3D-CRT group. Distant metastases (in liver, peritoneum and bone) are substantially equal in both groups (25% vs 28%).

Conclusions: IMRT showed lower rates of acute toxicity and better local control rates, as shown by the scientific literature data.

**PO126**

## THE NEW TECHNOLOGY IN RADIOTHERAPY OF BREAST CANCER: PRELIMINARY STUDY ON CONCOMITANT BOOST

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Aim: Whole breast radiotherapy (WBRT) is considered a standard therapeutic option for early breast cancer (EBC) in the postoperative setting after breast conservation (BCS). On the problem of the boost there is a large majority that believes that a boost to the lumpectomy cavity can further increase local control. At the moment the boost in our Center is performed with a beam of electrons with 3 cm around the surgical scar, but there is no agreement on this system, given the surgeon's habit to minimize the surgical scars (missing targets). For this reason therefore we have carried out a new method to identify and hit the boost. In the current analisys we studied the acute and late toxicity of concomitant treatment.

Methods: From May 2018 twenty-seven patients received 50 Gy to the whole breast in 25 fractions/4 weeks with 2Gy/fraction plus an additional concomitant daily boost of 0.3 Gy to the tumor bed, giving a total dose of 57.5 Gy.

Results: Three months after the end of radiotherapy, 59.2% and 40.7% of patients showed grade 0 skin toxicity and grade 1 skin toxicity, respectively. After 6 months, 70.4% and 29.6% of patients showed grade 0 and grade 1 skin toxicity. After 1 year, grade 0 skin toxicity was found in 77.7% of the patients and grade 1 skin toxicity in 22.2% of the patients. After a median follow-up of 12 months, all patients showed excellent cosmetic results with minimal breast edema and minimal skin changes. There have been no local relapses to date.

Conclusion: The schedule with a concomitant boost appears to be an acceptable alternative to the traditional longer schedule, with low local toxicity and by excellent to good short-term cosmetic results, although a much longer follow-up is needed to assess the local control rate. The problem remains on how to make the surgeons understand that the clips around the lumpectomy cavity are necessary for hit the boost.

**PO127**

## RADIATION TREATMENT FOR RARE CANCERS: OLDEST AND NEWEST INDICATIONS

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Aim: All paediatric cancers and 25% of tumours in adult are considered rare and the proper treatment approach is lacking due to the low incidence rate. However, the role of radiotherapy (RT) as a treatment approach for cancers is established, providing good results in terms of overall survival and tolerance. Moreover, in the present scenario of robust data missing, the scientific advances in RT, including modern techniques, provide an increasing in the utilization of RT also in this setting. Thus, based on the present background, aim of this analysis is to review the role of RT in the management of several rare tumours for adult patients.

Methods: A collection of available data regarding RT and rare tumours was made, by PubMed research, including oral-mucosal and ocular melanomas, trachea, neuro-endocrine and endocrine tumour, hepatobiliary tumour, soft tissue sarcoma and desmoid tumour.

Results: For mucosal melanomas, RT is mainly prescribed, being associated with lower local recurrence rate. Regarding ocular melanoma, historically, enucleation has been the first treatment modality in case of locally advanced disease. Plaque brachytherapy or stereotactic radiosurgery are common forms of definitive RT, ensuring a local control up to 90% in small lesions. For trachea tumours, surgery is considered as elective treatment, while RT was traditionally used as an adjuvant or as a salvage treatment for unresectable disease; however, the exact role of RT remains unclear. Neuro-Endocrine Tumours (NET) include a large variety of cancers, mainly developed in gastro-entero-pancreatic (pNET) and bronchopulmonary systems (bpNET). For pNET, RT can be a suitable option for post-surgical (positive margins or poor pathologic features) or unresectable/borderline disease. For bpNET, the role of adjuvant treatments is uncertain and should be evaluated in larger trials. In both cases, stereotactic body RT (SBRT) is a good alternative for patients not amenable to surgery. For endocrine tumours, adjuvant RT has demonstrated benefits through reducing recurrence risk.

For hepatobiliary malignancy, SBRT is a promising approach and there is a growing body of literature supporting its utilization. For soft tissue sarcoma, perioperative treatments are often indicated, and a growing role of SBRT in oligometastatic disease is recognized.

Conclusion: RT treatment option is a frequent indication in the setting of rare cancers; thus, the role of Radiation Oncologist must not be neglected.

## PO128

### SALVAGE RADIOTHERAPY WITH DOSE-ESCALATED SIMULTANEOUS INTEGRATED BOOST (SIB) MRI-GUIDED TO THE MACROSCOPIC LESION IN PATIENTS WITH LOCAL RECURRENCE AFTER RADICAL PROSTATECTOMY FOR PROSTATE CANCER

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Aims: The main treatment option for prostate cancer relapse after radical prostatectomy (RP) is salvage radiotherapy (SRT). Target volumes and delivery doses may be different when macroscopic recurrence occurs. Multiparametric magnetic resonance imaging (mpMRI) is a useful tool for detection of local relapse (LP), but also for contouring target volumes and treatment planning. The study aims to evaluate clinical outcomes and toxicity of SRT with SIB dose escalated in patients (pts) with local recurrence after RP.

Methods: Between May 2015 and November 2017, 18 pts with macroscopic local recurrence after RP, referred to our Institute for SRT. In all pts a pre-RT pelvic mpMRI was performed to detect local recurrence and matched with TC-SIM for defining target volumes. VMAT-IGRT technique, with daily CBCT, was used to delivery hypofractionated SRT (30 fractions with SIB): 60-67.5 Gy (2-2.25 Gy/fraction) to the prostatic bed and 69-72 Gy (2.3-2.4 Gy/fraction) to the macroscopic lesion;7 pts were also treated on pelvic nodes (1.8 Gy/fx). Concomitant ADT was prescribed in 8 pts. After RT pts were evaluated with PSA every 4-6 months and at least a pelvic mpMRI. Toxicity were assessed using CTCAE v. 4.03 scale.

Results: Median time from RP was 79 months (range 3-157) Median pre-RT PSA level was 0.745 ng/ml (range 0,13-6,52). Median follow up after SRT was 26 (range 3-46), Median time to mpMRI post-RT was 9 months (range 3-33). At time of the analysis we recorded 12 complete radiologic response (66,7%), 4 partial radiological response (22,2%), and in 2 pts local lesion was unchanged. All pts but one had biochemical control of the disease (PSA nadir + 0.2 ng/ml). Biochemical progression free survival was 100% at 1 year and 85% at 3 years. For the patient with biochemical failure (30 months after RT, and one year after the interruption of concomitant long term ADT), local recurrence was not detectable at mpMRI after 15 months post-RT. Late genitourinary toxicity was mild, only one pt had a stenosis G3; main late gastrointestinal toxicity was hematochezia, G2 in 1 pt, G3 in 1pt.

Conclusions: Dose escalated SRT with VMAT-IGRT (+/- ADT) for macroscopic LP after RP seems effective with good late toxicity profile. Pelvic mpMRI seems to be useful tool not only for diagnosis, despite low PSA levels, but also for treatment planning and follow-up; the optimal time for performing mpMRI after SRT is yet to be defined. Longer follow up and larger series are necessary.

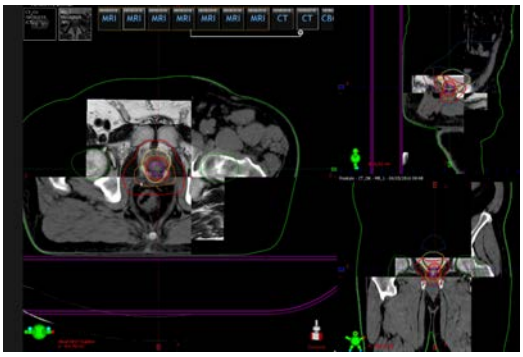

Figure 1.

## PO129

### EFFICACY AND SAFETY OF VMAT/SIB INTENSIFIED NEOADJUVANT CHEMORADIATION IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER

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Aims: To assess the pathological complete response (pCR) and the toxicity profile of preoperative capecitabine-based intensified volumetric modulated arc therapy (VMAT) radiotherapy using simultaneous integrated boost (SIB) technique in locally advanced rectal cancer (LARC) patients (pts).

Methods: Pts with cT2N+ or cT3T4N0-2 were enrolled into the protocol. Elective lymph nodes and the entire mesorectum received a total dose of 45 Gy at 1.8 Gy/fraction, while gross disease and the correspondent mesorectum were boosted with 57.5 Gy at 2.3 Gy/fraction. Capecitabine (1650 mg/mq/die) was prescribed throughout the whole radiotherapy treatment. Acute and late toxicities were recorded according to CTC-AE scale. Surgery was planned at least 7-8 weeks after the chemoradiotherapy (CRT) end.

Results: 21 LARC pts (median age: 67 years, range 42-81 years; Male/Female ratio:14/7) entered the analysis. The vast majority of pts had a cT3 tumor (N=16, 76%) with lymph nodal involvement in 90% of cases (cN1: 15 pts, cN2: 4 pts). All patients completed the prescribed treatment; overall, most of them (16 pts, 76%) suffered from mild gastrointestinal toxicity, while 2 pts (10%) from G3 adverse events. Genitourinary and hematological toxicities were less frequent, with 5 pts (24%) referring G1 dysuria and 1 pt (5%) G1 leucopenia. Twenty patients (95%) underwent surgery, after a median interval of 12 (range 7-19) weeks from the CRT's end. Anterior or abdominoperineal resections were performed in 18 (86%) and in 2 (10%) cases, respectively. One pt (5%), having metastatic disease at re-evaluation, was judged unfit for surgery and started to systemic therapy. Six pts (29%) obtained a pCR, while TRG 1-2 rate was 43%. Three pts (14%) suffered from perioperative complications (1 wound infection,1 anastomotic leak and 1 cardiac arrhythmia respectively). At the time of analysis, 9 pts (43%) referred mild inferior gastrointestinal discomfort (G1-G2) as late sequela. After a median follow-up of 26 months (range 5-47), all patients were alive; both the 2-year local control and the 2-year progression free-survival were 95%.

Conclusions: A moderately hypofractionated regimen up to a total dose of 57.5 Gy in 25 fractions with a mono-drug concomitant schedule achieves encouraging response rates and toxicity profile comparable to reported literature. With the limit inherent to the small sample size, these data can led to future scenarios on dose intensification treatments.

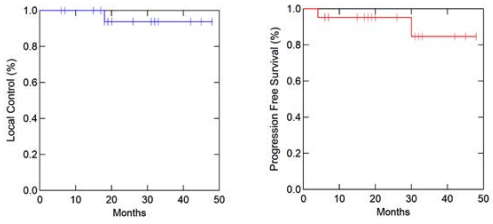


**Figure 1.**

**PO130**

## HYPOFRACTIONATED RADIOTHERAPY IN ELDERLY BREAST CANCER PATIENTS. PRELIMINARY EVALUATION OF CUTANEOUS TOXICITY

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Aims: Breast cancer (BC) is the most common cancer in the female population and in 17.2% of cases affects women over 65 years old. Sometimes, this group does not access to the whole therapeutic protocol. The use of Hypofractionated Radiotherapy (HyRT) could reduce patient discomfort and social costs of disease especially in elderly patients. The aim of this study is to evaluate radio-induced toxicity in older breast cancer patients treated with HyRT.

Methods: From January 2015 to October 2018, 104 consecutive BC patients treated at the "Istituto Nazionale per lo Studio e la Cura dei Tumori– Fondazione Giovanni Pascale" were enrolled. All treatments were evaluated by a Multidisciplinary Breast Unit. The patients were divided into 2 groups. The first group included 69 patients aged 70 to 79 years with a good Performance status (PS) and stage pT1-2 N0-1 M0. The second group (B) included 35 patients aged over 80 years old or 70 to 79 years with a poor PS and stage pT1-2 N0-1 M0. The group A received a HyRT with a dose of 42.56 Gy (2.66 Gy/fraction) in 16 fractions to whole breast without boost on the tumor bed while the group B received a dose of 28.5 Gy (5.7 Gy/fraction) in 5 fractions once a week on the whole breast without boost. Medical staff evaluated the cutaneous toxicity at the end of therapy, at 3 and 6 months according to the RTOG scale and the CTCAE criteria. Statistical analysis was performed to compare the cosmetic result between the 2 groups and to evaluate the impact of treatment characteristics on the development of skin toxicity.

Results: All patients' characteristics are summarized in Table 1. An excellent cosmetic result (G0) was recorded in 19 (17%), 66 (59%) and 96 (86%) breasts at the end of treatment, 3 months and 6 months respectively. No G4 was reported and skin toxicity did not cause any interruption of radiotherapy treatment. In additions edema, fibrosis, dyschromia and telangiectasia were rare events. No statistically significant difference was found between the 2 groups in terms of toxicity using the chi-square ($p>0.05$). Moreover, the same test showed that Trastuzumab negatively influenced toxicity at the end of RT ($p=0.015$).

Conclusions: This study confirms the safety and the benefits of HyRT in older breast cancer patients. We firmly believe that the use of these schedules will improve their quality of life, survival and mortality.

Table 1. Patient characteristics.

| Characteristics | Number of patients (n%) | |
|---|---|---|
| | A Group | B Group |
| Age | | |
| 70-79 | 69 | 10 (28%) |
| >80 | 0 | 25 (72%) |
| Disease site | | |
| Right | 29 (42%) | 12 (34%) |
| Left | 34 (49%) | 21 (60%) |
| Bilateral | 6 (9%) | 2 (6%) |
| Histological subtype | | |
| CI NST | 33 (44%) | 17 (46%) |
| CDI | 33 (44%) | 19 (51%) |
| CLI | 6 (8%) | 0 |
| Other | 3 (4%) | 1 (3%) |
| Molecular subtype | | |
| Luminal A | 44 (59%) | 22 (60%) |
| Luminal B | 25 (33%) | 13 (35%) |
| Triple Negative | 2 (3%) | 2 (5%) |
| HER2-like | 4 (5%) | 0 |
| Stage | 58(77%) | 23 (62%) |
| I | 17 (23%) | 13 (35%) |
| II | 0 | 1 (3%) |
| III | | |
| Grading | | |
| G1 | 8 (11%) | 8 (22%) |
| G2 | 54 (72%) | 24 (65%) |
| G3 | 13(17%) | 5 (13%) |
| Chemotherapy | | |
| Yes | 13 (20%) | 2 (5%) |
| No | 56 (80%) | 33 (95%) |
| Hormonal therapy | | 32 (92%) |
| Yes | 58 (85%) | 3 (8%) |
| No | 11 (15%) | |
| Biological therapy | 9 (13%) | 0 |
| Yes | 60 (87%) | 35 |
| No | | |

## PO131

### MODERATE HYPOFRACTIONATED RADIOTHERAPY IN BREAST CANCER: A SINGLE-INSTITUTIONAL EXPERIENCE

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*Radioterapia Oncologica Università di Pisa, Italy*

Aims: Radiotherapy prevents local recurrence of breast cancer after conservative surgery. We evaluated the rates of local recurrence and the toxicity among patients who received moderate hypofractionated radiotherapy after lumpectomy for early breast cancer.

Methods: Between jan-2011 and feb-2013 a total of 394 patients with stage I/II breast cancer (median age 60 yrs, range 33–87) treated in our institution, after lumpectomy and axillary dissection or SNB (sentinel node biopsy), with 3D-CRT hypofractionated radiotherapy (45 Gy to the whole breast in 2,25 Gy fractions over a 4 week period and an additional concomitant boost of 5 Gy to the tumor bed). We evaluated local recurrence rate and skin toxicity documented according to the common toxicity criteria (CTC)-score. Potential influencing factors were classified in 3 groups: patient-specific (age), tumor-specific (tumorsize, nodal status) and treatment-specific factors (axillary surgery, antihormonal therapy, chemotherapy, trastuzumab). Patients with pure carcinoma in situ or treated with neoadjuvant chemotherapy were not included.

Results: During a median follow-up period of 84 months, local recurrences were observed in 5 of the 394 patients. The 7-years rate of local recurrence were 1.2%. Distance recurrences were observed in 11 patients with a 7-years rate of 2.8%. At the end of our treatment 87.2% of patients showed erythema grade 1 (G1), 9.8% erythema grade 2 (G2) and 2.5% erythema grade 3 (G3). After at least 6 months from radiotherapy 12.9% of patients showed late side effects (low grade fibrosis, oedema, hyperchromia and pain). In multivariate analyse a significant influence on the development of acute skin toxicities (erythema G1 vs G2/G3) was observed only for nodal status (pN+ vs pN0; p=0,035) without correlation with the axillary surgery (dissection vs SNB). Factors associated with late toxicity were nodal status (p=0.052) and tumorsize (p=0.042). Neither patient age, nor choice of systemic therapy showed any significant correlation with higher grade toxicity.

Conclusions: In our analysis, in patients with early breast cancer who undergo conservative surgery and hypofractionated radiotherapy (45 Gy to the whole breast and additional concomitant boost of 5 Gy to the tumor bed), the risk of local recurrence appears low (1,2%). Breast moderate hypofractionation results well tolerated with high percentage of acute low grade toxicity (87,2%) and no late high grade toxicity.

## PO132

### THREE WEEKS SCHEDULE OF ADJUVANT BREAST RADIOTHERAPY: PRELIMINAR RESULTS IN TERM OF TOXICITY

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*Radioterapia Oncologica Università di Pisa, Italy*

Aims: Radiation therapy delivered with hypofractionation, which involves the delivery of a higher dose per fraction in fewer fractions over a shorter overall treatment time, is a valid option for early breast cancer patients after breast-conserving surgery. We herein report early outcomes of accelerated whole-breast radiation therapy with concomitant boost in our Institution.

Methods: We have compared a group “A” of 45 patients treated from January 2019 and May 2019 who received 40.5 Gy in 2.7 Gy fractions to the whole breast with a concomitant boost of 7.5 Gy in 0.5 Gy fractions with a group “B” of 394 patients who received 45 Gy of radiation to the whole breast in 2,25 Gy fractions and an additional concomitant boost of 5 Gy to the tumor bed.

Both grups of patients were affected by early breast cancer and after lumpectomy and axillary dissection or SNB (sentinel node biopsy) were treated with linear accelerator 3D-CRT. Patients receiving neoadjuvant chemotherapy were excluded. Outcome was analyzed in terms of toxicity with special focus on documented skin toxicity at the end of the treatment. Skin toxicity was documented according to the common toxicity criteria (CTC)-score.

Results: At the end of our treatment we observed • GROUP A: 84.5% of patients showed erythema grade 1 (G1), 15.5% erythema grade 2/3 (G2/G3); • GROUP B: 87.2% of patients showed erythema grade 1 (G1), 12.3% erythema grade 2/3 (G2/G3). There is not statistically significant differences between the two groups in terms of toxicity and tolerability.

Conclusions: In patients with early breast cancer who undergo breast-conserving surgery a shortened whole-breast irradiation schedule with concomitant boost of three weeks may be an alternative option with acceptable toxicity.

## PO133

### SMART DOSE ESCALATION WITH AN HDR-LIKE SBRT TECNIQUE FOR PROSTATE RE-IRRADIATION

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Purpose: Re-irradiation of intraprostatic failure remains a challenge. There is increasing interest in the use of stereotactic body radiation therapy (SBRT) in the re-treatment of intraprostatic relapse. The aim of this study was to evaluate the toxicity after salvage CyberKnife® (Accuray, Sunnyvale, Ca) (CK) based re-irradiation of patients with intraprostatic failure of pelvic malignancies.

Methods: Between June 2018 and May 2019 one patient with intraprostatic metastases from rectal cancer and four patients with prostate cancer failure previously treated with primary RT between 2006 and 2016 were re-irradiated using CK. All local relapses were confirmed by prostate biopsy (n=2) and/or radiologic staging images (n=3). Median prior RT dose was 68.73(45-78) Gy and the median interval to SBRT salvage therapy was 75 (45-116) months. Fiducial markers were implanted into the target in 4 of 5 patients. In one operated on patient the two relapses near surgical clips and in front of bladder were treated with spinal tracking. Median SBRT total dose was 35 (25-40) Gy in 5 fractions (EQD2=85 Gy, for $\alpha/\beta$ 1.5). Prescription isodose was 80% (63-81%). Rectal intraprostatic relapse was treated with 40 Gy in 5 fractions at isodose 78.5%. In three patients, 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. In 3 cases a precautionary therapy with steroids and alphalytics was used during the salvage treatment. Two patients received neoadjuvant or concomitant/adjuvant androgen suppressive therapy during their SBRT course (and is still ongoing). Toxicity was scored in accordance with CTCAE v 4.0.

Results: The median follow-up was 4.5 months (1-10 months). Acute toxicity was observed in 3 of 5 patients and was limited to grade 1 GU (minimal strangury, urgency and occasional urinary incontinence). No early late GU and GI toxicity was registered with this follow-up. Median post-salvage PSA level of 0.05 (0,02-0,07) ng/ml.

Conclusions: Our results suggest that prostate SBRT re-irradiation with intra-prostatic dose intensification is feasible. Longer follow-up is needed to establish the long-term benefits and late toxicity of the SBRT urethral-sparing HDR-like technique.

## PO134

### STEREOTACTIC RADIATION THERAPY IN TREATMENT OF RESIDUAL DISEASE AFTER 3D CONFORMAL RADIATION THERAPY IN PATIENTS WITH NSCLC. UPDATED RESULTS OF A PROSPECTIVE STUDY.

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Aims: to update the clinical results of the prospective study on stereotactic boost in unresectable lung cancer (Prot. SBRT post RTCT Numb. 0003722).

Methods: The protocol study started in 2012 and preliminary results have been presented during 2018 AIRO meeting.

Results: In the period of study, we treated sixteen patients: eight patients received concurrent chemotherapy and external beam irradiation; in eight patients radiotherapy alone whose delivered . In all patients, the cumulative delivered BED was >100. Patients treated with boost showed no significant acute toxicities. Median follow-up, including who died, was 48 months. A 1- year PFS was of 61.36%. 12- and 24-months actuarial survival rates were respectively 79.55% and 58%.

Conclusions: Escalation dose with SBRT boost is feasible. The results observed in our study have given evidence of being slightly better than the ones reported in literature on this issue since now.

PO135

## RADIATION THERAPY IN THE TREATMENT OF UNRESECTABLE PANCREATIC CANCER PATIENTS.

S. Parisi[1], C. Tamburella[1], I.Napoli[1], L. Molino[1], F. Arena[1], A. Cacciola[1], V. Davì[1], L. Campanelli[1], G. Chisari[1], S. Lillo[1], C. Severo[1], D. Cambareri[1], C. Vadalà[1], R.E. Vadalà[1], A. Brogna[2], A. Platania[2], C. Palazzolo[2], A. Santacaterina[2], G. Sansotta[1], G. Iatì[1], A. Pontoriero[1], S. Pergolizzi[1]

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Aims: To evaluate feasibility, toxicities, local control and overall survival of a stereotactic boost in unresectable pancreatic cancer patients previously submitted to external beam irradiation and chemotherapy.

Methods: From May 2016 to May 2019 we retrospectively analysed all patients affected by unresectable pancreatic cancer treated with radiotherapy (RT) in our centre. Among these we evaluated the records of patients submitted to stereotactic body (SBRT) boost after induction chemotherapy to external beam RT.

Results: In the period of observation ten unresectable pancreatic cancer patients, with histological diagnosis of pancreatic adenocarcinoma, were submitted to external beam irradiation. At the time of primary diagnosis all patients was staged cT4, cN0/1, cM0. All patients received neoadjuvant chemotherapy (5/10 GEM+ABRAXANE; 5/10 GEM) followed by external beam radiotherapy (V-MAT 4 patients; IMRT 6 patients). We delivered a median total dose of 50.6 Gy (range 48-51.25 Gy). Three patients showed an early progressive disease with liver metastases; one patient interrupted the treatment for uncontrolled diabetes mellitus with cardiovascular complication at the dose 48Gy. One patient had surgery for down-staging tumor after radiotherapy. Five patients were treated with consecutive stereotactic boost delivering a median total dose of 11Gy/1 fraction (range 10-12 Gy). Patients treated with boost showed no significant acute toxicities: 3/5 patient had nausea G1 and diarrhea G1. 2/5 patients had nausea and vomit G2. Local control was obtained in 4/5 patients (80%). A median overall survival of 15 months (range 7-34) has been obtained.

Conclusions: To the best of our knowledge this is the first study which evaluate the feasibility of the SBRT boost after induction chemotherapy to EBRT. These preliminary results seem to indicate that this kind of therapy could be emerge as a novel therapeutic option in this clinical scenario.

PO136

## LOCAL CONTROL AND SAFETY OF MODERATE HYPOFRACTIONATED RADIOTHERAPY IN IN SITU BREAST CANCER

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Aims: Radiotherapy prevents local recurrence of in situ breast cancer after breast-conserving surgery. We evaluated the rates of local recurrence and the toxicity among patients with pure carcinoma in situ who received radiotherapy after breast-conserving surgery.

Methods: Between jannuary 2011 and february 2013 a total of 47 patients with in situ breast cancer (93.7% had ductal carcinoma in situ, 2,08% had lobular carcinoma in situ and 2,08% had mixed ductal and lobular feature; median tumor size 7.7mm, range 2-20; histological grade 4,1% G1, 37,5% G2, 56,25% G3; median age 58 years, range 41–79) treated in our institution, after lumpectomy and SNB (sentinel node biopsy), with 3D-CRT hypofractionated radiotherapy (45 Gy to the whole breast in 2,25 Gy fractions over a four-week period and an additional concomitant boost of 5 Gy to the tumor bed). We evaluated local recurrence rate and skin toxicity documented according to the common toxicity criteria (CTC)-score.

Results: During a median follow-up period of 86 months, local recurrences were observed in 1 of the 47 patients. The seven-year rate of local recurrence was 2.1%. At the end of our treatment 85.1% of patients showed erythema grade 1 (G1), 6.4% erythema grade 2 (G2), 4.2% erythema grade 3 (G3). After at least six month from radiotherapy 27.6% of patients showed late side effects such as low grade fibrosis, oedema, hyperchromia and local pain. Only one patient developed a second tumor in the same breast with a completely different histology from the first one (lobular invasive carcinoma vs ductal carcinoma in situ).

Conclusions: In patients with in situ breast cancer who undergo breast-conserving surgery and receive moderate hypofractionated radiotherapy (45 Gy to the whole breast and additional concomitant boost of 5 Gy to the tumor bed), the risk of seven years local recurrence appears low with acceptable acute and late toxicity.

**PO137**

## VMAT PARTIAL BREAST IRRADIATION: ACUTE TOXICITY OF HYPOFRACTIONATED SCHEDULES OF 30 GY IN 5 DAILY FRACTIONS

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Aims: To report acute toxicities in breast cancer patients (pts) recruited in a prospective, phase II trial and treated with accelerated partial breast irradiation (APBI) using Volumetric Arc Therapy (VMAT) delivered with an hypofractionated schedule of 30 Gy in 5 daily fractions.

Methods: From March 2014 to May 2019 pts with early stage breast cancer (Stage I), who underwent breast conservative surgery, were recruited in a prospective phase II study started at National Cancer Institute of Milan. Pts received APBI with a hypofractionated schedule of 30 Gy in 5 daily fractions. Radiotherapy treatment (RT) was delivered using VMAT with a TrueBeam® (Varian Medical Systems, Inc.,CA) Linac. Acute Toxicity was assessed according to RTOG/EORTC criteria at the end of RT.

Results: 155 pts, treated from March 2014 to May 2019, were enrolled in this study. 81 women had right-side and 74 had left-side breast cancer. Median age was 69 (range 43-92). Pathological stage was IA in all the patients while molecular classification was Luminal A in 131/155 (84,5%) pts and Luminal B in 24/155 (15,5%) pts. Acute toxicity, assessed at the end of RT, consisted of G1 erythema in 31/155 (20%) pts and skin toxicities higher then G1 didn't occur. Fibrosis G1 was reported in 29/155 (18,7%) pts and Fibrosis G2 in 2/155 patients (1,2%). No episodes of pneumonitis or pericarditis were registered immediately after RT end and in the follow up time. Edema G1 occurred in 8/155 (5,1%) pts and asthenia G1 occured in 1/155 (0,6%) pts.

Conclusions: APBI using hypofractionated schedule of 30 Gy in 5 daily fractions showed, until now, a very low toxicity profile. APBI with VMAT proved to be feasible and can be a valid alternative treatment option after BCS in selected early breast cancer pts according to ASTRO guidelines. A longer follow-up is needed to assess late toxicity.

**PO138**

## SIMULTANEOUS INTEGRATED BOOST TO DOMINANT INTRAPROSTATIC LESION: LONG TERM RESULTS

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Aims: Several trials showed a benefit in prostate cancer survival outcomes with dose escalation, with a higher toxicity rate. Aim of this study was to show the results in terms of late toxicity and long term outcomes in prostate cancer patients treated by an integrated boost to the dominant intraprostatic lesion (DIL).

Methods: Inclusion criteria of the study were: histologically proven adenocarcinoma of the prostate; cT2/3N0M0 stage (on abdominal and pelvic Magnetic Resonance Imaging and bone scan); Gleason Score < 8; nodal involvement risk less than 20% (Roach formula); age >18 years; Eastern Cooperative Oncology Group performance status ≤2. The trial was approved by the Institutional Ethics Committee. Patients were treated using Intensity Modulated Radiotherapy, with a simultaneous integrated boost to the DIL, defined on the staging MRI. Prostate and seminal vesicles prescribed dose was of 72 Gy/1.8 Gy per fraction; while DIL received 80 Gy / 2 Gy per fraction. Androgen deprivation therapy was administered according to guidelines. The primary endpoint was to evaluate acute toxicity, in order to reduce the rate of acute grade > 2 GI toxicity as already reported in the preliminary analysis.[1] Secondary endpoints were late toxicity and biochemical disease-free survival. Kaplan-Meier product-limit method was used. RTOG scale was used to evaluate toxicity.

Results: Forty four patients were enrolled, with a median age of 73 (59-81). Median follow up was 66.5 months (25-144 months). The 34.1% of patients were classified in the intermediate risk group, while the others in the high and very high risk group, according the current guidelines. Actuarial 5-year late GI toxicity free survival was: 76.6% of G1; 100% of G3. Actuarial 5-year late GU toxicity free survival was: 88.8% of G1; 97.6% of G3. Nobody experienced G4 toxicity.

Biochemical Disease Free Survival was of 94.9% at 5 years, with all patients experimented local control. Five-year overall survival was of 94.6% and 96.9% the metastasis free survival.

Conclusions: The reported results, in term of toxicity and survival outcomes are encouraging. Further studies, even on-going or with the use of more accurate imaging methodologies could demonstrate the utility of a boost to DIL.

**Reference**

1. Ippolito E, Mantini G, Morganti AG, et al. Intensity-modulated radiotherapy with simultaneous integrated boost to dominant intraprostatic lesion: preliminary report on toxicity. Am J Clin Oncol. 2012 Apr;35(2):158-62.

## PO139

## MONO-WEEKLY HYPOFRACTIONATED RADIATION THERAPY IN EPITHELIAL SKIN CANCER: THE NEW FRONTIER IN LATE ELDERLY PATIENTS

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Aims: Epithelial skin cancer (ESC) can occur in late elderly population (> 80 years) and requires radiotherapy (RT) treatment, mainly in case of positive margin or inoperable disease. Standard RT obliges to daily attendance, but, these patients could be unable to easily attend hospital, due to their age and health status. Our purpose was to evaluate efficacy, tolerability and symptom control of a mono-weekly hypofractionated RT scheme. The aim was to reduce total treatment time while maintaining clinical response.

Methods: Late elderly patients with epithelial skin cancer who received RT were reviewed. Patients were treated with weekly RT to a total dose of 56 Gy (8Gy/fraction; BED10Gy =86 Gy) using electron beam or photons, based on tumor site, dimensions and depth. Toxicity was re-graded according to the Common Terminology Criteria for Adverse Events, version 5.0. Clinical evaluation was performed before, during, after treatment.

Results: From March 2015 to May 2019, a total of 9 patients were treated. Median age was 89 years (range 81-94). Most patients (n=6) had Performance Status of 2 and all but one had multiple co-morbidities. The vast majority of lesions were histologically proven squamous cell carcinoma and were located in the head region. At presentation, lesions were painful and/or bloody. Details are listed in Table 1. Median follow-up was 6 months (range 4-24). No treatment-related deaths occurred. All patients completed the planned treatment, without interruptions. After RT, partial (n=5) and complete (n=4) response was clinically recorded and lesions were no longer painful and bloody in all cases. Acute toxicity included grade 1 (G1) radiodermatitis (n=1), G1 fatigue (n=1) and G1 mucositis (n=1). No severe acute and late toxicity was recorded.

Conclusion: Mono-weekly hypofractionated RT is a valid treatment option, with low toxicity, high compliance and good treatment response. Further studies are needed to confirm our promising results in the management of late elderly patient with epithelial skin cancer.

**Table 1. Patient and tumor characteristics.**

| Characteristic | Patient (n) |
|---|---|
| **Gender** | |
| Male | 5 |
| Female | 4 |
| **Performance status** | |
| 1 | 2 |
| 2 | 6 |
| 3 | 1 |
| 4 | 0 |
| **Comorbidities** | |
| Cardiovascular disorders | 8 |
| Endocrine disorders | 3 |
| Genitourinary disorders | 3 |
| **Tumor localization** | |
| Head region | 8 |
| Extremities | 1 |
| **Clinical tumor classification** | |
| cT1 | 0 |
| cT2 | 3 |
| cT3 | 5 |
| cT4 | 1 |
| **Tumor histology** | |
| Squamous cell carcinoma | 8 |
| Basal cell carcinoma | 1 |
| **Visual analogue scale (VAS)** | |
| < 5 | 0 |
| 5 | 5 |
| 6 | 4 |
| > 6 | 0 |
| **Clinical lesion status** | |
| Bloody | 5 |
| Non bloody | 4 |

## PO140

## FIVE- YEAR OUTCOMES OF HYPOFRACTIONATED ADJUVANT FORWARD-PLANNED INTENSITY MODULATED RADIOTHERAPY WITHOUT BOOST IN PATIENTS WITH EARLY STAGE BREAST CANCER

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Aims: To report 5-year outcomes in early breast cancer (BCA) patients (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 02/2009-03/2018 1054 pts with pTis-pT2, pN0-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 (28-90) years. 7% of pts had ductal carcinoma in situ (CDIS), 7.6% lobular invasive carcinoma (CLI), 74.1% ductal invasive carcinoma (CDI), 3% mixed invasive carcinoma (CLI+CDI) and 8.3% other histology (mucinous, tubular, papillary, ecc.). Right sided were 46% and left sided tumors 54% (2.2% bilateral). Chemotherapy was prescribed in 28.4% of patients, hormonal therapy in 80.3% of pts. Histologic subtypes of invasive tumors were: 7.0% in situ, 47.5% Luminal A, 28.6% Luminal B Her 2 neu negative, 5.3% Luminal B Her 2 neu positive, 4.1% Erb 2 overexpression, and 7.5% Basal like. Toxicity was evaluated with RTOG scale (acute) and SOMA-LENT score (late).

Results: Median follow up was 67.9 (interquartile range: 45-93) months. A median number of 4 (2-6) segments with wedges were used and bolus was admitted for the first 500 pts to obtain a homogeneous dose distribution and improve skin dose distribution. Acute toxicity and late toxicity divided into edema-hyperpigmentation and fibrosis-telangiectasia-pain are described in Table 1. The observed proportion of local relapses (LR) in CDIS pts was 4.23%, in Luminal A 0.8%, in Luminal B Her 2 negative 2.97%, in Luminal B Her 2 positive 5.36%, in Erb overexpression 11.63% and in Basal like 3.8%. In pts younger than 50 years the LR rate was 3.39%. Five-year Kaplan-Meier estimate of local relapse-free survival was 97.9%, regional (nodal) relapse-free survival was 98.7%, and distant relapse-free survival was 96.6%. The 5-year Kaplan-Meier estimate of overall survival was 97.3% and cancer specific survival 98.9%

Conclusion: The de-intensification of BCA radiotherapy, without boost, with WBHF-IMRT after BCS demonstrated low toxicity and good local control for Luminal A and Luminal B Her 2 negative pts but in young age, Erb overexpression and Basal like histologic subtypes 5-year LR is still high. Our protocol was modified to include a simultaneous integrated boost in these pts.

**Table 1.**

| Toxicity | G0 | G1 | G2 | G3 |
|---|---|---|---|---|
| Acute | 16.8% | 70.2% | 12.1% | 0.9% |
| Early late (edema and hyperpigmentation) | 67.0% | 30.8% | 2.1% | 0.1% |
| Late (teleangiectasia, fibrosis and pain) | 88.0% | 10.2% | 1.2% | 0.5% |

**PO141**

## EVALUATION OF ACUTE AND LATE TOXICITY IN PATIENTS WITH LUNG CANCER TREATED WITH HYPOFRACTIONATED RADIOTHERAPY

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Aims: The objective of the study is to evaluate acute and late pulmonary and esophageal toxicity in patients with locally advanced or metastatic lung disease undergoing hypofractionated radiotherapy (RT) treatment.

Methods and Materials: In our study we analyzed 24 patients who underwent hypofractionated radiotherapy treatment in the period between July 2016 and May 2019. Seventeen patients had a NSCLC histology and seven had a SCLC histology in a locally advanced or metastatic stage. Mean total dose was 45Gy (range 25-60 Gy) with mean BED of 48Gy (range 32.5-62.5) and a mean dose per fraction of 300 cGy (range 250-500cGy). For the evaluation of pulmonary and esophageal toxicity the CTCAE vers 4.03 scale was used. We also evaluated the response to treatment by Response Rate TC or PET-TC.

Results: The median age of the patients was 71 years (range 45-87). All patients had a PS 1-2, multiple cardiovascular and pulmonary comorbidities (some of them in oxygen therapy) and were smokers. Three patients underwent concomitant chemotherapy. Acute pulmonary toxicity was reported in 5 patients. Only one patient presented G3 toxicity after ten days the end of the RT treatment, four of them presented G2 toxicity of which two are being treated at the dose of 15 Gy and 20 Gy and two after about 15 days after the end of therapy. Acute esophageal toxicity was reported in five patients. Four patients presented G2 toxicity and only one patient G1 toxicity. No patient, at the time of evaluation, presented late pulmonary or esophageal toxicity. Only one patient interrupted RT treatment in advance due to worsening of the general clinical conditions. No patient presented local progression and two patients presented systemic disease progression. Four patients died from causes related to the disease, the rest are alive with illness.

Conclusions: In our analysis the hypofractionated RT has documented good local disease control and no significant acute pulmonary and esophageal toxicity was documented in our patients. No late toxicity was recorded. This treatment can be used for patients who have comorbidities and cannot be subjected to standard treatments or with integrated approaches.

## PO142

### INTERNAL ORGANS AT RISK ASSESSMENT WITH 4D CT IN LUNG STEREOTACTIC ABLATIVE RADIOTHERAPY: DO THEY RESPECT DOSE CONSTRAINTS?

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Aim: To calculate retrospectively generated internal organs at risk volumes (IOAR) and to evaluate whether IOARs in SABR plans respect dose contraints.

Methods: In this study, we retrospectively generated respiratory IOARs for our cohort of patients that underwent 4DCT for thoracic radiotherapy at our Department betweeen august 2018 and february 2019. We generated IOARS for heart, trachea, esophagus and spinal cord and we performed dosimetric evaluations taking into consideration these volumes.

Results: We included 38 patients with a median age of 70 years (mean 68, SD± 13,4, range 43-89), 18 patients were females (47%) and 20 males (52%). IOARs were significantly bigger than standard OARs (p-value<0,001 for all the IOARs). The IOARs that did not respect the dose contraints were, respectively, 8/38 (21%) for Heart IOAR, 2/38 (5%) for Esophagus IOAR, 6/38 (15%) for Trachea IOAR and 0/38 (0%) for spinal cord IOAR, taking into account the recently UK SABR dose contraints.

Conclusions: IOARs could be useful to understand the real volume of OARs that is actually irradiated, especially in SABR for central lesions. Our results need to be further validated in prospective trials.

## PO143

### RISK OF RECURRENCE AFTER HIPPOCAMPAL SPARING WHOLE BRAIN RADIOTHERAPY: A MONO-ISTITUTIONAL CASE SERIES

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Aims: Recently, hippocampal avoidance during whole-brain radiotherapy (HA-WBRT) is performed to prevent neural stem cell injury causing neurocognitive dysfunction. Nevertheless, the estimated risk of metastases in hippocampal avoidance area is unknown. The purpose of this study is to determine the risk of hippocampal recurrence in patients undergoing panencephalic radiotherapy with hippocampal sparing.

Methods:We identified patients with advanced solid tumors with brain metastases. All patients received HA-WBRT panencephalic radiotherapy with hippocampal sparing. Treatment was performed with a linear accelerator (Varian Medical System) in a photon regimen, with a 6 MV nominal energy and Rapid Arc technique with multiple planar and nonplanar beams. During the follow up patients underwent periodic brain MRI.

Results: Between July 2017 and May 2019 from our institution, we identified 26 patients receiving HA-WBRT: 14 with brain metastases (6 (23.1%) Non Small Cell Lung Cancer, 16 (61.5%) Small cell Lung Cancer, 3 (11.5%) breast cancer, 1 (3.8%) melanoma) and 12 undergoing Prophylactic Cranial Irradiation (PCI). Prescribed dose was 30 Gy in 10 fractions for HA-WBRT and 25 Gy in 10 fractions for HA-PCI. The median dose to the under dosed peri-hippocampal area was 19.5 Gy (range= 15,7-23,0). Maximum dose median value to the hippocampus was 16.0845 Gy (range=13,328 -23,545). We did not observed metastases in patients undergoing PCI (n=12, 46.1%) with a median fup of 8 months. We observed 4 metastatic patients (15.4%) with intracranial recurrences, two of these (7.7%) presented recurrence in the hippocampal area (see Table 1 for details). Both patients presented intracranial progression with multiple metastases.

Conclusions: Current data are not sufficient to define the safety of treatment in terms of perhippocampal recurrence. In our case series we observed recurrence in the hippocampal areas only in patients with massive intracranial progression. Therefore, in these patients hippocampal relapse accounted for less than 1% of intracranial progression. Larger patients population are needed to investigate the risk of isolated hippocampal relapse in patients undergoing HA-WBRT.

**Table 1.**

| PATIENT | PRIMARY TUMOR | BRAIN RT DOSE (Gy) | RECURRENCE SITE | DOSE IN RECURRENCE AREA (mean, Gy) | INTRACRANIAL PROGRESSION |
|---|---|---|---|---|---|
| 1 | Breast Cancer | 30 | Right hippocampus<br>Left hippocampus | 17,664<br>17,379 | yes |
| 2 | NSLC | 30 | Left hippocampus | 15,175 | yes |

**PO144**

## RADIOTHERAPIC BOOST IN BREAST CANCER: TARGET DELINEATIONS AND RELATE MISTAKES

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Aims: The aim of present study is to asses wether the actual procedure used in our hospital was adequate for a correct treatment of the radiotherapy boost. Methods In the breast unit of San Givanni Calibita Hospital of Rome, we treated 61 sequential patients between January and July 2018 with defined breast cancer; these patients performed quadrantectomy and adiuvant radiotherapy. Tumor bed was identified by means a CT post-operative scan, radiological, surgical and anatomo-pathological description and surgical clips positions. The different surgical approaches were: 59 (97%) simple lumpectomy (without move surgical bed), 2 (3%) oncoplastic surgery (with great move of surgical bed). The clips were placed in the pectoralis major fascia in 52 (85%) patients, in 7 (12%) cases the surgical repere were placed in surgical bed and in 2 (3%) patients no clips were implanted. The tumor bed was contoured considering tissue inhomogeneities (s.e. sieroma) and inner clips. If the sieroma was not visible, the CTV was delineated using the area around the clips. Electron treatment was performed in 50 patients (82%), in 6 cases (10%) the photon treatment was chosen, in 5 patients (8%) the tumor bed area couldn't be identified so no boost treatment was delivered. Results In 19 (31% of total) we couldn't find the tissue inhomogeneities. For 28 (46%) patients we weren't able to match the target position; in 40 cases (66%) the tissue inhomogeneities were detected. In 17 (42%) cases the clips positions were well fitted all around the sieroma. Conclusions According to the collected data, a not properly implantation of the surgical clips can greatly effects the tumor bed delineation and consequently increase the probability of a target missing. In this scenario we could expect a therapeutic reduction of boost treatments. Taking into account the 19 cases, where no evidence of the sieroma position was found (such those patients whose treatment is delivered late after the surgical intervention), the real target position and the dosimetric consequences remains difficult to explore. A last consideration concern the possible limitations that occurs, when the clips are not properly positioned, in using the simultaneous intensity modulated boost approach. Summarizing, to avoid those kind of mistakes and to reduce the related risks, a synergic cooperation between the surgeon and the radiotherapist is needed so as to achieve an ideal and useful clips implantation.

**PO145**

## CONSTRICTORS SPARING OR NOT IN POSTOPERATIVE RADIOTHERAPY IN SUPRAGLOTTIC CARCINOMA PATIENTS UNDERGOING CONSERVATIVE SURGERY: DOSIMETRIC EVALUATION

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Aims: The purpose of this study was to investigate dosimetric differences between conventional Non-Constrictors Sparing VMAT (NCS-VMAT) and Constrictors Sparing VMAT (CS-VMAT) plans in supraglottic carcinoma patients, undergoing Open Partial Laryngectomy (OPL).

Methods: We performed a retrospective analysis of squamous cell carcinoma patients treated at our Radiation Oncology Unit between January 2018 and January 2019 with postoperative RT following Supracricoid Laryngectomy (SCL) with Cricoioidopexy (CHP) or Cricoioidoepiglottopexy (CHEP). All patients were treated with a non-optimized NCS-VMAT plan for constrictor muscles. A moderately accelerated VMAT-SIB to 54-60 Gy in 30 fractions was our strategy. The neo-larynx and the high-risk node area was included in the high dose CTV60. The low dose CTV54 included bilateral low risk neck nodes. A 2-3 mm planning target volume was uniformly added to each CTV as per our institution's standard when daily IGRT was applied. Organs at risk (OARs) included the spinal cord, thyroid gland, parotid glands and mandible. A VMAT plan was generated using 2 partial arcs with full 360° gantry angles using 6-MV photons prescribed to the PTV mean . We retrospectively performed an atlas-based contouring of the upper, middle and lower constrictors on MIM Software INC and then we created a CS-VMAT plans with optimization for the constrictor muscles, to reduce the constrictors Mean Dose as low as possible.

Results: 10 consecutive patients (8M e 2F) with a pT3-4 pN1-3b M0 squamous supraglottic carcinoma were enrolled in our study. Dose to PTV and to the other Organs at Risk was maintained close as possible to original plans. In CS-VMAT plans, the mean constrictors dose was decreased by an average of 2.1 Gy. After the replanning, all patients showed a higher reduction of uPCM mean dose (3.8 Gy) but an obvious

smaller mPCM and iPCM mean dose reduction (1 Gy and 0.3 Gy respectively), considering the overlapping between PTV and mPCM/iPCM. In both set of plans, the mean Monitor Units (MUs) values were similar: 913±140 and 925±156 for NCS-VMAT and CS-VMAT respectively.

Conclusions: Our study suggests that the constrictor muscles sparing approach in post-operative radiotherapy following open partial laryngectomy is feasible and resulting in a decrease in dose to constrictor muscles whitout any loss in conformity or increase in treatment time.

## PO146

### PREOPERATIVE INTENSITY-MODULATED SIB RADIOTHERAPY CONCOMITANT WITH CAPECITABINE IN LOCALLY ADVANCED RECTAL CANCER: OUR INITIAL EXPERIENCE

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Aim: Preoperative radiotherapy (RT) in combination with fluoropyrimidine-based chemotherapy (CT) is the standard of care in patients with locally advanced rectal cancer (LARC). The treatment intensification is content of the research, given the correlation between RT dose-tumor response and the prognostic role of the tumor regression grade (TRG) highlighted in several studies. The aim of the study was to analyze the correlation between RT dose-intensification and feasibility of treatment and acute toxicity (AT).

Methods: We retrospectively analyzed patients with LARC treated with intensity-modulated radiotherapy (IMRT) and simultaneous integrated boost (SIB) and concurrent Capecitabine, between September 2018 and April 2019. Acute toxicity was evaluated according to the RTOG scale. The feasibility was evaluated with compliance of patients to RT and CT.

Results: A total of 25 patients (median age 77yrs, range 54- 86) were identified for this analysis. A dose of 45 Gy was prescribed to the entire mesorectum and pelvic lymph nodes with a median SIB dose of 56 Gy (range 50–56Gy) to the tumor and corresponding mesorectum. All patients completed planned RT and 24 completed CT. Acute Gastrointestinal (GI) and hematological (HT) toxicities were analyzed. 23 patients developed AT GI Grade 2, 2 patients developed AT GI Grade 1. In terms of HT toxicity, we reported AT G1 in all patients except one patient with HT grade 2.

Conclusions: Despite we present a retrospective study, our results are according to the literature confirming the feasibility of this approach. We reported good tolerance to IMRT-SIB technique for the improvement of small bowel sparing. Furthermore, IMRT dose intensification did not modify the compliance to adjuvant chemotherapy. Long-term toxicity and the impact on disease control and on survival will be evaluated with a longer follow-up time.

## PO147

### EFFICACY AND TOXICITY OF STEROTACTIC BODY RADIOTHERAPY (SBRT) FOR CENTRALLY LOCATED PULMONARY LESIONS: A RETROSPECTIVE ANALYSIS OF A MONOCENTRIC EXPERIENCE

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Aims: Recently SBRT has become the standard of care for inoperable peripheral or central Non Small Cell Lung Cancer (NSCLC). However, it is well recognized that patients (pts) with centrally located pulmonary lesions remains a challenge because of the increased risk of treatment-related adverse events. Aim of this study is to evaluate safety, tolerability and efficacy of SBRT for centrally pulmonary lesions.

Methods: Between August 2014 and September 2018 14 pts were submitted to SBRT for centrally located pulmonary lesions. Median age was 72 years (range 54-87 years). Twelve pts were male, 2 Female. Eigthy-nine percent of patients were former smoker, while 11% were still active at time of treatment. Thirteen pts have a Performance status equal to 0 or 1 (ECOG scale) and only 1 pt had PS two. All patients were submitted to complete staging (chest abdominal CT and/or 18 FDG PET CT) including pulmonary function tests before SBRT. Patients were then stratified According to Global Initiative of Chronic Obstructive Lung Disease: stage 0 (29%), 1 (14%), 2 (43%), 3 (14%). Eleven pts (79%) had primary (6 pts) or loco-regional relapsed (5 pts) NSCLC of which 9 patients had adenocarcinoma while 2 squamous carcinoma. Three patients were treated for lung metastases. A total dose of 60 Gy in 8 daily fractions was delivered to all patients with Image-guided Intensity modulated Radiotherapy using Tomotherapy®.

Results: At a median follow up of 17.5 months (7-21 months) 13 patients are still alive, while 1 died to other causes. Overall response rate was 100%. One pt had a complete response, 10 patients a partial response and 3 stable disease. During regular follow up 4 patients developed local progression, while 6 developed metastases (4 had both). All pts completed radiotherapy

treatment course with good tolerance and no interruptions. No acute pulmonary, cardiac or esophageal toxicity ≥ G3 were reported according to CTCAE scale v4.0. Concerning late toxicities we found only 1 case of G3 pulmonitis; no late cardiac or esophageal toxicity G2 or greater were found.

Conclusions: In selected pts affected by centrally located pulmonary lesions SBRT seems to be feasible, well tolerated and effective representing an efficient treatment. Higher RT doses seem to achieve better results than conventional RT. More clinical data are awaited from on going international clinical trials.

## PO148

### VOLUME DE-ESCALATION IN RADIATION THERAPY: STATE OF THE ART AND NEW PERSPECTIVES

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New RT techniques and data emerging from follow-up for several tumor sites suggest that treatment volume de-escalation may permit to minimize therapy-related side effects and/or obtain better clinical outcomes with a high incidence. We reviewed the main evidence around volume de-escalation in RT: for Lymphoma large-volume techniques (extended- and involved-field RT) are being successfully replaced by involved-site RT and involved-node RT; in head and neck carcinoma spare a parts of elective neck is controversial; in early breast cancer, partial breast irradiation has been established as a treatment option in low-risk patients; for pancreatic cancer stereotactic body radiotherapy may be used to dose escalation; for rectal cancer a recent consensus provides a recommendation for irradiation of elective regional lymph node level. Anyway, further clinical trials are necessary to improve the identification of suitable patient cohorts and the precise amount of possible volume de-escalation that does not compromise tumor control.

## PO149

### HELICAL TOMOTHERAPY• ULTRA-HYPOFRACTIONATION STEREOTACTIC BODY RADIOTHERAPY (USBRT) TREATMENT FOR LOCALIZED PROSTATE ADENOCARCINOMA: A MONOISTITUTIONAL EXPERIENCE

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Aims: To assess the feasibility and safety, in terms of acute toxicitiy of a short uSBRT image-guided intensity modulated radiation therapy (IG-IMRT) in prostate adenocarcinoma (PCa).

Patients and methods: Sixty patients (pts) with clinically localized PCa were treated with uSBRT in retrospectively selected way. Inclusion criteria for this analysis were: histologically confirmed PCa, low-(LR), intermediate risk(IR) according to 2019 NCCN risk categories, selected high risk (HR)pts. Pts with at least one of the following features were excluded: cN1 or cM1 stage, severe urinary obstructive symptoms; previous pelvic RT; severe systemic disorders, chronic urinary or intestinal inflammatory conditions. All pts received Tomohelical® uSBRT for a prescription dose of 36,25 Gy in 5 fx on alternate days. Toxicities were recorded by RTOG scale at the end of RT, at 6 and 12 months after.

Results: From 2015 to 2018, 60 pts met the inclusion criteria. Median follow up (F-U) was 16 months (range 0-42). Median age was 76 (59-87). 14 pts were at LR, 23 were favorable IR, 16 were unfavorable IR and 4 HR. 28 pts received androgen deprivation therapy with a median duration of 5 months (range 1-27). All pts completed the treatment, the median overall treatment time was 9 days (7-19). Acute toxicity was as follow: GI, G0 48/60 (80%) pts, G1 11/60 (18%), G2 1/60 (2%); GU, G0 26/60 (43%), G1 24/60 (40%), G2 10/60 (17%). No pts had G3-G4 acute toxicities. At 6 months, 48 pts were available. Toxicity was as follow: GI, G0 47/48 (98%) pts, G1 1/48 (2%), G2 0/48 (0%); GU, G0 42/48 (87,5%), G1 6/48 (12,5%). No toxicities ≥ G2 were reported. At 12 months,37 pts were available. Toxicity was as follow: GI, G0 35/37 (95%) pts, G1 2/37 (5%), G2 0/37 (0%); GU, G0 33/37 (89%), G1 4/37 (11%). No toxicities ≥ G2 were reported. At the last F-U, all pts but one were biochemical and clinical free from disease, one patient experienced bone metastasis. One patient died without evidence of disease.

Conclusions: Helical Tomotherapy® uSBRT is safe and offers excellent tumor control. Taking account the geographical characteristics of our Region, uSBRT allows to deliver the whole RT over 10 days with a sensible impact in waiting list and pts quality of life by reducing the number of Hospital visits.

## PO150

### MULTIDISCIPLINAR MANAGEMENT OF ELDERLY PATIENT WITH CANCER: THE RADIATION ONCOLOGIST'S POINT OF VIEW

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In the future decades the percentage of older people will increase worldwide, causing a shift in global epidemiology with a significant rise in cancer incidence. On the other hand, older subjects are seldom represented in clinical trials of novel oncological treatments, which often leads to inappropriate therapeutic strategies for cancer care in this important subset of patients. Additionally, cancer therapies are often chosen considering chronological age only, which can lead to over- or under-treatments. With the purpose of optimizing the oncological therapy in every single aged subject, it's strongly advisable to consider a global assessment of the patient, taking into account the performance status, comorbidities, functional and cognitive status and also economic and social-familiar support. An increasing amount of data in literature is showing that such a strategy confers excellent results in outcome as well as quality of life of aged patients with cancer.

## PO151

### STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN INOPERABLE PANCREATIC CANCER: A RETROSPECTIVE ANALISYS

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Aims: Evaluating safety and efficacy of SBRT in not metastatic inoperable pancreatic cancer

Methods: Patients (pts) with pancreatic adenocarcinoma without metastases that were considered inoperable in a multidisciplinary tumor board were treated with SBRT. Pts received 3 fractions of 8, 10 or 12 Gy (total dose 24-36 Gy) or 25 Gy in 5 fractions of SBRT based on tumor location in relation to stomach and duodenum. Toxicity was scored according to CTCAE v4.0. Progression free survival (PFS), freedom from loco-regional progression (FFLRP), freedom from distant metastasis (FFDM) and overall survival (OS) were calculated using the Kaplan-Meier method.

Results: Between April 2014 and March 2019 23 pts were treated with SBRT. Total SBRT dose was: 36 Gy in 2 pts, 30 Gy in 6 pts, 24 Gy in 14 pts and 25 Gy in 1 pt. Nineteen pts received an induction chemotherapy gemcitabine-based (alone or with oxaliplatin). Median age was 73 (range54-86 years). Twenty-two pts had a Performance status (PS) equal to 0 or 1 according to ECOG scale and only 1 pt had PS two. At a median follow up of 18 months (range, 6-52 months) 9 pts are still alive, while 14 died. Median FFLRP, FFDM, PFS and OS rate were 25.6, 16.1, 16.7, 23.3 months respectively. Estimated 1-year FFLRP, FFDM, PFS and OS rate were 81%, 66%, 63%, 86% respectively. No pts developed G3 or greater acute or late toxicity, 2 pts developed G2 gastric or duodenal ulcer and 1 pt a G2 gastric haemorrhage that were medically managed.

Conclusions: SBRT in inoperable patients with pancreatic cancer reported good tolerance with low rate of acute or late toxicity. Moreover seem to have good rate of loco-regional control disease and to improve survival outcomes.

## PO152

### STEREOTACTIC RADIOTHERAPY (SBRT) FOR UNRESECTABLE LOCALLY ADVANCED NON SMALL CELL LUNG CANCER (LA-NSCLC)

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Aims: Conventional fractionated radiotherapy (cRT) concurrent with chemotherapy (ChT) is the standard of care in unresectable LA-NSCLC.The majority of patients (pts) cannot tolerate this treatment due to its toxicity, so sequential ChT followed by cRT is the more frequent choice in clinical practice. Recently, SBRT has been used instead ofcRT in NSCLC offering superior control with less toxicity. We present our experience with SBRT in LA-NSCLC.

Methods: Between June 2015 and December 2018, 28 LA-NSCLC pts who underwent SBRT were analyzed . 25/28 (76%) pts received neoadjuvant ChT before SBRT. All pts had CT-PET before SBRT. In pts submitted to neoadjuvant ChT the target volume was the residual disease defined on the basis of CT-PET images. The technique was intensity modulated arc therapy(IMAT) and volumetric modulated arc therapy (VMAT) in 11(39%) and 17 (61%) pts, respectively. A specific treatment planning (IMRT-SIB) for primary tumor (T) and lymph-node/s (N) was done for 18 (64%) pts, while in remaining 10 (36%)the planning target volume (PTV) included both T and N. All pts repeated CT-PET 3 months after treatment and thereafter every 4-6 months. The toxicity was evaluated using CTCAE scale.

Results: Median age was 63 years (54-81). 9(32%), 14(50%) and 5(18%) pts had clinical N1, N2 and N3 stage at diagnosis, respectively. 21 (75%) and 7 (25%) had central and peripheral tumor. Median PTV for T and N separately treated were 17.2 cc (8.7-67.96) and 15.02cc (9.9-72.3), while for T and N treated in the same target was 91.86 cc (53.2-165.9). Median prescribed dose was 40 Gy (35-55) and 35 Gy (35-45) in 5 fractions to T and N, respectively.After a median follow-up of 9 months (4-39) 4 of 28 (14%) pts had local recurrence (LR), 6 (21%) regional node (RN) recurrence and 8 (28%) distant progression (DP). Median LR

free survival (FS), RN-FS and DP-FS were 9 months (4-48), 9 months (4-48) and 9 months (4-48), respectively. Median overall and cancer specific survival were 9 months (4-48). Of note 2 patients who had hemoptysis before SBRT resolved the symptom after treatment. No patients developed > grade 2 toxicity.

Conclusions: SBRT was a feasible,safe and effective treatment in selected unresectable LA-NSCLC pts. Although clinical outcomes were very promising both in terms of results and toxicity,larger and more mature studies are needed to adopt this treatment in clinical practice.

**PO153**

## RADIOTHERAPY FOR SUBCUTANEOUS METASTASES FROM PANCREATIC NEUROENDOCRINE TUMOR: A CASE REPORT

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Aims: Skin metastases from neuroendocrine tumors are rare and the optimal palliative approach is uncertain. Systemic therapies and supportive cares are administered in the majority of cases. In this report we describe our experience in the multidisciplinary management of a case of pancreatic neuroendocrine tumor with multiple subcutaneous metastases, highlighting the advantages achieved with palliative radiotherapy delivered to symptomatic skin metastases.

Methods: A 61-year-old woman affected by a pancreatic small cell neuroendocrine carcinoma with multiple hepatic and subcutaneous metastases was referred to our Radiation Oncology Unit after a multidisciplinary evaluation. Indeed, the patient had obtained an initial partial response of her visceral lesions with chemotherapy (Cisplatin- and Etoposide-based), but a progression of subcutaneous metastases was detected. Two different RT treatments were planned and delivered for a skin mass at the right fronto-temporal region of the scalp and for two lesions at the right scapular region and at the back of the left thoracic wall, respectively. All lesions were large (at least 10 centimeters in diameter) and easily bleeding.A total dose of 30 Gy in 10 fractions was prescribed for the scalp lesion, while a total dose of 20 Gy in 5 fraction was delivered to each back lesions, simultaneously. Both the radiation treatments were planned with 6-MV non-coplanar photon beams tangent to the skin, ensuring a useful dose-sparing of normal tissues. Second-line chemotherapy schemes were administered but soon discontinued due to hematological toxicity (especially thrombocytopenia).

Results: The treated lesions stopped bleeding and showed a progressive shrinkage. The skin became progressively crusted and remained stationary until patient's death. The patient did not show treatment-related side effects and experienced a sensitive improvement of her quality of life. During chemotherapy administration, an overall diffuse reduction of skin lesions was also observed. Unfortunately, the patient died about two months after completion of RT due to cachexia.

Conclusions: Palliative radiotherapy delivered to symptomatic skin metastases from neuroendocrine tumors could allow a satisfactory local response, as well as an improvement of patient's quality of life. For these reasons, this approach could be considered for selected patients and should be re-evaluated in the multidisciplinary management of these rare tumors with poor prognosis.

**PO154**

## THE EFFICACY OF STEREOTACTIC BODY RADIATION THERAPY IN OLIGO-METASTATIC PROSTATE CANCER PATIENTS: PRELIMINARY EXPERIENCE IN ABANO TERME CENTRE

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Aims: To evaluate the efficacy of stereotactic body radiation therapy (SBRT) in oligo-recurrent (OR) and oligo-progressive (OP) metastatic prostate cancer patients.

Methods: We conducted a retrospective analysis of two settings of oligo-metastatic (one to four metastasis) prostate cancer patients: OR, defined as the presence of bone and/or lymphatic lesions, detected with choline or Ga^68-PSMA (Prostate Specific Membrane Antigen) positron emission tomography following biochemical recurrence; OP, defined as the presence of the same type of metastasis detected in the same way after a prostatic-specific antigen (PSA) rise during androgen deprivation therapy. All patients underwent to ablative radiation therapy delivered with volumetric technique; the median BED(2) (Biological Effective Dose using an $\alpha/\beta$ of 2 Gy) was >120 Gy. Primary endpoints were local control (LC) and progression-free survival (PFS) in both groups; ADT-free survival in OR group; second-line systemic treatment-free survival (STFS) in OP group.

Results: From May 2016 to May 2019 we treated 15 OR and 5 OP metastatic prostate-cancer patients, for a total number of 24 metastases (9 bone and 15 lymphatic lesions). The median PSA level before SBRT in OR group was higher than in OP group (3.29 ng/ml Vs 2.27 ng/ml), 80% of the patients in OR group was without ADT. In both groups the median PSA doubling time was definitely inferior to 6 months. Three patients (1 in OR and 2 in OP) after a progression of PSA underwent a second course of SBRT in out-field region. One patient in OR group showed an in-field relapse, not suitable to re-irradiation. Median follow-up was 6 and 13 months in OR e OP group respectively. The rates of LC were 92.3% and 100% in the OR and OP group respectively. We observed a PFS at 6- and 12 months of 76.9% and 51.3% respectively in OR series, 80% and 53.3%

respectively in OP group. ADT-FS at 6- and 12 months was 83.9% and 55.9% respectively. STFS at 6- and 12 months was 80% in OP group.

Conclusions: in our limited and recently experience, SBRT seems to be effective in terms of LC and in terms to defer the use of ADT or new generation hormonal therapy.

## PO155

### MANAGEMENT OF BRAIN METASTASES (BM) FROM OVARIAN CARCINOMA (OC) WITH STEREOTACTIC RADIOTHERAPY (SRT)

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Aims. BM from OC are uncommon and consensus regarding optimal management is lacking. SRT allows to delivery focused ablative radiation doses in one (SRS) to five fractions (FSRT). We evaluated outcomes after SRT in OC patients (pts) with BM.

Methods. Between August 2006 and November 2018, 11 pts OC underwent SRT on 24 BM. At the time of OC diagnosis all patients were submitted to surgery and at least one line of chemotherapy (range, 1-4). Median age and KPS were 63yrs (range, 43-79) and 90 (range, 70-100), respectively. Primitive histology was sieropapillar and endometrioid carcinoma in 9 and 2 pts, respectively. Median time between first diagnosis and BM progression was 49m (range, 12-126), 3 (27%) pts had only BM and 8 (73%) pts with other metastatic sites. At time of SRT, 8 pts were naïve for BM, whereas 3 had already received whole brain RT (10x3Gy), and were re-irradiated with SRS for brain relapse. After SRT, brain control was achieved if there was a lack of in-field progression. The duration of response was assessed separately for each lesion and was measured from the date of SRT until MRI documentation of failure at the treated site.

Results. Median number of treated lesions was 1 (range, 1-3). Maximum diameter of BM resulted ≤20 and 21–30mm, in 20 (84%) and 2 (8%) lesions treated with SRS, the remaining 2 (8%) BM which had a diameter >30mm were submitted to FSRT. Median SRS dose was 18Gy (range, 15-21Gy), FSRT was administered in 5 fractions of 5Gy and 7Gy single doses, respectively. After a median follow-up of 23 months, 10 pts had died, and 1 is alive without disease. All BM responded to SRT: 6 (25%) had a partial remission and the remaining 18 (75%) a stabilization. Median duration of response and brain control was 23m (range, 5-35) and 8m (range, 5-35), respectively. Overall survival ranged from 5 to 36m (median 19), 6 (60%) and 4 (40%) pts died for systemic or brain progression of disease, respectively. No acute brain toxicity was registered, whereas 1 patient developed a symptomatic radionecrosis on 1 BM 6m after SRS (21Gy). This diagnosis was confirmed after surgical excision.

Conclusions. SRT is safe and effective for the treatment of BM from OC. In selected cases already submitted to whole brain radiotherapy, also reirradiation with SRT can be done.

## PO156

### RESPONSE AND IMPACTION ON QUALITY OF LIFE TO PALLIATIVE RADIOTHERAPY TREATMENT IN NON-COMPLICATED SYMPTOMATIC BONE METASTASES

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Aims: Bone is one of the most common target organs for cancer metastasis (mts). This patients (pts), with advanced disease, have pain, difficult to control , with functional limitation that severely impairs health-related quality of life. The aims of this study are estimate the quality of life (QoL) and pain resolution after palliative radiotherapy treatment in this patients.

Methods: From January 2016 to April 2019 were treated 156 pts (65 women and 91 men), average age 68 years (range 22 \ 94 years) with-symptomatic bone mts. In 42 pts the primitive lesions was mammary, in 52 was genitourinary tract (kidney, bladder, prostate, penis, cervix, endometrium), in 12 was gastrointestinal tract (stomach, colon, rectum, anus, liver), in 3 was head-neck district, 1 case was Sarcoma, 1 case was melanoma, in 4 pts was multiple myeloma and in 2 pts the primitive tumour was unknown. The treated seats were: vertebrae in 123 pts, femur in 9 pts, sternum in 6 pts, ribs in 12 pts, pelvis bones in 42 pts, cranial reliquary in 5 pts, tibia in 2 pts, homer in 2 pts, shoulder in 6 pts, 38% of our pts performed treatments in multiple locations. The fractionation schemes used were: 3-30 Gy, 4-20 Gy, 6-30 Gy, 5-25 Gy, 2-40 Gy, 8 Gy using the 3DCRT technique, IMRT-Vmat and SBRT. The indications to the technique and the type of fractionation were given according to age, Performance Status (PS), VAS (visual analog pain scale) and disease site. The evaluation of the treatment response was carried out by analyzing the pre and post treatment VAS and considering the possible association with Pain Therapy (PT)

Results: From the datas' evaluation of the pre and post radiotherapy (RT) VAS to one month, we have recorded an improvement of the algic symptomatology in 89,6% of PTS; in 6.9% of the cases the VAS remained unchanged and only in 3.5% of the pts we experienced an increase in pain; of the latter, 3 had to interrupt the treatment and one died before the end of the RT for disease progression. 42% assumed PT.

Conclusions: The RT, assessed according to the treatment site and the therapeutic objectives, results in a decrease of the VAS scale values with better QoL. A multimodal approach is necessary to guarantee a better

PS, good pain control and to help the pts cope with RT treatment before it has manifested its efficacy.

## PO157

### FOCAL RADIOTHERAPY FOR OLIGOPROGRESSIVE MALIGNANT PLEURAL MESOTHELIOMA. A SINGLE-INSTITUTION EXPERIENCE

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Purpose: No standard treatment option is available for patients with malignant pleural mesothelioma (MPM) progressing after upfront treatment. This retrospective mono-institutional study explored the role of focal radiotherapy (FRT) as a treatment modality for oligoprogressive MPM.

Materials and Methods: Patients were all pretreated with 1 or 2 lines of chemotherapy (CHT). Oligoprogressive MPM was defined as an unresectable disease with radiological progression at a maximum of 3 sites according to a chest-abdominal computed tomography. Patients were treated with either stereotactic body radiation therapy (SBRT, > 4 Gy per fraction) or hypofractionated radiotherapy (hypoRT, 30 Gy/10 fractions or BED equivalent). Local control (LC) and time to further systemic treatment (TFST) after FRT were the primary endpoints of the study. Progression free survival (PFS), overall survival (OS) and toxicity were also evaluated. Radiologic progression was assessed according to modified RECIST criteria for MPM.

Results: From 01/2012 to 11/2018, 21 pleural lesions were treated in 17 patients (10 males, 7 females). Median age was 69 yrs (range 54-78). 15/17 patients (88%) had an epithelioid histology. 13/17 (76.5%) underwent FRT at progression after first-line CHT with platinum/pemetrexed; 4/17 (23.5%) received FRT progressing after second-line CHT. Of note, 3/17 patients were re-treated with a second course of FRT for further oligoprogression. 10/21 lesions were treated with SBRT (range 5-7 Gy per fraction); median BED (calculated with an alfa/beta=3) was 80 (range 60-144). 11/21 lesions received hypoRT. 6-mo and 1yr-LC was 87.5% and 65.6%, respectively. 6-mo-TFST was 65.2% with a median value of 6.7 months. 6- mo-PFS was 23.1% with a median PFS of 2.9 months. 6-mo and 1yr-OS after FRT were 69.2% and 51.9%, respectively. No G3 acute or late toxicities were reported.

Conclusion: According to our study, FRT in this selected group of patients with oligoprogressive MPM was feasible and effective, allowing a disease control comparable to currently available second- or third-line systemic therapies.

## PO158

### 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 2019 they were treated 42 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.

## PO159

### VMAT FRACTIONATED HALF-BODY PALLIATIVE IRRADIATION (HBI) IN WIDESPREAD SYMPTOMATIC PELVIC BONE DISEASE : A PRELIMINARY EXPERIENCE

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Aims: Fractionated half-body irradiation (HBI) for widespread (WS), symptomatic, metastatic bone can-

cers has been found a faster and convenient way for palliation using 15 Gy/5Fr/5 days . The most common irradiated site in our experience is a volume including the pelvic bones with or without the lumbar tract and or femour heads with conventional 2D-3D isocentric modality . But the dose to the bowel impacts on acute toxicity due to the whole abdomen included in the fields.. VMAT modality could be an effective, fast and safe modality in palliative radiotherapy on a whole pelvis as we found in our case.

Materials and Methods: A 48 yrs old woman with widespread bone metastatic breast cancer came to our attention for symptomatic widespread lesions on pelvic bones and lumbar spine, refractory to medical therapy. Palliative radiotherapy with dose of 3 Gy for 5 consecutive days was prescribed on a whole volume including the whole pelvis with the lumbar spine from the top of L1 to the femoural left head. Three delivery modalities were adopted and compared : a 2D technique with two opposed isocentric AP-PA (2d –ap-pa) MLC customized fields and 10 MV photon beams ; a 3D isocentric MLC customized 4fields box technique 6-10 MV photon beams (3D 4 F box) and a dual arch 6 MV photon VMAT( d-VAMAT). PTV coverage and dose to the bowel as peritoneal cavity were analysed and compared.

Results: The dose to the rectum , bladder and peritoneal cavity were reducted in the VMAT modality. The V95 improved in d-VMAT (V95 = 99.9% d-VMAT vs 96.7% 3D-4F box vs 95% 2D-AP-PA); the peritoneal cavity V15 (EQD2) was 1.960 cc for d-VMAT, 2350 for 2D-AP-PA e 2500 cc for 3D-4 F box . In VMAT the dose distribution was strictly conformed to the anatomy of the target. This modality was chosen to treat this patient. Improvements in PS, pain, and narcotic scores and no acute toxicity were recorded . At six months after treatment the patient still remains asymptomatic.

Conclusions: In terms of response and toxicity VMAT based whole pelvis radiation could be considered as a faster and much more easy HBI schedule for the palliation of pain in widespread bone metastatic cancer.

**PO160**

## FRACTIONATED STEREOTACTIC RADIATION THERAPY (FSRT) FOR RESECTED BRAIN METASTASES: A PRELIMINARY REPORT

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Aims: Cavity stereotactic radiosurgery (SRS) or fractionated stereotactic radiation therapy (FSRT) are emerging treatment options after surgical resection of brain metastases (BM). Recent randomized trials, aimed to clarifying the adverse effects of postoperative whole-brain radiation therapy (WBRT) for BM have confirmed the association of neuro-cognitive and quality of life decline with WBRT. The recent phase 3 NCCTG study comparing SRS and WBRT for resected BM showed comparable overall survival and superior preservation of cognitive function after SRS, supporting the rationale for limiting WBRT to only patients where it is clinically essential. We present a preliminary report of our experience on surgical cavity FSRT.

Methods: Between May 2011 and May 2018, 30 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 (12 pts), breast cancer (6 pts), gastrointestinal cancer (7 pts), others (5 pts). All patients were evaluated by Karnofsky performance status (KPS) and neurologic functional score (NFS). Localization was obtained using fusion imaging from computed tomography (CT) and magnetic resonance imaging (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 was GTV/CTV plus an additional 2-3 mm in all directions (average PTV 28.6 cc). Pts were treated with a 6-MV linear accelerator fitted with a dynamic micro-multileaf collimator. Fifteen pts received 5x6 Gy and fifteen 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 surgical 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 13 months (range 2-89), 24 of 30 pts were evaluable because two were lost to follow up and four have a short follow up. 11 pts (45,8%) had LC and BC, 12 (50%) reached LC without BC, one (4,1%) had in- and out-field relapse. So, in 23 (95,8%) pts, postoperative FSRT reached a LC of whom one-half had BC. All pts in progression were re-irradiated, eight with SRS, two with WBRT and two with WBRT followed by SRS for a second progression. Altogether, after cavity stereotactic radiotherapy, 21 new lesions registered outside irradiated cavity were treated with SRS. No acute neither late toxicity was registered, no treatment-related NFS decline was observed.

Conclusion: Our preliminary report showed that surgical cavity FSRT for resected BM achieves an excellent LC and a satisfactory BC with a good neurocognitive outcome. WBRT and/or SRS can be reserved to pts with further brain progression of disease.

**PO161**

## STEREOTACTIC RADIOTHERAPY IN ISOLATED BONE METASTASES FROM PROSTATE CANCER: A TWO CLINICAL TRIALS INTERIM ANALYSIS

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Aim. To determine the efficacy and safety of stereobody radiosurgery (SRS) in the treatment of isolated bone metastases (mts) in prostate cancer (PC) patients (pts).

Methods. Data from PC patients with <3 bone mts undergone single fraction stereotactic radiosurgery (SRS-DESTROY-2 phase I clinical trial) as exclusive treatment, or boost (SRS-vertebra phase I clinical trial) after conformal external beam radiotherapy (3D-CRT), were collected and analyzed. From October 2010 to December 2018, as per trials design, PC pts received SRS according to skeletal site (vertebral versus other bone lesions). In particular, vertebral mts received a 3D-CRT dose of 25 Gy in 10 fractions followed by a SRS dose of 8 Gy, 10 Gy, or 12 Gy, in subsequent escalated cohorts; other bone lesions were treated by subsequent escalated SRS doses ranging from 12 Gy to 24 Gy. Best radiologic response to SRS was evaluated by computed tomography (CT) scan, Magnetic Resonance (MR) or positron tomography (PET) scan, and classified according to the RECIST or PERCIST criteria. Objective response rate included complete response (CR) and partial response. Actuarial local control (LC) was defined as the time interval between the date of SRS and the date of inside SRS field relapse/progression of disease or the last follow-up visit. Toxicity was evaluated by CTC-AE scale.

Results. Forty-six pts carrying a total of 68 bone mts were selected for the enrolment. The median age was 73 years (range: 56-86), and the majority of patients (96%) presented Eastern Cooperative Oncology Group performance status 0-1. The most frequent anatomical districts were the pelvis (40%) followed by vertebral mts (35%), and a miscellanea of other sites, mainly ribs, sternum and scapula (17,25%) Overall, dose prescription to the Planning Target Volume ranged from 12 to 37 Gy (median dose: 24 Gy) and all lesions were treated with a volumetric arc radiotherapy technique. With a median follow-up of 18 months (1-66) no severe (> grade 3) acute or late toxicities were recorded, with only 3 pts reporting G2 toxicity (2 esophagitis and 1 ematological). The overall objective response rate was 75.0% (CI 95%: 60.1-84.8) with a CR rate of 62%. The 2-years actuarial LC was 94%.

Conclusions. This study confirms the activity and safety of SRS in the treatment of bone metastases in oligometastatic PC pts. Optimal SRS schedules should be defined taking into account the need to guarantee the best personalized radiation dose.

**PO162**

## STEREOBODY RADIOTHERAPY IN PROSTATE CANCER ISOLATED NODAL RECURRENCES: AN INTERIM ANALYSIS FROM TWO PHASE I CLINICAL TRIALS

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Aim: To determine the efficacy and safety of stereobody radiotherapy (SBRT) in the treatment of isolated lymph nodal recurrences in prostate cancer (PC) patients (pts).

Methods: Data from PC pts with nodal recurrences undergone 5 fractions (SBRT-DESTROY-1 phase I clinical trial) or single fraction radiosurgery (SRS-DESTROY-2 phase I clinical trial) as exclusive treatment, retreatment or boost after external beam radiotherapy, were collected and analyzed. From November 2003 to January 2018 ptts were enrolled in different arms based on tumor site and previous treatment as per SBRT and SRS trials design. Doses ranged from 20 Gy to 50 Gy (maximum planned dose) at 4-10 Gy per fraction in DESTROY-1, while patients enrolled in DESTROY-2 trial received a single fraction dose ranging from 12 Gy to 24 Gy. Best radiologic response to treatment was evaluated by computed tomography (CT) scan, Magnetic Resonance (MR) or positron tomo-

graphy (PET) scan, and classified according to the RECIST (version 1.1) or PERCIST criteria. Objective response rate included complete response and partial response. Actuarial local control (LC) was defined as the time interval between the date of SBRT and the date of inside SBRT field relapse/progression of disease or the last follow-up visit. Toxicity was evaluated by CTC-AE scale.

Results: Thirty-seven pts carrying a total of 60 lymph nodal lesions were selected for the enrolment. The median age was 67 years (range: 62-86), and the majority of patients (93%) presented Eastern Cooperative Oncology Group (ECOG) performance status 0-1. The most frequent anatomical districts were the pelvis (N=35, 58.3%) followed by abdomen (N=17, 28.3%), and thorax (N=8, 13.4%). Overall, dose prescription to the Planning Target Volume ranged from 16 Gy/single fraction to 50 Gy/5 fractions. The vast majority of lesions (85%) were treated with a volumetric arc radiotherapy technique. With a median follow-up of 21 months (4-89) no severe (> grade 3) acute or late toxicities were recorded, with only one patient reporting G2 toxicity (nausea). The overall objective response rate was 83.3% (CI 95%: 68.9-92.2) with a complete response rate of 80%. The 2-and 4-years actuarial LC was 88% and 69%, respectively.

Conclusions: This study confirms the activity and safety of SBRT in the treatment of isolated lymph nodal recurrences in PC patients. Optimal SBRT schedules should be defined taking into account the need to guarantee the best personalized radiation dose.

**PO163**

## STEREOTACTIC RADIOTHERAPY FOR TREATMENT OF BRAIN METASTASES: A MONOCENTRIC EXPERIENCE

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Aims: Brain metastases are a well-established cause of morbidity and mortality, affecting 20%-40% of patients (pts) with cancer. In this retrospective study, we investigate the local control and radiation-induced brain necrosis in pts with brain metastases who received single-fraction or multifraction (SRS).

Methods: Between September 2010 and January 2019, a total of 103 pts(mean age 66 years, range 39-86) presenting with 154 metastases (provenance: 101 lung, 22 breast, 9 melanoma, 9 colonrectum, 5 kidney, 4 thyroid, 2 bile duct, 2 endometrium) were submitted to SRS at Department of Radiation Oncology in Pisa. All of them had KPS ≥70. For all pts, we calculated the Graded Prognostic Assessment (GPA), a prognostic index for pts with brain metastases. Gross tumor volume (GTV) was defined as macroscopic contrast enhancing lesion on T1-MRI. Planning tumor volume was obtained by adding to GTV an isotropic margin of 3 mm in all directions. The RT treatment was performed with True Beam LINAC VARIAN System with VMAT technique, using 6MV photons. We utilized a head thermoplastic mask as immobilization system. In this analysis we evaluated results in terms of local control and radiation-induced brain necrosis, trying to find a correlation with the delivered dose and the planning volume. In order to conform the delivered dose, we calculated the equivalent dose in 2 Gy (EQD2) considering an alfa-beta ratio of 5 (colonrectum), 4.6 (breast), 3 (lung and endometrium) and 1(cholangiocarcinoma and melanoma).

Results: Median overall survival (OS) was 13 months. The GPA index was significantly associated with OS (p = 0.014). Radiological response on MRI was assessed by a neuroradiologist according to the RANO-BM criteria. Local control was defined as the absence of new radiographic enhancing abnormality in the irradiated areas on MR imaging. After a mean follow-up of 9,8 months (range: 2,2-79,2), 29 metastases (18%) were in progression. The local control (complete/partial response/stable vs progression disease) was statistically related to a value of EQD2 ≥100 (p=0,049). Nineteen pts (12.3%) showed a radionecrosis at MRI performed during follow-up. This reaction was not statistically related to GTV-volume(p=0,350) but was strongly related to a value of EQD2 ≥150 (p=0,054).

Conclusions: Local control appears to be dose dependent with significantly better control observed in tumors receiving EQD2 ≥100. The risk of developing radionecrosis increases with EQD2 ≥150.

**PO164**

## EFFICACY AND SAFETY OF STEREOTACTIC RADIOSURGERY MONOISOCENTRIC TECHNIQUE TREATMENT FOR MULTIPLE BRAIN METASTASES

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Aims: To investigate the efficacy and safety of stereotactic radiosurgery (SRS) using a monoisocentric technique (Elements Multiple BrainMets SRS from BrainLab), with or without immune-checkpoint inhibitors (ICI) in patients with multiple brain metastases from melanoma, lung cancer, colorectal cancer and renal cancer.

Methods: From November 2018 to March 2019, seven patients with controlled systemic disease, good performace status and multiple brain metastases (range 4-13) of dimensions between 3 and 20 mm experienced SRS with dose prescription from 18 to 22 Gy. The treatment planning was performed by means of the Elements automatic planning software, dedicated for treating multiple brain metastases with SRS using a single isocenter with non-coplanar dynamic conformal arcs. Only three patients administered concurrent nivo-

lumab at doses of 3 mg/kg every two weeks. Endpoints of the study were early Local Control, Neurological Toxicity (radionecrosis) evaluated with magnetic resonance (MR) performed 60 days later SRS treatment and neurocognitive disorders.

Results: We obtained in four patients partial response (PR); only greatest lesions were stable or reduced dimensions while small lesions (<1cm) had disappeared, one patient had stable disease (SD), no patients showed early radionecrosis and/or neurocognitive disorders and two patients died, one for systemic progression disease and one for comorbidity.

Conclusions: In our brief experience, SRS using monoisocentric technique for multiple brain metastases treatment showed short-term good local control and concurrent treatment with ICI is mostly well tolerated without early neurological toxicity and neurocognitive disorders. A longer follow-up is needed to confirm these data.

**Table 1.**

| | | | | |
|---|---|---|---|---|
| **7 pts (4-13 les)** | | | | |
| **3-20 mm** | **PR** | **SD** | **Dead** | **Neurologic Tox** |
| **18-22 Gy** | | | | |
| **FUP 2 mth** | **4 pts** | **1 pt** | **2 pts** | **0 pts** |

## PO165

### STEREOTACTIC RADIOTHERAPY IN OLIGOMETASTATIC OVARIAN CANCER PATIENTS: A PRELIMINARY DATA OF RETROSPECTIVE STUDY IN A SINGLE INSTITUTION

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Aims: We report our preliminary experience with stereotactic radiosurgery (SRS), fractionated stereotactic radiotherapy (FSRT) and stereotactic body radiotherapy (SBRT) in oligometastatic ovarian cancer patients in terms of feasibility, toxicity and efficacy.

Methods: Retrospective data collection from a single institution was performed. The inclusion criteria were as follows: ovarian cancer, oligometastatic recurrent disease after systemic therapy, no previous irradiation. The intracranial and extra-cranial target were treated in frameless Radiosurgery modality with robotic arm LINAC (Cyberknife System). Manual contouring of the tumor and the organ-at-risk was performed on the co-registered CT datasets with MRI (intracranial target) and PET/CT (body target). All patients were followed up with magnetic resonance or PET/CT and clinical evaluation every 3 months after treatment.

Results: Between 2008 and 2017, 15 women and 29 targets (20 Brain Metastases and 9 pelvic/paraortic nodes - 17 SRS, 3 FSRT and 9 SBRT) were treated in our Centre. The median age was 52 years (range, 44-74); the median follow-up time was 43 months (range, 15-126) for brain metastases and 38 months (range, 15-50) for body target. Brain Metastases were treated with a median prescription dose of 20Gy/1Fx (range, 16-21Gy) in SRS modality and 30Gy/5Fx in FSRT modality. Lymph nodes were treated with a median dose of 21Gy/3Fx (range, 20-27Gy). Among 29 evaluable lesions, a complete radiologic response, partial response and stabilization were observed in 25 (86%) targets. Progressive disease was observed in 4 (20%) brain targets. One patient underwent to surgical resection and in 3 patients a re irradiation for recurrence was delivered. No grade 2-3 or 4 acute or late toxicities were observed. The median overall survival time was 16.5 months (range, 4-58) and 47 months (range, 23-58) respectively in brain and lymph nodes targets. The median time to local progression was 30 months (range, 17-35) and 32.5 months (ranges, 14-55) respectively, in brain and lymph nodes targets. The pattern of failure was predominantly in brain metastases.

Conclusions: SRS, FSRT and SBRT in oligometastatic ovarian patients is a safe and effective treatment. Stereotactic radiotherapy modality is a valid alternative to delay a second line systemic therapy.

## PO166

### DISTANT METASTATIC SECONDARY GLIOBLASTOMA: A CASE-REPORT OF A YOUNG PATIENT

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Aims: To report the case of a young patient with bone and nodes metastases of secondary glioblastoma multiforme (GBM).

Methods: In 2015 a 29-year-old female underwent surgery for a low grade glial lesion in the right frontal region with residual disease. The residual tumor remained stable until 2017 when magnetic resonance imaging (MRI) detected a progression that was subsequently totally removed. Histology revealed a diffuse astrocytoma (grade II). The following MRI documented a new recurrence and the patient received a third craniotomy. A diagnosis of GBM was made with the following molecular biology: 1p/19q non-codeleted, presence of IDH1 mutation, absence of IDH2 mutation, methylated MGMT. Three months after radiochemotherapy treatment, she presented with painful right cervical lymph nodes enlargement. She also suffered from widespread bone pains. Temozolomide-based therapy was disconti-

nued after six months because of hematologic toxicity. Node biopsy confirmed the diagnosis of glioblastoma metastasis with the same cytomorphological features. A full-body CT scan was performed and it was negative for other sites of disease. First, a cytoreductive radiation treatment of the right side of the neck up to a total dose of 30 Gy in 6 fractions was performed. Then she started a Procarbazine and Lomustine-based therapy which was stopped because of G3 hematological toxicity. Due to persistent widespread bone pain, after 4 months she was subjected to a 18F-FDG-PET which documented a diffuse bone uptake. Bone biopsy documented GBM metastasis.

Results: Currently she is alive and a III-line systemic therapy has been proposed. Neck lymph nodes are in complete response after radiation therapy. Bone pain is still not controlled and she has been referred to palliative care. Brain MRI is still negative with a progressive increase in extension of the T2/FLAIR signal alteration surrounding the surgical bed.

Conclusions: We reported a case of a malignant extracranial evolution of a secondary GBM in a young patient to point out that metastatic disease is rare but can occur also in secondary GBM which usually have a better prognosis than primary ones.

## PO167

### STEREOTACTIC ABLATIVE RADIOTHERAPY IN SPINAL AND NON-SPINAL BONE OLIGOMETASTASES: OUR EXPERIENCE

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Aims: Thanks to pharmacology, surgical and radiotherapy progress patients with bone oligometastases have a better life expectancy. Stereotactic Ablative Radiotherapy (SABR) has an ablative and antalgic role in this setting. Our aim is to investigate about local and systemic control and acute toxicity in bone oligometastatic patients(pts).

Methods: From February 2017 to May 2019 we enrolled 57 pts (20 female and 37 male) with bone oligometastases (spinal and non-spinal) who underwent to SABR in our institution. Median age was 66 years old (37-83 years), the primitive tumor was prostate (40,5%), lung (17,5%),breast (16%), uterus (5,2%), bladder and ureter rectum (3,5%), ovary (3,5%), multiple myeloma (3,5%), head and neck (1,7%), liver (1,7%), melanoma (1,7%). 28% had spinal metastases, 72% had non spinal metastases. The diagnosis occurred in 47,4% with Positron emission tomography (PET), 22,8% with Magnetic resonance imaging (MRI), 1,7% with bone scintigraphy, 21% with both PET and MRI, and 7% with computerized tomography (CT). The treatment was administered with Linear Accelerator 6MV with Volumetric Modulated Arc Therapy (VMAT) technique. Only 7% received one single fraction (15-21 Gy), 5,2% received three fractions (18-30 Gy), in 75,4% of pts five fractions (30-37.5 Gy) was delivered.

Results: At a median follow up of 10 months (0.1-25.9 months) only 5,2% experienced acute toxicity (1,7% nausea, 1,7% erythema, 1,7% exacerbation of the pain), 83% had pain control 17% experienced pain persistence. Four pts died for systemic progression of disease. About local response: 65,3% had complete remission (RC), 13,5% had partial response (RP), 19,5% had progression disease (PD), one patient was lost to follow-up. About systemic response: 66,6% had PD and 33,3% RC.

Conclusion: The observed data showed that SABR is a safe and feasible treatment, with a good profile of acute toxicity and local control.

## PO168

### ONCE-WEEKLY RADIOTHERAPY FOR UNFIT OR METASTATIC/RECURRENT PATIENTS: COMPLIANCE AND CLINICAL OUTCOMES OF A MONO-INSTITUTIONAL PILOT TRIAL

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Aim: To evaluate efficacy and clinical outcome in patients treated with once-weekly radiotherapy (RT) fractionation, due to their unfitness for surgery and/or standard treatments or to metastatic or recurrent illness presentation.

Methods: This retrospective analysis reports 27 patients enrolled in a pilot trial who undergone once per week RT, from 2011 to 2019, seen their impossibility to sustain guidelines-planned cures. Individual dose and fractionation were chosen on the basis of patients general clinical condition, previous irradiation, aim and lesions characteristics; patients were treated throughout 3DCRT, IMRT or VMAT technique. The primary endpoints were to determinate efficacy and acute toxicities. Efficacy was clinically evaluated, while toxicity examination was based on RTOG scale.

Results: Patients median age was 77 years (range: 45-94), 17 were male and 10 female. 21 patients underwent 3DCRT, 3 IMRT and 3 VMAT technique in once-weekly RT fractionation; 24 therapies were palliative (of which 4 retreatments) and 3 were adjuvant. Median dose to high-risk CTV, in first RT cycle, was 27 Gy (range: 10-50)while average fraction amount was 6 (range: 4-10).22 patients had acute toxicities (non more than G2, one), while 5 patients didn't have any RT induced side effects. Clinical response was observed in 59% of patients: 17% had clinical and/or radiological complete response, 17% partial response, 25% disease stability; 41% had disease progression; moreover, at the time of writing, 17 patients are dead (of these only 10 were disease-related cause) and 10 are alive. (See Table 1 for more details) .

Conclusions: Our analysis shows that once-weekly RT fractionation might represent, in selected patients, a treatment characterized by good clinical results and relatively-mild toxicities; moreover, this schedule may

also reduce logistic impact both for the patients (especially for those ones with comorbidities and/or difficulties in reaching the hospital) both for the Centre (in order to limit Radiation Oncology Centre-waiting list). Further investigations about this fractioning and its impact are ongoing.

**Table 1.**

| | |
|---|---|
| Number of Patients | 27 |
| Male | 17 |
| Female | 10 |
| Age (Median; Range) | 77 (45-94) |
| KPS (Median; Range) | 80% (70-100%) |
| Symptoms before RT | Present in 21 patients |
| RT aim | 24 palliative (4 retreatments)<br>3 adjuvant |
| RT body district | H&N, 16<br>Thorax, 3<br>Abdomen, 2<br>Pelvis, 4<br>Other, 2 |
| Follow-up (Median; Range) | 4 months; 0-22 months |
| Clinical Outcome | 17% CR<br>17% PR<br>25% SD<br>41% PD |
| Acute Toxicity (according to RTOG scale) | 85% of patients (22/27) Grade 1 |
| RT Technique | 3DCRT, 21<br>IMRT, 3<br>VMAT, 3 |
| Dose to high-risk CTV (Median; range) | 27 Gy (10-50 Gy) |
| Number of fraction (Median; range) | 6 (4-10) |
| Status of Patients | 17, dead<br>10, alive |

## PO169

### SACRAL PLEXUS SPARING IN STEREOTACTIC RADIOTHERAPY AFTER PELVIC EXTERNAL BEAM RADIOTHERAPY

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Aim: In oligometastatic patients (pts), stereotactic body radiotherapy (SBRT) is more often used with a "radical" intent, sometimes in previously treated regions. The aim of this retrospective analysis was to evaluate the problem of sacral plexus sparing in pts with lumbosacral metastasis, near to the pelvic node area formerly treated. Radiation toxicity of the lumbosacral plexus has been little described in the literature and there is no agreement regarding the dose constraints for this critical structure.

Methods: From November 2017 to April 2019, 9 lumbosacral bone metastasis (8 pts) from prostate cancer were treated with SBRT as curative intent. All pts previously received a 51.8 Gy RT on pelvic nodes. The median interval between the two irradiation was 50 months (range 25.1-180.1). The treatment was performed with CyberKnife (Accuray, Sunnyvale, CA) with a schedule of 25 Gy in 5 fractions in 5 cases, 24 Gy in 3 fractions in 3 cases and 18 Gy in 1 fraction in 1 case. The dose was prescribed to 80% isodose (range 75-82%). In 5 pts also a MRI was performed, in order to delineate as exactly as possible the course of the nerve. In 3 pts (4 lesions), the contouring of sacral plexus was delineate according to anatomy atlas. Since there are no indications in literature about dose constraints in case of reirradiation, the dose prescribed to sacral plexus was "as low as possible". In the treatment plan preparation we tried to conform the dose to the target, with sacral plexus sparing even at the expense of the PTV coverage.

Results: In our series the target coverage was 97% (range: 86-100%). Dmax to the lumbosacral plexus was 74% of the prescription dose (median, range: 13.6-84.2%). The treatment was very well tolerated, with no acute side effect. Six lesions were evaluated with imaging 4 months (range 10.2-1.8) after the completion of RT, with stable disease in term of dimensions (SD according to RECIST1.1).

Conclusion: Even though the follow up period is too short to be sure that pts will not develop major complication such as sacral plexus neuropathy, we can preliminary conclude that the hypo SBRT reirradiation of pelvic bone metastasis is feasible and safe even in pts previously irradiated on pelvic nodes.

## PO170

### STEREOTACTIC RADIOTHERAPY WITH VMAT TECHNIQUE IN PATIENTS WITH MULTIPLE LOCALIZATIONS

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Aim: The aim of the study is to show the results obtained by treating patients with multiple lesions using a single TPS.

Method: The method used for this work was to develop a single plan able to conform the dose to all the lesions in full compliance with the dose limits for the organs at risk. In particular, the case of two patients is reported: 1. patients with multiple brain lesions, highlighted by the fusion of TC and RM; 2. patients with multiple abdominal lesions, in particular a lymphnode, a vertebra and a further lesion on the vertebra, centering carried out in PET / TC. In both cases stereotaxic therapy was required. The TPS was processed with VMAT technique with 6MV FFF energy. In the first case the dosage was 8Gy in 3 fractions. Since three lesions are fairly close together, in order to be able to carefully assess whether there were problems with dose overlap, various isocentric regions with a center in the target were considered, but with ever-increasing rays so as to be able to impose a degradation of the most important dose out of the target. In the second case the dosage was different for each lesion, in particular: • 6Gy in 5 fractions for the lymphnode, • 5Gy in 5 fractions for the paravertebral lesion, • 4Gy in 5 fractions for the vertebra. Given the need to treat the vertebra, in order to better assess the spinal corde dose, it was decided to consider an internal target in order to achieve dose gradients such as to save the corde as much as possible. The three targets were treated at the same time, in particular, the entire vertebra and paravertebral lesion on

spinous process were treated simultaneously considering the lesion as an integrated boost.

Results: In both cases good results were obtained, with regard to the dose delivered to the target (coverage of the prescribed dose to 95% of the volume) and also concerning compliance with the limits for organs at risk. The patients treated did not show any side effects during the treatment nor did they report problems at the first follow up.

Conclusions: The method used seems to give excellent results both in terms of dose to target and savings in OARs. This leads our research group in Cosenza to use this technique as an elective approach in stereotaxic modulated treatments.

## PO171

### STEREOTACTIC BODY RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST (SBRT-SIB) IN PATIENTS WITH BONE SPINE METASTASES. A RETROSPECTIVE EVALUATION IN A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Stereotactic Body Radiation Therapy (SBRT) delivered in homogeneous target volume dose distribution in patients with spine metastases maximizes local tumor control and preserves neurologic function. A novel approach could be the use of an "inhomogeneous" SBRT using a Simultaneous Integrated Boost (SIB) delivering modality; the so-called "HDR brachytherapy-like" treatment. Aim of the present study is to retrospectively report our experience in the treatment of spine metastases using a frameless radiosurgery system delivering SBRT/SIB technique.

Methods: We reviewed the clinical records of all patients treated with SBRT/SIB for vertebral metastases in our center from December 2007 to July 2018.The primary end-point was to evaluate Time to Local Progression (TTLP); the secondary one were the Overall Survival (OS), toxicity and pain control.

Results: A total of 20 patients with spine metastases and 22 metastatic sites were treated in our Center with SBRT-SIB. The median follow-up was 35 months (range, 12-110). The median TTLP for all patients was not reached and the actuarial 1-, 2- and 3-years local free progression rate was 86.36%. The median OS was 38 months. None of the patients experienced neither radiation adverse events (grade 1-4) nor reported pain flair reaction. In 17/20 patients a complete pain remission (CR) was observed and 3/20 had partial pain remission (PR) (CR+PR: 100%).

Conclusions: Spine radiosurgery with SBRT-SIB is safe. The use of this modality in spine metastases patients provides an excellent local control.

## PO172

### POSSIBLE ABSCOPAL EFFECT AFTER STEREOTACTIC BRAIN RADIOTHERAPY IN WOMAN AFFECTED BY METASTATIC CANCER. A CASE REPORT

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Aims: We here report the case of an abscopal effect occurred in our clinical practice.

Methods: A 70 year old woman initially presented with multiple pathologic supradiaphragmatic nodes. She underwent surgery on the left neck in 2014, with the diagnosis of nodal metastases of likely a poorly differentiated breast cancer. Diagnostic exams failed to identify a primary site of disease. The patient started a systemic treatment with 6 cycles of carboplatin and gemcitabine, because of an allergy to taxanes, and letrozole, with a poor response. A revision of histologic specimen suggested a possible origin of the disease from skin annexes. Due to a following slight progression, the patient underwent 6 cycles of chemotherapy with adriamycin and cyclophosphamide, achieving a complete response. After over one year without any progression, an enlargement in right neck nodes was identified. A biopsy confirmed the nodal metastases of poorly differentiated carcinoma. The patient was referred to our clinic to evaluate a radiotherapy of the right neck: the radiation oncologist requested an FDG-PET, which confirmed the progression in right neck and suggested a possible brain secondary lesion. So a brain MRI was performed, pointing out a 17 mm metastases in right occipital region. The patient underwent a stereotactic treatment on the brain metastases (21 Gy in single fraction) in march 2018. After one month a planning CT was performed in order to prepare the treatment of the right neck, showing a major response in nodal volume. No further radiation nor systemic treatment was performed, and the patient underwent a close follow-up. Eight months later the brain lesion was still controlled, and a slight increase of two right neck nodes was identified. Therefore the patient underwent radiation treatment of the right neck (45 Gy in 15 fractions) in january 2019. A CT performed four months after radiotherapy showed no enlarged nodes in the neck nor other sites of disease.

Results: The patient achieved a major response on neck nodes soon after stereotactic radiation on the brain, which lasted for about eight months, without any further treatment.

Conclusions: Abscopal effect after radiotherapy is a rare phenomenon, and usually occurs when immunotherapy is administered close to radiation. Nevertheless it can be seen in few cases, even without any immune-stimulating drug.

## PO173

### A NEW INTEGRATED HEALTHCARE MODEL: RADIOTHERAPY AND PALLIATIVE CARE (RAP) OUTPATIENT CLINIC

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Aims: Over the last century radiotherapy (RT) has been successfully used to control symptoms caused by cancer. With advances in cancer care, the distinction between curative and palliative goals has become blurred. There is substantial evidence that palliative care (PC) combined with standard cancer care improves patient and caregiver outcomes in terms of quality of life (QoL), survival, use of healthcare services and costs.

**Table 1. Irradiated sites: 170 for 140 patients.**

| | | |
|---|---|---|
| Colonna | 63 (37%) | 121 (71%) |
| Osso | 58 (34%) | |
| Encefalo | 22(14%) | |
| Linfonodi addominali | 8 (5%) | |
| Lesioni pelviche | 7 (4%) | |
| Lesioni polmonari | 4 (2%) | |
| Latero-cervicali | 4 (2%) | |
| Altro | 4 (2%) | |
| TOTAL | 170 (100%) | |

**Table 2. Dose and Fractionation.**

| Single dose | | Total Dose | | n. Fractions | |
|---|---|---|---|---|---|
| 8Gy(+7,5 Gy) 98 ls (58%) | | 8Gy(+7,5 Gy) 98ls (58%) | | 1 | 98 ls (58%) |
| 4Gy | 36 ls (21%) | 20Gy | 36 ls (21%) | 5 | 53 ls (31%) |
| 5Gy | 23 ls (13,5%) | 25Gy | 19 ls (11%) | 3 | 12 ls (7%) |
| 6 Gy | 6 ls (4%) | 18Gy | 6 ls (4%) | 10 | 6 ls (4%) |
| 3Gy | 6 ls (4%) | 15Gy | 4 ls (2%) | | |
| 10Gy | 1 ls (0,5%) | 30Gy | 7 ls (4%) | | |

**Table 3. Techniques.**

| | | |
|---|---|---|
| VMAT : 79 (46%) | | 117 (69%) |
| TOMO: 38 (20%) | | |
| 3D: | 53 (31%) | |

Methods: From April 2016 to April 2018 a radiation oncologist and PC physician made 291 joint evaluations in the weekly Outpatient Clinic. Consecutive patients with advanced cancer were assessed for palliative RT and timely referral for PC. Before each clinical visit, the 2 physicians first reviewed the patient's clinical history and imaging studies while a nurse received the patient and administered the Edmonton Symptom Assessment System Scale(ESAS) and a QoL questionnaire (EORTC ; C 15-Pal). Data on clinical and disease characteristics, RT administered and follow-up information on date and place of death were inserted in a dedicated database. When palliative RT was not indicated, an appointment was scheduled at the Outpatient Clinic for the following month.

Results: 260 patients were evaluated in the integrated RT and PC Outpatient Clinic. Median age was 69 years. 83 patients had lung cancer, 27 patients were irradiated in more than one site. 121 (71%) of the 170 irradiated lesions were bone metastases. The dose and techniques characteristics are shown in the attached tables. In the 291 joint evaluations RT was considered not indicated in 137(47%) and 87 patients were referred immediately for home-care or hospice PC. In September 2018 142 had died, 96(68%) of whom in a PC setting (hospice or home-care). Median survival of irradiated patients was 10.2 months and median overall survival of the entire group was 8,5 months.

Conclusion: This new integrated approach improved the quality of care and QoL of our advanced cancer patients. The systematic analysis of all data collected will hopefully provide the answer to the many open questions remaining in this challenging healthcare area.

## PO174

### STEREOTACTIC RADIOTHERAPY FOR RE-IRRADIATION OF RELAPSED INTRACRANIAL LESIONS

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Aims: Stereotactic Radiotherapy (SRT) is increasingly used for the treatment of patients (pts) with recurrent primary brain tumors or metastasis (mts) after previous radiotherapy (RT). We analyzed the outcomes in pts treated in our Institute.

Methods: From 01/2018 to 04/2019, 65 intracranial lesions in 11 pts were treated with SRT Cyberknife® (Accuray, Sunnyvale, CA)(CK). Four pts presented recurrent mts from breast cancer, 5 pts from NSCLC, 1 patient glioblastoma (GBM) and 1 patient intracranial hemangiopericytoma (HPC). Previous RT on the same volume was performed with: Gamma Knife radiosurgery (GK) in 3 pts, VMAT SRT in 3 pts, CK in 2 pts, whole-brain RT (WBRT) in 4 pts, post-operative

Tomotherapy on tumor bed in 1 patient, post-operative 3D-CRT on tumor bed in 1 patient. Median time from the last RT was 12 (3.2-40.5 months). Gross tumor volume (GTV) and planning target volume (PTV) were delineated by the fusion of CT and MRI in all pts. Median GTV size was 0.15 (0,02-36,76) cc. PTV was obtained adding an expansion of 1 mm to GTV. Median PTV size was 0.43 (0,07-60,96) cc. Median prescribed dose was 35 (24-35) Gy in 1-5 fractions, at a median isodose of 77% (70-80%). Prophylactic corticosteroid therapy was prescribed to all pts and antiedema therapy with mannitol to 1 patient simultaneously treated on 21 lesions.

Results: Median follow-up after re-irradiation was 4 (2-18) months. SRT was delivered on a median number of 2 (1-21) lesions; 3 pts underwent SRT on > 5 lesions simultaneously (9, 19 and 21 lesions, respectively). Acute toxicity was G2 cefalea in 3 pts (GTV>1cc or >3 lesions), successful treated increasing the dose of corticosteroids. Radionecrosis occurred in only one patient (GTV>1cc, 2 previous VMAT SRT), symptomatic for seizures, treated with corticosteroids and levetiracetam. Local control, evaluated with MRI was: partial response in 7 pts, stable disease in 3, progressive disease in one patient. Seven pts presented intracranial disease progression (pts treated on >3 lesions). Four pts were dead at the last follow up, 2 for systemic progression and 2 for intracranial progression. Six months and 1 year OS were 27% and 18% respectively.

Conclusions: SRT for re-irradiation is feasible, with only 1 case of radionecrosis registered, and effective, with SD or PR in the majority of patients. An accurate patient selection is warranted in order to avoid toxicity and a longer follow-up is needed to confirm the low radionecrosis rate.

**PO175**

## PROGNOSTIC SCORE IN RADIOTHERAPY PRACTICE FOR PALLIATIVE TREATMENTS: PROPHET STUDY (FINAL ANALYSIS)

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Aims: The choice of Palliative radiotherapy (PRT) for bone metastases is complex. Prognostic scores can help to customize the treatment. We investigate the decision-making process after the application of the Mizumoto Prognostic Score (MPS) to 9 clinical cases, through a prescription simulation based on real data.

Methods: Radiation Oncologists (RO) with different degree of experience was subjected to a questionnaire to analyze which treatment scheme they had chosen before and after receiving information of the prognostic data. 9 cases were selected from clinical practice. A complete indication of the parameters required by the MPS was drawn up: 3 cases were of class A (better prognosis), 3 cases of class B (intermediate prognosis) and 3 cases of class C (poor prognosis). Each case was presented to each interviewed RO; then asked to choose one of the 4 options (Question 1); then revealed how the MPS codified the clinical case; then asked if he wanted to change the first choice (Question 2); and finally which final indication to confirm (Question 3). The experience classes defined for the Oncology Radiotherapists (RO) interviewed are 5: i) Specialized RO (RO-Spec), ii) senior RO, member of team dedicated to palliation (RO-S-D); iii) RO junior, team member dedicated to palliation (RO-J-D); RO senior, not dedicated to palliation (RO-S-NON-D); iv) RO junior, not dedicated to palliation (RO-J-NON-D). RO junior and senior have been respectively defined if with specialist assistance seniority of less than 8 years or higher / equal to 8 years. Treatment options for each clinical case included: a) Gold Standard 1 (40 Gy in 5 fractions); b) Gold Standard 2 (8 Gy in 1 fraction); Good Clinical Practice (30 Gy in 10 Fractions); "Other". The conversion rates of the prescription were analyzed after notification of the MPS data (Conversion Rate), and the agreement values (Agreement) between the various operators both globally and in subgroups (RO- Spec; RO-SD; RO-JD; RO-S-NON-D; RO-J-NON-D). The agreement was analyzed in absolute value and percentage using the Fleiss kappa test to discriminate the variance of the responses among the groups The ROs interviewed were contacted through the AIRO Palliative Study Group.

Results: 207 questionnaire was administered. The median conversion rate of the PRT prescription after MPS among all the ROs is: 11.6%. For RO-Spec was 18%. The agreement between all the ROs did increase of + 4.84%, corresponding to a shift from a low agreement level (k=0.18) to the level of 'sufficient agreement' (k=0.24) to the global analysis after the MPS application. The evaluation of the agreement for each subgroup confirmed an agreement increase corresponding to a

change from level of 'poor agreement' (k = 0.18) to the 'sufficient agreement' level (k = 0.24) to the global analysis after the MPS application. Further detailed analyzes will be notified at the conference.

Conclusions: Prognostic scores seem useful and shoul be encourged

**PO176**

## PRELIMINARY ANALYSIS OF TOLERANCE AND INTRACRANIAL LOCAL CONTROL IN A RETROSPECTIVE SERIES OF 39 OLIGOMETASTATIC PATIENTS TREATED WITH SINGLE SESSION STEROTACTIC RADIOTHERAPY (SRT) FOR BRAIN METASTASES: IMPACT OF GTV VOLUME AND BRAIN V12 GY

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Aims: To evaluate tolerance and intracranial local control in a retrospective series of 39 consecutive oligometastatic patients (pts) treated with SRT in single session for brain metastases from primary tumors of various sites and histology.

Methods: We retrospectively analysed 39 consecutive oligometastatic patients with radiological diagnosis of brain metastases who received SRT in single session with image-guided volumetric modulated arc therapy (VMAT) from 2016 to 2018. The tumor/patient/treatment characteristics are summarized in Table 1. GTV to PTV margins were of 2 mm for all pts. SRT doses to PTVs were prescribed as median dose, with V99 of PTV=D90 and brain V12 ≤10 $cm^3$. 30 pts received SRT to 1 single lesion and 9 pts had 2 lesions treated. Mean prescription dose according to literature (RTOG 9005) was 20 Gy (range: 15-24).

Results: All patients completed the scheduled SRT without acute side effects. No G2+ late toxicity was registered. At the end of the treatment we found a detriment of Karnofsky Performance Score (KPS) in only 1 patient (KPS 60 to 40) out of 39 pts (2.6%). With a median follow-up of 8 months (range:1-31 months) intracranial local control was achieved in 28/39 pts (72%): 4 pts with complete response, 6 pts with partial response and 18 pts with stable disease, respectively. Analysis of dose/PTV diameter showed the following Results: mean dose (MD) of 22 Gy±2.08 SD for lesions < 2 cm; MD of 19.13 Gy±3.10 SD for lesions of 2.1-3 cm; MD of 16.25 Gy±2.50 SD for lesions of 3.1-4 cm. Brain V12 ranged from 3.16 $cm^3$ to 10.5 $cm^3$, in particular the patient with detrimental KPS had a brain V12 of 9.77 $cm^3$.

Conclusions: Our preliminary data show that Single Session SRT for brain metastases in oligometastatic pts is a safe treatment with no major acute/late detrimental side effects, provided that RTOG dose/volume parameters of PTV and brain V12 are respected.

**Table 1. Tumor/ Patient/Treatment characteristics.**

| | | N=39 |
|---|---|---|
| Median age at diagnosis (y) (interquartile range IQR) | | 69 (61-72,8) |
| Sex | Male | 21 (53,8%) |
| | Female | 18 (46,2%) |
| Location of primary tumor | | |
| | Lung | 23 |
| | Breast | 8 |
| | Kidney | 2 |
| | Ovaries | 1 |
| | Skin | 2 |
| | rectum | 3 |
| Histology of primary tumor | | |
| | Adenocarcinoma | 20 |
| | squamous cell carcinoma | 3 |
| | invasive ductal carcinoma | 8 |
| | clear cell carcinoma | 2 |
| | melanoma | 2 |
| | other | 4 |
| Initial surgery | Yes | 23 (59%) |
| | No | 16 (41%) |
| Initial chemiotherapy | Yes | 29 (74,4%) |
| | No | 10 (25,6%) |
| Initial radiation | Yes | 9 (23,1%) |
| | No | 30 (76,9%) |
| Immunotherapy | Yes | 20 (51,3%) |
| | No | 19 (48,7%) |
| Karnofsky Performance Status | | |
| | pre SRT >60 | 35 (89,7%) |
| | pre SRT <60 | 4 (10,3%) |
| | post SRT>60 | 34 (87,2%) |
| | post SRT<60 | 5 (12,8%) |
| Number of treated lesions | | N=48 |
| | 1 | 30 |
| | 2 | 9 |
| Treatment dosimetric parameters | | |
| | Median dose/fx (IQR) , Gy | 20 (18-24) |
| | Median GTV (IQR) , cm3 | 1,62 (0,67-2,91) |
| | Median PTV (IQR) , cm3 | 3,73 (1,97-6,03) |
| | Median PTV diam (IQR), mm | 19,2 (15,56-22,59) |
| | Median PTV (IQR), Gy/mm | 1,13 (0,79-1,38) |

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## GAMMAKNIFE RADIOSURGERY AND SYSTEMIC THERAPY (INCLUDING TARGET THERAPY) FOR BRAIN METASTASES FROM LUNG CANCER: RETROSPECTIVE ANALYSIS OF TREATMENT FEASIBILITY AND OUTCOME AT NIGUARDA CANCER CENTER

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Aims: Stereotactic radiosurgery (SRS) is considered a standard treatment for the management of brain metastases (BM) from non-small cell lung cancer (NSCLC) and other solid tumors. Preliminary data suggest that radiosurgery for BM provides optimal local (in-field) disease control, and also that systemic medical treatment with target therapy (TT) improves survival of patients with NSCLC. Both treatment modalities may be associated with limited toxicity, providing a solid rationale for their use in clinical practice. The aim of this retrospective analysis is to evaluate the feasibility and the clinical outcome of the addition of SRS with the GammaKnife (GK) equipment to systemic treatment with TT.

Methods: Between 1/2015 and 12/2017, 70 patients (pts) with a histological diagnosis of NSCLC were treated for BM using GK at Niguarda Cancer Center. This series includes 42 males and 28 females with a median age of 66 years (range 37-83) and a relatively good performance status (PS 0-2). Of these 70 pts, 16 were medically treated with a combination of TT and chemotherapy (CT), 52 with CT only, and 2 with a combination of CT and immunotherapy. The median follow up of 30 surviving pts was 20.5 months (range 0-48).

Results: Pts were divided into two groups depending on overall survival (OS): group A less than 12 months OS (41 pts), and group B more than 12 months OS (29 pts). In group A, only 2 pts (4.8%) were treated with TT, in one case before and in the other after SRS; the median number of BM treated with GK was 2 (range1-10) with a median target volume (TV) of 0.82 cc (range 0.05-36.8 cc). 5 pts relapsed locally (12%). In group B, 14 pts (51.8%) were treated with TT, SRS being delivered before TT in 12 cases and after TT in 2 cases; the median number of BM was 3 (range 1-11), TV in this group was 1.51 cc (range 0.01-19.5cc). In this second group only 3 pts relapsed locally (10%).

Conclusions: The results of this preliminary retrospective analysis show that the use of SRS in the context of a systemic medical treatment with TT is feasible and is associated with good rates of OS and good local control as compared to other medical treatment modalities.

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## ABLATIVE RADIOTHERAPY FOR OLIGOMETASTATIC PROSTATE CANCER: PRELIMINARY RESULTS OF AN OBSERVATIONAL STUDY

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Aims: The purpose of the study was to assess biochemical response, local control and toxicity of stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer patients.

Methods: Between January 2017 and February 2019, 33 lesions (12 bone and 22 lymph nodes) detected by Ga68-PSMA positron emission tomography (Ga68-PSMA PET), magnetic resonance (MR), computed tomography (CT) were treated in 25 patients (pts). Pts included were: oligometastatic at diagnosis (2 pts), oligorecurrent castration-sensitive (15 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 the 15 castration-sensitive pts hormone therapy was not associated. We evaluated toxicity using Radiation Therapy Oncology Group (RTOG) scale, local control by radiologic imaging and biochemical response according to prostate serum antigen (PSA) level every 3 months after SBRT.

Results: Median follow-up was 11,4 months (range 3-24). At 3-months, biochemical complete response (PSA decrease > 50%), partial response (PSA decrease > 10%) and progression (PSA increase > 10%) were observed in 10/25 (42%), 8/25 (29%), and 7/25 (29%), respectively. At median follow-up of 13 months (range 9-24), 8/10 of the 3-months complete responders remained progression-free. Of 8 pts with an initial partial response, 2 pts developed progression disease with out-of-field nodal and bone metastases: new lesions were treated with SBRT. In 17/25 (68%) pts, a new radiologic imaging was performed with in-field progression occurring in only 2 cases. Androgen deprivation in oligorecurrent castration-sensitive (4/15 pts) and systemic therapy in oligorecurrent castration-resistant pts (3/6 pts) was delayed by an average of 8 months (range 4-16) after SBRT. 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. Further data and longer follow-up are necessary to confirm efficacy of SBRT.

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## STEREOTACTIC RADIOTHERAPY IN A SINGLE TREATMENT PLAN FOR MULTIPLE BRAIN METASTASIS : A MONO-INSTITUTIONAL EXPERIENCE

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Background/Aims: In recent years stereotactic radiosurgery (SRS)/ radiotherapy (SRT) prescription was extended to patients with more than 5 brain metastases. To report our early experience with single treatment plan stereotactic radiotherapy (SRT) delivered with Cyber knife® (Accuray, Sunnyvale, CA) in pts with multiple brain metastasis.

Methods: From March 2018 to January 2019 a total of 87 brain metastases in 8 pts (five females and three males) were treated with a single treatment plan SRT in our institution. Patient's median age was 73 (29-81) years and median Karnofsky Performance Status (KPS) was 90% (70-100). Primary site of tumors was melanoma in three pts, breast in two pts, lung in two pts, and one patient had lung and breast cancer. Three 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.

Results: Median number of brain metastasis was 8 (6-21). Median GTV volume was 0,16 cm3 (0,02-17,45 cm3), and median PTV volume 0,42 cm3 (0,07-20,89 cm3). All pts received preventive steroid therapy, median dose was 4 mg/day (2-16 mg). Median prescribed radiotherapy dose was 32,5 (22-37.5) Gy, at a median isodose of 77% (65%- 89%), in a median number of 5 fractions (1-5 fr). All fractions were delivered in consecutive days. Median estimated treatment delivery time was 75 (43-114) minutes, depending not only on volume and number of lesions, but also on setup and performance status of the pts. With a median follow of 5.3 months (0.5-11.1 months), none of the patients presented acute or early late toxicity after SRT. In five patients evaluated with contrast-enhanced MRI all presented CR, PR or SD in the irradiated lesions. No patient presented radionecrosis. Two patients presented intracranial progression due to new lesions at the first control, three months after treatment. Four patients were dead at the last follow up, one with heart failure two weeks after the treatment, one with systemic progression and two with intracranial progression.

Conclusions: Single plan SRT in pts with more than five brain metastases is feasible with a good toxicity profile and it is a promising option of treatment in these pts.

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## GAMMAKNIFE RADIOSURGERY OF BREAST CANCER BRAIN METASTASES, A SINGLE CENTER EXPERIENCE

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Aims: The aim of our study is to assess safety and efficacy of GammaKnife Radiosurgery (GKRS) for brain metastases (BMs) in primary breast cancer (BC) patients.

Methods: From an institutional database, we retrospectively identified patients with breast brain metastases treated with a single session of GKRS. Lesion and patient specific outcomes including response, lesion control, brain control and overall survival were recorded; patients, disease and treatment characteristics affecting clinical outcome were analyzed.

Results: Forty-five breast cancer patients received GKRS for brain metastases from January 2012 to March 2018. Characteristics of primary disease were reported in Table 1. At first GKRS treatment median age was 58 years (range: 27-80); 20% of patients received GKRS after surgery. A single metastasis was diagnosed in 53.3% of patients, 46.7% of patients had 1-4 BMs. Notable, 55.6% of patients had controlled extracranial disease at time of BMs occurrence. 73.3% had systemic treatment within 4 weeks from RS. Mean number of brain metastases treated per course of GKRS was 2.3 (range: 1-16); median BMs volume was 0.72 cc with a median dose of 20 Gy. About a half of patients (52.3%) treated with GKRS did not change chemotherapy regimen at the time of BMs diagnosis. None of patients had symptomatic radiation necrosis, seven (15%) patients developed radiological evidence of radionecrosis without neurological symptoms. Mean follow up was 1.9 years (range:0.01-6.3), at last follow up five (11.1%) patients developed local progression, Local Progression Free Survival (LPFS) was 84.4%, at statistical analysis none factor was statistically significant for LPFS. At last follow up 12 (26.7%) patients developed distant brain failure (DBF), median time to DBF was 7 months (range:4-14), at the time of DBF four (8.9%) patients received a second session of GKRS while 11 (24.4%) patients required salvage Whole Brain Radiotherapy, none factor was an independent prognostic factor of DBF. Twenty-three (51.1%) patients were dead at last follow up, overall survival (OS) was 21.2%, DS-GPA >2 was an independent prognostic factor of survival (HR= 0.24 (95% CI 0.08-0.74, p=0.013).

Conclusions: GKRS treatment for BMs in metastatic breast cancer is safe and achieves good rates of local control; patient selection with prognostic scale such as DS-GPA is confirmed an important instrument to select brain metastases patients who could benefit from a

local treatment.

**Table 1. Characteristics of primary breast cancer.**

| | | |
|---|---|---|
| **ER*** | **N** | **%** |
| Negative | 21 | 46.7 |
| Positive | 24 | 53.3 |
| **PgR** | | |
| Negative | 17 | 37.8 |
| Positive | 28 | 62.2 |
| **Her-2§** | | |
| Not amplified | 18 | 50.0 |
| Amplified | 27 | 60.0 |
| **Ki67** | | |
| ≤20% | 10 | 22.2 |
| >20% | 35 | 77.8 |
| **Luminal** | | |
| A | 6 | 13.3 |
| B | 12 | 26.7 |
| Her-2 | 20 | 44.4 |
| #TN | 7 | 15.6 |
| **BRCA status** | | |
| Not mutated | 41 | 91.1 |
| Mutated | 4 | 8.9 |
| **Stage** | | |
| I | 13 | 28.9 |
| II | 19 | 42.2 |
| III | 11 | 24.4 |
| IV | 2 | 4.5 |

**ER: Estrogen Receptor °PgR: Progesterone Receptor*
*§HER-2: Human Epidermal growth factor Receptor 2*
*#TN: Triple Negative*

## PO181

### STEREOTACTIC BODY RADIATION THERAPY FOR BRAIN METASTASES FROM PRIMITIVE TUMORS OF DIFFERENT NATURE

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Aims: Brain Metastasis (BM) are usually refractory to aggressive combinedmodality therapy and death rate after treatment is very high. Stereotactic intensity-modulated radiation therapy is now available to deliver a high dose of radiation to the tumor with relative preservation of surrounding tissues and minimal toxicity. We aimed to determine the efficacy of Stereotactic intensity-modulated radiation therapy (SBRT)-VMAT to control BM and report on the patients (pts) outcomes.

Methods: we retrospectively evalueted 12 pts who, between March 2017 and November 2018, had undergone SBRT-VMAT at our istitution Villa Santa Teresa in Bagheria for the treatment of BM from different primitives tumors. All the patients performed preoperative RM-brain integrated with the CT of centering to optimize the care plan. We treated BM from primitive tumors of different nature: breast in 4pts, small cell lung cancer in other 4 pts, adenocarcinoma in 2 pts, urothelial carcinoma in other two. Radiation was delivered in daily fraction of 5 or 6 Gy, to a total median dose of 28,3 Gy at the 95% median isodose line. We evaluated all the patients with the Karnofsky Performance Status (KPS).

Results: The median overall survival time was 6 months from the date of stereotactic treatment. At the beginning of the SBRT the KPS was 60, while at the end was 70 with a mild improvement of the quality of life even if epilectic crisis was observed in 4 patients.

Conclusions: SBRT-VMAT could be considered as the treatment of choice for the management of brain metastases as it produces results comparable to other currently used radioterapic techniques.

## PO182

### STEREOTACTIC ABLATIVE RADIOTHERAPY FOR OLIGOMETASTATIC SOFT TISSUE SARCOMA PATIENTS

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

Methods: We retrospectively review data of oligometastatic sarcoma patients treated in our institution between April 2001 to December 2016, collecting 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.

Results: 33 patients with oligometastatic sarcoma were treated with SBRT, accounting for 56 metastases, including 37(66%) lung, 15 (29.9%) bone and 4 (7.1%) lymph node metastases. Median age was 64 years (range 18-83). Eight (23.5%) patients had metastatic disease at diagnosis. Nine (26,5%) patients received concomitant chemotherapy for metastatic disease during SBRT. Median follow-up from first SBRT was 10 months (range 1-112). Median number of metastases treated per radiation course and median SBRT fractions were 2 (range 1-3) and 4,5 (range 3-12), respectively. Median prescribed dose was 40Gy (range 25-54) and median BED was 75Gy (range 48-151). Local control (LC) rates at 6 months, 1 and 2 years was 85.4%, 82.3%, and 73.6%, respectively. At univariate statistical analysis central tumor location identified patients with poorer LC (p=0.02). Twenty-two (66,7%) patients developed distant relapse with a median time to relapse of 2 months. Distant relapse free survival (DRFS) at 6 months and 1 year was 21.2% and 3%, respectively. No factors affected DRFS at statistical analysis. Overall survival at 1 year, 2 and 3 years was 29.8%, 22.4% and 8.4%, respectively. A number of metastases > 4 (HR 3.1, CI 95 1.1-8.7 p=0.032) and more than 2 courses of chemotherapy (HR 3.9 CI 95 1.6-9.7 p=0.028) admini-

stered before the time of SBRT were independent prognostic factors of survival. No acute or chronic grade ≥3 toxicities were observed.

Conclusions: In patients with oligometastatic sarcoma, SBRT yields satisfying LC with minimal toxicity. There is a subset of patients with slowly progressive tumors in which SBRT alone can lead to a good local control, an extended disease-free interval and a delay of chemotherapy changes.

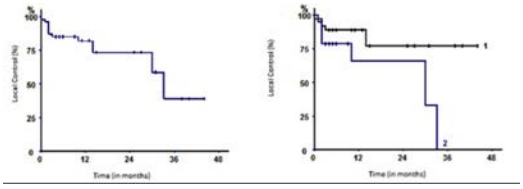

**Figure 1.**

## PO183

### STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH NON SMALL CELL LUNG CANCER BRAIN METASTASIS: OUR EXPERIENCE

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Aims: Brain metastases (BM) are a common complication in a wide range of cancers, but they are particularly common among patients with lung cancer. In recent decades, stereotactic radiotherapy (SRT) has become an attractive non-invasive treatment for patients with BM. Only the BM is irradiated to an ablative dose, sparing healthy brain tissue. In this retrospective study, we want to evaluate the role of SRS in patients with non-small-cell lung cancer (NSCLC) BM.

Methods: Between November 2010 and January 2019, a total of 72 patients (mean age 65,8 years, range 40-85) presenting with 101 metastases of NSCLC were treated with SRT at Department of Radiation Oncology in Pisa. Inclusion criteria were: KPS ≥70, follow up > 2 months, previous whole brain, SRT delivered to surgical cavity. For all patients we calculated the Graded Prognostic Assessment (GPA), a prognostic index for patients with brain metastases. The RT treatment was performed with True Beam LINAC VARIAN System with IMRT technique, using 6MV photons. We utilized a head thermoplastic mask as immobilization system. Planning tumor volume was obtained by adding to GTV an isotropic margin of 3 mm in all directions. Radiological response on MRI was assessed by a neuroradiologist according to the RANO-BM criteria. Local control was defined as the absence of new radiographic enhancing abnormality in the irradiated areas on MR imaging. In this analysis we evaluated results in terms of local control, overall survival and radiation-induced brain necrosis, trying to find a correlation with the histology, the delivered dose and the planning volume.

Results: After a mean follow-up of 15,3 months, 15 metastases (14,8%) were in progression. A better local control was statistically related to lower GTV-volume (p=0,023). Median OS was 15 months (range 2-62). The GPA index was significantly associated with OS (p=0,019). A longer OS is correlated with adenocarcinoma histotype (p=0,154) and development of radionecrosis (p=0,065). Twelve patients (11,8%) showed a radionecrosis at MRI performed during follow-up. This reaction wasn't statistically related to GTV-volume or delivered dose.

Conclusions: GPA index is a good method for NSCLC patients selection candidate to SRT that represents a reliable, effective, and minimally invasive approach. A better local control is related to smaller GTV-volume.

## PO184

### STEREOTACTIC RADIATION THERAPY IN OLIGOMETASTATIC OVARIAN ADULT-TYPE GRANULOSA CELL TUMOR (AGCT)

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Aim: show that SBRT is a feasible and potentially effective treatment in oligometastatic adult-type GCTs (aGCTs) patients.

Materials and Methods: we performed a retrospective analysis of 9 patients with recurrent aGCTs with 21 lesion treated with SBRT using Vero system. Follow-up was calculated from the last day of SBRT to the last follow-up visit. Progression free survival (PFS) was defined as the time interval between the last day of SBRT and the first diagnosis of progression or the last follow-up visit. Overall survival (OS) was calculated from the date of diagnosis of oligometastatic disease. Time to local progression (TTLP) and Time to out-field progression were also calculated.

Results: The median age at the time of SBRT was 65 years. Treated lesions were 19 visceral metastases and only 2 lymph nodes. Patients underwent a median of two treatments with a median dose prescription of 30 Gy given in 3 fraction. Median GTV volume was 2,5 (range 0,2-58,9 $cm^3$); PTV volume was 20,9 $cm^3$ (range 3,8 – 64,6 $cm^3$). After a median follow-up of 39 months, five patients were NED, three alive with out-field disease and only one was dead with in-field disease. Radiologic evaluation (RECIST) post SBRT, showed CR in 13 lesions, PR in 7 an SD in 1 lesion, therefore we observed an overall clinical benefit (CR+PR+SD) in 100% treated lesion. In-field control was observed in 20 out of 21 evaluable lesions, with a LC rate of 100% up to 3-years with a median local control of 32 months (using RECIST criteria). No grade 3 or 4 acute or late

events were observed. Acute toxicity, grade 1 or 2, observed in 14 cases included mostly fatigue and gastrointestinal events (nausea, diarrhea). Late toxicity (14 cases) include grade 1 or 2 gastrointestinal events (according to CTCAE criteria)

Conclusions: Granulosa cells cancer is an indolent tumor with a favourable prognosis, but with a tendency to give multiple relapses. Usually its recurrences are treated with surgery or chemotherapy with a higher risk of moderate/severe toxicity and comorbidity. Use of SBRT can delay systemic treatment and become a useful alternative to the more invasive surgical techniques. Based on our experience RT could be a valid and active treatment option of recurrent GCTs to improve patient's clinical outcome with a good local control of disease and a very low toxicity profile.

## PO185

### STEREOTACTIC BODY RADIATION THERAPY FOR ABDOMINO-PELVIC OLIGOMETASTATIC LYMPH NODES OF GYNECOLOGICAL MALIGNANCIES: A MONO - INSTITUTIONAL EXPERIENCE

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Aims: The aim of this study was to evaluate the role of stereotactic body radiotherapy (SBRT) in a series of oligometastatic lymphnodes of gynecological malignancies.

Methods: Clinical records of patients affected by oligometastatic lymph nodes of any gynecological primary treated with SBRT were retrospectively reviewed. From 2011 to 2018, a total of 40 patients with single or multiple abdomino pelvic lymph node metastases for a total of 53 lesions were treated in our Center. Primary cancer were 28 ovarian, 8 endometrial, 3 cervical and 1 vulvar cancer. Toxicities were graded according to Common Terminology Criteria for Adverse Events version 4.0. Tumor response was evaluated by CT/ PET and/or MRI, according to Response Evaluation Criteria in Solid Tumors (version 1.1)

Results: Median follow-up was 24 months (range 6-88). Complete radiologic response, partial response, stable disease and progressive disease were observed in 62.3%, 22.6%, 11.3% and 3.8% of cases, respectively. The median LC was not reached. One year- and three year- LC were 96.6%. Median distant control was 35.5 months. Median OS was 59.9 months. All of patients completed the prescribed treatment with a low toxicity profile: only 12.5% experienced G2 acute toxicity, most common adverse effect was abdominal pain (5.2%), fatigue (4.2%) and nausea and vomiting (3.1%). None of the patients had grade 3 or 4 acute or late toxicity.

Conclusion: SBRT is a feasible and safe approach in selected cases of lymph nodes oligometastatic gynecological cancer with satisfactory results in terms of LC and DFS.

## PO186

### STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC HORMONE-SENSITIVE PROSTATE CANCER (MHSPC) PATIENTS WITH ISOLATED LYMPH NODES INVOLVEMENT: A MONO-INSTITUTION EXPERIENCE

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Aims: Oligometastatic prostate cancer represents a distinct subset of metastatic disease with a potentially more indolent biology, where metastases are limited in number and location. SBRT is emerging as a widely treatment option in oligometastatic prostate cancer. Several retrospective studies have reported the benefit of SBRT for local control and for replacing or delaing the introduction of androgen hormone therapy (ADT). This analysis describes our experience with treating nodal oligometastatic HSPC patients with SBRT alone.

Methods: Between January 2016 and January 2019 fourteen mHSPC patients were treated with exclusive SBRT, delivered by LINAC with daily cone beam CT. All patients underwent [(11)C] choline or PSMA positron emission tomography (PET) for biochemical relapse after local primary treatment (RT or surgery). All patients had isolated abdominal or pelvic nodal disease. Prescribed dose was 36 Gy in 6 fractions or 35 Gy in 5 fractions. Response to treatment was assessed with periodical PSA evaluation. Patients with a reduction or a stability of PSA level were considered responders and a further PET-CT was done in patients with biochemical increase. Toxicity was evaluated according to CTCAE vers. 4.02.

Results: The median age was 69 years (range 57-83); the median follow-up was of 21 months (range 3-36) and the median PSA pre-SBRT was 2.56 ng/ml (0.67-5.78). The median PSA post-RT was 0.90 ng/ml (range 0.02-5.30). All patients had local control and decrease of PSA level after SBRT. 6/14 (43%) patients had a PSA increase due to an out-field progression confirmed by Choline-PET/CT. Of these last, 4 patients started ADT for multimetastatic disease progression after SBRT; other 2 patients required a second salvage SBRT for metachronous nodal relapse. Median ADT – free survival was 10.5 months and b-PFS at 24 months was 40%. Acute and late toxicities greater than G1 were not recorded.

Conclusions: Despite the small number of patients and the short follow-up, our experience shows that salvage PET-guided SBRT for isolated lymph nodes involvement is safe and effective to improve response rate and to defer the start of ADT in selected low-volume mHSPC patients.

**PO187**

## ROLE OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC PROSTATE CANCER PATIENTS WITH ISOLATED SPINE METASTASES: A PRELIMINARY EXPERIENCE

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Aims: SBRT has a consolidate role in increasing biochemical and local control rate in oligometastatic prostate cancer. Several studies suggest that using SBRT to spine metastases it is possible to achieve high levels of control both pain and disease in close proximity to the spinal cord. The purpose of this study is to report an initial clinical experience with SBRT in selected oligometastatic patients with isolated spine metastases treated at our center in Barletta.

Methods: Between December 2016 and January 2019, 6 oligometastatic prostate cancer patients with a total of 7 spine metastases were treated with SBRT, delivered by LINAC with daily cone beam CT. All patients underwent [(11)C] choline or PSMA positron emission tomography (PET) for biochemical relapse after local primary treatment (RT or surgery). 3 patients received androgen deprivation therapy(ADT) concomitant to SBRT and remaining 3 underwent exclusive SBRT. All spine metastases were localized in the anterior portion of the vertebral body and CTV included the entire vertebral body. The treatment sites were: lumbar spine for 4 patients and thoracic spine for 2 patients. 3 patients had high cancer-related pain before SBRT. Prescribed dose and schedule of fractionation was 30 Gy in 5 fractions . Response to treatment was assessed with periodical PSA evaluation and a further PET-CT was done in patients with biochemical increase. Toxicity was evaluated according to CTCAE vers. 4.02.

Results: The median age was 72 years (range 63-73). The median follow-up was of 12 months (range 3-25). Median PSA value before SBRT was 2.2 (range 0.5-4.3). A significant reduction of PSA was observed in 4 cases, while PSA was stable in 1 case and raised in 1 case who experienced a relapse of disease in other sites .All symptomatic patients reported significant pain reduction during the six months post-SBRT. SBRT was well tolerated: one patient experienced G1 acute gastrointestinal toxicity. Late toxicity was evaluated in patients with more than 6 months of follow-up, and no toxicity was relevated. At the time of analysis, all patients are alive.

Conclusions: This preliminary experience shows that SBRT can be administered safely and represents an effective treatment option in order to improve symptomatic and clinical benefit in oligometastatic prostate cancer with spine metastases.

**PO188**

## CLINICAL OUTCOMES AND TOXICITY OF HYPOFRACTIONATED STEREOTACTIC BODY RADIATION THERAPY DELIVERED WITH HELICAL TOMOTHERAPY IN OLIGOMETASTATIC/OLIGORECURRENT DISEASE

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Purpose: The published studies about the treatment of oligometastases with stereotactic radiotherapy, showed hopeful results. Here we investigated clinical outcome of hypofractionated stereotactic body radiation therapy (SBRT) delivered with Helical Tomotherapy (HT) in patients affected by oligometastatic and oligorecurrent disease.

Methods: From April 2014 to October 2018, 59 lesions in 50 patients with a median age of 71 years (range 27-85) were treated with HT-SBRT at our center. We considered eligible for this treatment only patients with ≤ 2 lesions. According to tumor site and using a strategy of risk-adapted dose prescription, different treatment regimens were administered: 36-60 Gy in 5-10 fractions for lung metastases, 25- 60 Gy in 5-10 fractions for nodal lesions and 18-36 Gy in 3-6 fractions for bone metastases. Toxicity profiles were evaluated using CTCAE v4.0 criteria during treatment and at follow-up. Tumor response was evaluated by CT-scan every three months and/or 18FDG-PET/CT, according to RECIST or PERCIST criteria. Kaplan–Meier method was used to generate Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS) rates.

Results: Of 59 lesions, 35 were pulmonary metastases, 18 lymph nodal and 5 bony lesions. 39 patients had a single site, while 11 patients had 2 lesions simultaneously treated. The most frequent primary tumor was Non-Small Cell Lung Cancer (n=19) followed by prostate (n=10), colorectal (n=6), ovarian cancer (n=3), larynx (n=3), bladder (n=2), breast (n=2); melanoma, pancreas, liver, germ cell tumor and parotid gland tumor in the remaining 5 cases. With a median follow-up of 14 months (range 3-51), no acute or late toxicity ≥ G3 were reported. We observed only one case of acute G2 chest pain and 2 cases of late G2 dysphagia and chest pain resolved after short time steroid therapy. At the time of analysis, LC rates at 1- and 2-years were respectively of 94.2% and 85.7% for lung lesions, 83.3% and 83.3% for nodal lesions. For bone metastases, we reported a 1-yr LC rate of 80%. 1-yr and 2-yrs PFS were 62.7% and 47.4%. OS rates at 1-yr and 2-yrs were 88% and 74%.

Conclusions: This study observed encouraging survival rates with limited toxicity. Oligometastatic patients may benefit from a more aggressive approach. Long term follow-up is awaited.

## PO189

### STEREOTACTIC RADIOTHERAPY FOR MULTIPLE BRAIN METASTASES: COMPARISON AMONG DIFFERENT TECHNIQUES AND PLANNING SYSTEMS IN VOLUMETRIC MODULATED ARC THERAPY (VMAT)

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Aim: Multiple brain metastases can be treated even with stereotactic radiotherapy techniques combined with inverse planning. We compared different technologies and techniques: non-coplanar arc against coplanar arcs, multiple isocenter against unique isocenter, Autoplanning (AP-TemaSinergie) against Element2.0 (E2- BraniLab) treatment planning consoles. We compared plan results in terms of target coverage, OAR sparing, delivery and set-up time.

Materials and Methods: We treated all our 34 patients with multiple brain metastases (2-13) with mono isocenter technique in combination with Autoplan. For each patient we also added plans with multiple isocenter technique, either double coplanar arc or with five no-coplanar arc, both with Autoplan and Elemnts 2.0. In all cases we prescribed single fraction of 18-24Gy or three-fraction 21-27Gy at isodose of 80%. For all treatments, we evaluated the PTV coverage with dose-volume histogram and conformity index (CI) as defined by Radiation Therapy Oncology Group. We evaluated all OAR constraints above the entire dose to normal brain (V12). We compared also the number of monitor unit (UM) delivered by the linac and the set-up time.

Results: For all the techniques used, the dose distribution is highly conformed and the CI is always under the value of 1.17±0.03. We noted the combination of single isocenter techniques with VMAT- AP produces reduction in terms of MU and delivery time. The blend of single isocenter techniques with the software E2 demonstrates the better sparing of normal brain in terms of V12. On the other hands multiple isocenter techniques, independently of the software used, provides the better respect of V12 but the longer treatment time in term of set-up and delivery.

Conclusions: Our judgement about the choice of the optimal combination for treatment could be guided by patient's characteristics and disease's and last but not least the center's expertise.

## PO190

### THE ROLE OF MULTI-FRACTION STEREOTACTIC RADIOTHERAPY IN THE TREATMENT OF BONE METASTASES: PAIN CONTROL AND RADIOLOGICAL RESPONSE

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Aim: To report treatment outcome of multi-fraction stereotactic radiotherapy (SRT) in the treatment of bone metastases in patients with oligometastatic or oligoprogressive disease.

Methods: From May 2016 to April 2019, oligometastatic or oligoprogressive patients with bone metastatic lesions < 5 cm were treated using SRT. Tumor responses were evaluated according to the RECIST criteria. Local disease control was defined as lesions that were not classified as progressive disease on RECIST criteria. The numerical rating Scale (NRS) was used to evaluate pain status.

Results: Primary tumors were as follows: breast (11, 35.5%), kidney (5, 16.1%), lung (9, 29%), prostate (2, 6,5%), gallbladder (1, 3.2%), sarcoma (3, 9,7%). Treated site was spine in 3 patients (9.7%), non spine in 28 patients (90.3%). Concomitant immune therapy was performed in 5 (16,1%) patients, target therapy in 7 (22.6%) patients, chemotherapy in 6 (19,4%) patients. NRS improved in 27 patients (preRT mean value=4.58, SD=1.8; post RT value= 1.0, SD=1.9; p=<0.001). The radiological response was evaluated by PET-TC in 15 (48.4%) patients and by TC-MRI in 17 (51,6%) patients. Ten (32,3%) had a partial or complete response on imaging, 16 (51,6%) stable disease and 5 (16,1%) disease progression according to the RECIST criteria. Only 1 (3,2%) patient with a iliac bone metastases experienced fracture at 4 months from SRT. No other treatment related toxicity was recorded. The Median follow-up was 6 months (range=2-20 months). No patients interrupted systemic treatment due to delivery of radiotherapy course.

Conclusions: This stereotactic radiotherapy regimen for bone metastases showed to be safe and well tolerated. Its impact on progression free survival in this subset of patients (oligometastatic or oligoprogressive) need to be assessed in prospective studies.

**PO191**

## OUTCOMES OF INTENSITY MODULATED RADIOTHERAPY WITH HYPOFRACTIONATED DOSE-ESCALATION USING A SIMULTANEOUS INTEGRATED BOOST TECHNIQUE FOR TREATMENT OF LARGE BONE METASTASES

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Aims: To evaluate the efficacy and toxicity of intensity modulated radiation therapy with simultaneous integrated boost (SIB-IMRT) for large lesions not suitable for stereotactic radiotherapy.

Methods: We retrospectively evaluated patients with bone metastases treated at our institute with SIB-IMRT. Radiological response was described according to RECIST criteria. Pain response was assessed by means of Numerical Rating Pain Scale (NRS). Toxicity graded according to the Common Terminology Criteria for Adverse Events (CTCAE) vers 4.02.

Results: Eleven patients with twelve lesions were treated at our institution from April 2017 to April 2019 with SIB-IMRT. Primary tumors were as follows: breast cancer (42%), prostate (33%) and lung (25%). Treated sites was 8 spine (66.7%), 3 pelvic bone (25%) and 1 cranial bone (8.3%). Ten patients (90.9%) were subject to drugs regimens during the treatment. NRS improved in all patients (pre-RT mean value = 3.75, SD =3.22; post-RT value =1.0, SD =1.95; p=< 0.001). The radiological response was evaluated by CT-scan in 4 patients (37%), PET/CT in 4 patients (37%), MRI in 3 patients (26%). The GTV and CTV were prescribed at mean dose of 39.47 Gy (range 30-45 Gy) and 29.98 Gy (range 25-32.4 Gy), respectively, in 10 fractions. Six patients (54%) had a partial or complete response on imaging, 4 patients (37%) stable disease and only 1 patients disease progression in according to the RECIST criteria. The Median Follow-up was 3 months (range 1-30 months).

Conclusions: SIB-IMRT is an effective, safe and well tolerated option for treatment of large bone metastases not eligible for stereotactic treatment. But this observation needs to be validated in future studies with more patients.

**PO192**

## TOMOTHERAPY STEREOTACTIC RADIOSURGERY FOR PATIENTS WITH BRAIN OLIGOMETASTASIS

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Aims: To evaluate the feasibility, tolerance and report preliminary results of stereotactic radiosurgery (SRS) using helical Tomotherapy (HT) for patients with 1-5 brain metastasis (BM).

Materials and Methods: Inclusion criteria included pts with radiological diagnosis of BM, KPS ≥ 80%, number of 1-5 metastases, diameter ≤ 3 cm, absent or controlled (after primary treatment) extracranial disease, measurable brain disease. Eligible pts received mean prescription dose 21 Gy (range 12-23Gy) in a single fraction SRS using HT. Toxicity was scored according to CTCAE 4.0 while radiological response evaluation was done by MRI every 3-6 months.

Results: From April 2016 to March 2019, 32 pts were enrolled. Pts characteristic were as follows. Male/female 15/17; median age 63 yy (range 44-81); median KPS 100% (range 80-100); median GPA class 2 (range 1.0-3.0); primary tumor site: lung 15/32; breast 5/32; 5/32 primary brain tumors; kidney 3/32; melanoma 2/32 and 1/32 ovary; total number of BM: 46; site of BM: frontal 12/46, temporal 5/46, occipital and parietal 3/46, cerebellar 10/46, other 13/46. 10 pts received cisplatin-based chemotherapy, 8 immunotherapy, 5 previous whole brain radiotherapy and 2 partial brain irradiation up to 60 Gy. Median GTV volume was 0,65 cc (range 0,13-3,56) and median dose delivered was 21 Gy (range 12-23 Gy). No patient experienced severe acute toxicity; Among 30 pts evaluable for radiological response, as having at least a minimum 3-month follow-up, only two experienced radionecrosis, 7/30 had died (disease progression).

Conclusion: The preliminary results of this monoinstitutional experience on HT SRS seem to show the feasibility and good tolerance of this SRS HT technique in terms of acute toxicity.

## PO193

### RADIOMICS AND PREDICTIVE MODELS APPLIED TO HEAD AND NECK RADIOTHERAPY: AN OVERVIEW OF ONGOING TRIALS

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Aims: In radiation oncology practice, comprehensive information on tumor genomic profile and tumor characteristics extractable by imaging can improve treatment planning and clinical response evaluation. Current studies on radiomics and predictive models of radiation-induced side effects (RISE) and/or tumor response will provide more informative results. In this paper we report a short overview of current modeling studies in patients subjected to radiotherapy (RT) for head and neck cancers (HNC) with the main scope to provide a preliminary explorative analysis on these topics.

Methods: In April 2019 we performed an advanced search on clinicaltrials.gov website using the following keywords and strategy: "Head and Neck Radiotherapy" AND "Predictive models OR Mathematical models OR Radiomic features". Studies in the following recruitment status: Suspended, Withdrawn and Unknown Status, as well as trials enrolling pediatric patients, were excluded. Both studies assessing RISE and tumor response have been selected and analyzed. We extracted data regarding study type, patients' number, recruitment status, model assessment, inclusion criteria, primary and secondary outcome measures.

**Table 1. Summary of ongoing trials.**

| Study identifier | Location | Study type | Estimated patients number | Recruitment status | Model assessment | Intervention/ treatment | Main inclusion criteria | Primary outcome measures | Secondary outcome measures | Study results |
|---|---|---|---|---|---|---|---|---|---|---|
| NCT03294122 | Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy | O/C/P | 400 | Recruiting | MICRO-LEARNER (MICROtoxic, self-Learning Environment, Clinical), and Radiomic features in Prediction of Normal Tissue Response in RT for Prostate and HNC) | Radical/ adjuvant RT (standard regimens) and possible concomitant chemotherapy | HNC patients, 18-75 year, metastatic-stage (AJCC VII ed.) (I-II pharynx and larynx patients if neck lymph nodes or oral mucosa are included) | Acute toxicity according to CTCAE grading system and its association with the investigated variables and absorbed dose | Late toxicity according to CTCAE grading system, and its association with the absorbed dose and additional variables | Not available |
| NCT02489084 | University Medical Center Groningen, Groningen, Netherlands | O/C/P | 2000 | Recruiting | SNP (PM for RISE in HNC based on Single Nucleotide Polymorphisms - SNP) | PM implementation using SNP profiles (blood sampling); Primary/ postoperative RT either or not combined with systemic treatment | HNC patients candidate to primary/ postoperative RT (either or not combined with systemic treatment) | Improvement of PM performance in late RISE evaluation by adding SNP profiles. Change in acute toxicity, patients symptoms and QoL | | Not available |
| NCT03656133 | H Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States | I/NR | 60 | Recruiting | PM (Use of a Proliferation Saturation Index - PSI - to Determine Personalized RT Fractionation for Patients With HPV+ Oropharyngeal Cancer) | PSI-based conventional fractioned or hypofractionated RT | Patients with p16+ or HPV+ squamous cell Oropharynx carcinoma, T1-3, N0-1 M0 AJCC 8th ed. | Increase of response rate of (52% at 4 weeks to 63% of patients, above the expected 49% | Rate of complete response at 2-3 months (CT or PET/CT evaluation) | Not available |

*O = Observational, P = Prospective, C = Cohort, I = Interventional (Clinical Trial), NR = Non-Randomized . PM = Predictive Models, RISE = Radiation-induced side effects, QoL = Quality of Life.*

Results: Our search provided 3 studies (Table 1). All trials were recruiting at the time of our search. A total of 2460 patients were expected. No definitive results were available. The NCT03294122 and NCT02489084 studies are assessing models to predict RISE in HNC, regardless of the primary tumor site. In this setting, we observed an emerging interest on the role of the microenvironment (e.g. microbiota, inflammatory markers), as well as on tissue features extracted by radiomic analyses and DNA profiles. Another study (NCT03656133) is specifically assessing tumor response of p16+ or HPV+ squamous cell oropharynx carcinoma by determining whether a mathematical model based on the individual patient "proliferation saturation index" is able to predict rapid tumor response and support the decision of personalized RT fractionation.

Conclusion: Comprehensive database of clinical, genetic, biological, imaging, dosimetric data are needed to match the collected information. The management of big data to aid the decision-making in clinical practice requires a multidisciplinary approach and experts' support. Tolerance and effectiveness of RT for HNC could be improved by using these innovative approaches. Definitive results and further validations of the proposed models are necessary.

## PO194

### IN UNOPERABLE SSCC, RADIOTHERAPY SCHEDULES COULD BE CHOSEN USING DERMOSCOPIC FEATURES?

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Aims: Radiotherapy is an optimal option for unoperable SSCC (Skin Squamous Cell Cancer) with excellent local control and good cosmetic outcomes. A lot of different fractionation and total doses had been used to treat SSCC, according to several clinical and histological parameters. Dermoscopically, these kind of lesions are often characterized, by atypical vascular pattern and/or deep ulceration that some authors correlate with the severity of the neoplasm. In our study, we decide to use different radiotherapy schedules for our patients with SSCC, performing a "dose escalation" in those who had negative dermoscopic features.

Methods: 43 patients (age> 60yo) with unoperable SSCC were enrolled in this study. Based on negative dermoscopic features (ulceration, bleeding, irregular vessels), signed by a skilled dermoscopist, we divided them in two groups: those with no negative dermoscopic features (20 patients) and those with negative one (23 patients). The lesions were on the trunk (9), on upper/lower limbs (12) or on the face (22). None of these lesions had nodal involvment (N0). No lesione were >5cm. In the first group we use an electron beam schedule of 2.5 Gy/22fx (55Gy) while in the second group we prescribe 3Gy/20fx (60Gy).

Results: All the patients ended treatment. In the group A (standard) the LC was observed (at 1 year follow up) in 15 patients (75%) and in 9 patients (45%) at 2 years follow up. Skin toxicity > grade 3 was not seen in these patients. No late toxicity was registered, with good cosmetical outcome. In the group B (negative features) the LC was observed in 16 patients (69%) at 1 year follow up and in 10 patients (43%) at 2 years follow up. 4 patients had grade 3 skin toxicity in this group

with 2 cases of late hypopigmentation.

Conclusion: Dermoscopic examination could be used to perform a dose excalation schedule in unoperable SSCC, with similar LC and accettable toxicity. More patients and a longer follow up are the main future topics to enhance this kind of approach.

## PO195

### RADIOMIC PREDICTIVE FACTORS USING MRI IMAGING IN LOCALLY ADVANCED CERVICAL CANCER TREATED WITH EXCLUSIVE RADIO-CHEMOTHERAPY

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Aims: The aim of this study was to analyze radiomic features, using MRI images, as predictive factors of disease progression (PD) in patients with locally advanced cervical cancer treated with exclusive radio-chemotherapy.

Methods: we analyzed radiomic features from MRI images performed before and after treatment in 37 women (median age of 56 years) affected by LACC (FIGO Stage IB2-IVA) underwent definitive radio-chemotherapy 45-50.4Gy (in 25-28 fractions) + HDR intracavitary BT boost 21-28 Gy (in 3-4 fractions). 70.2% patients received neoadjuvant chemotherapy; and 78.4% 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 subsequently more statistically significant features ($p<0.01$) were analyzed in a multivariate discriminant model, based on Mahalanobis distance method, to define the clusters related to the progression. D-scores were calculated too.

Results: Twenty-eight features were extracted from each T2-weighed MRI images performed before and after treatment. In multivariate analysis, after a median follow-up of 23.5 months (range 11-71 months), volume value was the only feature significantly correlated ($p=0.045$) with PD. The discriminatory model showed that a discriminant score (D) >2.55 was correlated with the 85% of risk of progression, a value of D between 2.55 -1.45 with the 70-85% and finally, a value of D between 1.45-0.17 with the 50%-70% of risk of progression. Pearson linear analysis showed a statistically significant correlation ($r=0.326$; $p=0.022$) between the feature VOLUME and the tumor volume (median volume 72 $cm^3$; range 11-269 $cm^3$).

Conclusions: Volumetric morphological characteristic was the main predictive factor regarding progression disease in LACC. Our results suggest that radiomics features related to clinical outcomes are predictive models to be used in the clinical setting. However, prospective studies with higher number of patients and longer follow-up are necessary to confirm our results.

## PO196

### EVALUATION OF ROBUST RADIOMIC FEATURES FOR LOCAL-RECURRENCE PREDICTION IN ORO- AND NASO-PHARYNGEAL CANCER PATIENTS AFTER IMRT TREATMENT: STUDY PROTOCOL FOR A RETROSPECTIVE ANALYSIS OF 79 CONSECUTIVE PATIENTS

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Aims: Radiomics is the high-throughput extraction of large amounts of quantitative features from medical imaging whose analysis can be used for clinical decision.Several papers show that inclusion of radiomic features in the models improve their prognostic power. However features are highly correlated to pre-processing steps, leading to a lot of false discovery rate in radiomic studies. In this study,we will extract only robust feature from CT-planning GTV of oro- and nasopharyngeal patients treated with IMRT, in order to evaluate local recurrence. In order to select only robust features, the influence of different gray-level discretization, resampling and interpolation methods on their values and their stabilitywill study.

Methods: Radiomic features will be extracted from phantom and patientsimages. Catphan®600 module 404is acquired using standard clinical CT protocol. 250 featuresare extracted from acrylic target, including First Order Statistics (19 features),Shape-based (16 ),Grey Level Cooccurence Matrix (24), Grey Level Run Length Matrix (16), Grey Level Size Zone Matrix (16), Neigbouring Grey Tone Difference Matrix (5) and Grey Level Dependence Matrix (14). All the reported features, except Shape-based, will be calculated on either the original and derived image obtained applying Wavelet and Laplacian of Gaussian filters.The same extraction will be done from a primary GTV of 94 head and neck patients, to confirm phantom results.The features will be extracted using different bin width (5,10,15,20,25 HU), resampling (original voxel dimensions, 1x1x1, 2x2x2, 3x3x3 $mm^3$) and interpolation algorithm (linear, spline and nearest neighbor interpolation). Moreover the variation of feature values in presence of metal artifacts will be evaluated. In order to evaluate correlation between robust radiomic features and treatment response, we will retrospectively evaluated 79 planning CT of oro- and naso- pharyngeal cancer patients treated from 2010 to 2018 (Table 1), with a mean follow-up of 37.3 months (range 6 - 95 months).

Results: This project is actually underdeveloping, therefore results are not already available.We expect to be able to reduce the number of features to the most reproducible, robust and non-redundant ones.

Conclusions: Correlation between radiomic features

and local recurrence will be investigated, in order to create a prognostic model including also dosimetric and clinical data.

**Table 1.**

| | |
|---|---|
| **Sex** | |
| M | 66 (83.5%) |
| F | 13 (16.5%) |
| **Median age at diagnosis (min-max)** | 63 (38 - 84) |
| **Smoking status (on 70 pts)** | |
| Former | 50 (71.4%) |
| Current | 33 (47,1%) |
| Never | 20 (28,6%) |
| **Oropharinx staging (62 of 79 pts)** | |
| T1 | 0 |
| T2 | 21 |
| T3 | 13 |
| T4 | 28 |
| N0 | 6 |
| N1 | 7 |
| N2 | 45 |
| N3 | 3 |
| Nx | 1 |
| **M0** | 62 |
| **Nasopharinx staging (17 of 79 pts)** | |
| T1 | 10 |
| T2 | 3 |
| T3 | 3 |
| T4 | 1 |
| N0 | 7 |
| N1 | 3 |
| N2 | 3 |
| N3 | 4 |
| Nx | 0 |
| **M0** | 17 |
| **Therapeutic combination** | |
| Radiation alone | 13 |
| RT-Concomitant CHT | 59 |
| RT-immunotherapy | 5 |
| Neoadjuvant CHT + RT-immunotherapy | 1 |
| Neoadjuvant CHT + RT-CHT | 1 |
| **Neck dissection after IMRT** | |
| Yes | 7 (8,9%) |
| No | 72 (91,1%) |
| **Vital status** | |
| Alive | 52 (65.8%) |
| Deceased | 27 (34.2%) |
| **Local control** | |
| Yes | 63 (79,7%) |
| No | 16 (20,3%) |
| **Time to local failure (mean (min-max))** | 8 (2-21) |

**PO197**

## INTRADUCTAL PROSTATE CARCINOMA (IDC-P): HISTOPATOLOGICAL ANALYSIS OF EGR AND P63

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Aim: Intraductal Prostate Carcinoma (IDC-P) is considered an intraductal spread of malignant cells into the otherwise benign ducts and is strongly associated with high Gleason Score (GS), large tumor volume, advanced disease stage, extraprostatic extension and increased risk of recurrence. TMPRSS2-ERG is the most common erythroblast transformation-specific (ERG) gene fusion in prostate cancer and represents an early event in prostate cancer progression; P63 is a homologue of the p53 gene and is a reliable marker of basal cell layer. Both ERG and P63 expression can be considered as IDC-P biomarkers. Objective of this retrospective analysis was to asses correlation between IDC-P and ERG/P63 overexpression with adverse clinical outcome.

Methods: We evaluated the presence of IDC-P in 79 patients with prostate cancer treated at Pisa University Hospital between 2004 and 2015, its putative correlation with molecular features (ERG and p63 expression) and the major prognostic factors (high GS, positive surgical margin, extraprostatic extension, seminal vesicle invasion, lymph node metastasis). All patients were treated with adjuvant (63,3%) or salvage (36,7%) radiotherapy. Treatment was performed using a Varian TrueBeam® platform and 6-MV photons. RapidArc® system was used for treatment planning. PTV was prostatic lodge in 45 patients, prostatic lodge and whole pelvis in 22; 12 patients were submitted to M1 lymph node boost. All the patients with whole pelvis PTV were treated with hormonotherapy too. Moderate hypofractionation schedule (28 fractions of 225 cGy, 230 cGy, 235 cGy) was chosen in 86,4% of patients; remained 13,6% was treated with conventional fractionation. Mean EQ2 dose was 70 Gy (range 68-74).

Results: At data analysis median follow up was 52,8 months (range 20,3-87,0). After a stratification according to D'Amico risk class, presence/absence of recurrence and presence/absence of IDC-P, all treated patients were analysed for biochemical control (PSA) after radiotherapy. Sixteen out of 34 with ERG hyperexpression experienced disease progression, whereas 4 out of 45 patients without IDC-P did not ($P<0.001$).

Conclusion: In our study, IDC-P and high ERG expression was associated with aggressive disease and adverse clinical outcomes (biochemical and disease recurrence). If confirmed in other studies, this feature can be considered as a risk factor in the decision of prostate cancer treatment.

**Table 1.**

## PO198

### CIRCULATING BLOOD CELLS AS BIOMARKER FOR PATIENT WITH GLIOBLASTOMA

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Purpose: In this study, we investigated the role of neutrophil to lymphocyte ratio (NLR) as a prognostic factor in patients with Glioblastoma (GBM) who were treated with upfront concomitant radio-chemotherapy (RCT) at Pisa University Hospital. Moreover, we evaluated how the change of platelet count pre RCT and post RCT, according with MGMT methylation status, can be related with overall survival (OS).

Methods: 50 patients treated from 2010 to 2018 (median age 59 ,range 33-85,M:F 1:1), with pathologically proven GBM, MGMT methylation status evaluated (32 out of 50 MGMT methylated) and KPS >70 were included in this analysis. All patients underwent upfront RCT with concomitant temozolomide. Neutrophili and lymphocyte counts were extracted from pathology laboratory records and were obtained for each patient at baseline. Platelet count was collected at baseline and after RCT(until two weeks from the end of the treatment). Cut-off value was determined as 2,95 for the pre-CRT NLR.

Results: We evaluated the platelet drop, observing higher significative fall of platelet count. Median difference in platelet count were -104000 and -44500, in methylated and unmethylated group, respectively (p=0,014). Our results were not associated with a significant improvement of OS. Patients were also grouped as follows regarding pre-CRT NLR: group A, pre-CRT NLR ≤ 2,95 and group B, pre-CRT NLR > 2,95. The OS rates showed significant differences between the NLR groups (OS median: 21 months vs. 12 months, for group A and B respectively, p=0.003).

Conclusion: NLR value has been evaluated such as a prognostic factor in many different cancers. Our study shows that a NLR value >2,95 at baseline is associated with poorer long-term survival. It has been reported in literature that platelet fall is a promising biomarker in delineating patients with better prognosis. We have seen that there was significant difference between the methylated and the unmethylated group about the platelet drop after RCT, but we didn't find any association with OS.

## PO199

### SARCOPENIA AS A PROGNOSTICATOR IN LOCALLY ADVANCED OR METASTATIC NSCLC ELDERLY PATIENT

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Aim: To evaluate sarcopenia using psoas muscle on CT imaging at the time of diagnosis as a prognosticator in elderly patients with locally advanced or metastatic NSCLC undergoing chemotherapy or radio/chemotherapy.

Methods: We included elderly patients (over 65 years old) with NSCLC undergoing palliative radiation therapy at our Department betweeen january 2010 and december 2017. We contoured on first diagnosis CT the volume of right and left psoas volume from the cranial border of L4 till the caudal border of L5. We calculated the median volume between the sides and we divided the median volume for the height of the muscle (Median Area, MA). We analyzed overall survival (OS) with these parameters (using the median value as cut-off) and the known prognosticators (age, ECOG, stage, previous surgery, number of metastases), with Kaplan Meier method (univariate) and Cox Regression Analysis (multivariate).

Results: We included 86 patients (63 males and 23 females), with a median age of 72 years (mean 73 years, range 65-90 years). At univariate analysis of OS, the significant parameters were the ECOG (p<0,001), the MA (p:0,011), previous surgery (p:0,001), number of metastases (p<0,001). At multivariate analysis, only ECOG (p<0,001), MA (p:0,031), number of metastases (p<0,001) and previous surgery (p:0,002) resulted significant.

Conclusions: Psoas muscle in elderly NSCLC patients could represent an independent prognosticator of survival, and could help to stratify the patient's prognosis.

PO200

## CLINICAL AND MOLECULAR CHARACTERISTICS OF HIGH-RISK DIFFERENTIATED THYROID CANCERS: RESULTS OF A SINGLE-CENTER EXPERIENCE

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Background: Differentiated thyroid carcinoma (DTC) usually carries an excellent prognosis, with only a minority of cases having a poor clinical outcome. A thorough knowledge of the clinical, pathological and molecular features of aggressive DTC is essential to improve the diagnostic process and ensure tailored therapy and follow-up protocols.

Materials and Methods: An analysis of the BRAF, RAS, TP53, PTEN and PIK3CA genes and TERT promoter was conducted in 105 high-risk DTC (tumors >40 mm in size and/or metastatic) and 144 low-risk DTC, comparing the clinical outcomes and molecular features of the two groups. Results: Within the high-risk group, patients whose cancers were large and/or metastatic had a worse outcome than those with large but non-metastatic cancers. The former had persistent disease or died during the follow-up in 64% and 85% cases, as opposed to 12% of the latter; they were more likely to undergo a second treatment (67% and 85% as opposed to 8%); and they had a shorter disease-free survival (DFS). High-risk DTC patients as a whole had a worse clinical outcome than low-risk patients: here again, they were more likely to have a second treatment and they had a shorter DFS. Metastatic DTC had a higher prevalence of TERT promoter mutations than large non-metastatic tumors (27% vs 14%, p=0.0398). High-risk DTC was associated with a lower frequency of BRAF (27% versus 61%), and a higher frequency of TERT promoter (21% versus 3%) and RAS mutations (11% versus 2%) than low-risk DTC. On multivariate analysis, only lymph node involvement, distant metastases and TERT promoter mutations emerged as independent predictors of a worse outcome. Conclusions: Patients with high-risk tumors, particularly if metastatic, had the worst outcomes. TERT mutations, lymph node involvement and distant metastases proved to be independent predictors of a poor prognosis. No link emerged between the other molecular events considered and patients' clinical-pathological features.

PO201

## PRO-DIFFERENTIATING AND 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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Aims: To characterize the ability of PXD-101 (Belicostat) as radiosensitizer for rhabdomyosarcoma treatment.

Methods: PXD-101 alone or in combination with radiotherapy (RT) was investigated in rhabdomyosarcoma (RMS) cells PAX3/FOXO1 fusion protein positive (RH30) or negative (RD).

Results: *In vitro*, a low concentration of PXD- 101 induced reactive oxygen species (ROS), double-strand breaks (DSBs) and up-regulated mad2, marker of defects in mitotic spindle assembly. PXD-101 concomitantly induced intrinsic caspase-mediated apoptosis, and G2 arrest. Surviving RMS; i) reduced their migratory/invasive capacity reducing the expression of c-Myb, beta-catenin and Integrin-beta1; ii) did not formed enriched-in-cancer-stem-like cells rhabdosphere, and down-regulated the expression of CD133, CXCR4, Nanog and Oct-3/4 stem cell markers; iii) acquired a myogenic-like phenotype, promoting the expression of myogenic-related markers in RD; iv) inhibited ERKs and AKTs. PXD-101 radiosensitizes by inhibiting the ability of RMS to trigger checkpoint activation, detoxifies from ROS accumulation and repair DSBs. Notably, PXD-101 transcriptionally and post- transcriptionally affected c-Myc expression, keymaster regulator of rhabdomyosarcomagenesis and radioresistance. Combining PXD-101 and RT showed cytotoxic effects in vivo on tumour xenografted mice.

Conclusions: Taken together, our data suggest that inhibiting HDACs by PXD-101 might represent a potential pro- differentiating therapeutic strategy that could potentiate the action of anti-mitotic chemotherapies and certainly that of RT.

## PO202

### CONSOLIDATION THERAPY WITH DURVALUMAB AFTER RADICAL CHEMORADIATION TREATMENT IN STAGE IIII, LOCALLY ADVANCED, NSCLC: A PRELIMINAR ANALYSIS ON THE TOXICITY PROFILE AND THE REAL LIFE IMPACT

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Aims: The PACIFIC trial investigated consolidation treatment with Durvalumab after radical chemoradiation treatment (CCRT) in patients with unresectable, stage III, NSCLC, PDL1 >1%, who did not progressed after CCRT. The relevant overall survival benefit obtained in the Durvalumab arm sensibly influenced the standard management of the patients treated with a curative intent. The aim of this study is the preliminary evaluation the critical issues related to the treatment with Durvalumab as consolidative immunotherapy.

**Table 1. Characteristics of patients.**

| | *N (%)* |
|---|---|
| Age | |
| ≤ 65 yo | 6 (46,15%) |
| > 65 yo | 7 (53,84%) |
| Comorbidity Index | |
| ≤ 4 pt. | 10 (76,9) |
| > 4 pt. | 3 (23,1%) |
| COPD | |
| NO COPD | 2 (15,4%) |
| GRADE I | 6 (46,2%) |
| GRADE II | 3 (23,1%) |
| GRADE III | 2 (15,4%) |
| GRADE IV | 0 |
| Stage (TNM VIII° ed.) | |
| TxN2 | 2 (15,4%) |
| T0N2 | 1 (7,7%) |
| T1bN2 | 2 (15,4%) |
| T2N2 | 3 (23,1%) |
| T3N2 | 3 (23,1%) |
| T2N3 | 1 (7,7%) |
| T4N2 | 1 (7,7%) |
| CHT | |
| 4 cycles | 4 (30,8%) |
| 5 cycles | 5 (38,5%) |
| 6 cycles | 1 (7,7%) |
| on going | 3 (23,1%) |
| PDL1 status | |
| unknown | 2 (15,4%) |
| < 1% | 1 (7,7%) |
| 1-50% | 8 (61,5%) |
| ≥ 50% | 2 (15,4%) |

Methods: From September 2018 to date, all the patients with unresectable, stage III, NSCLC treated in a single Institution with CCRT were evaluated. The ones eligible to Durvalumab as maintenance treatment were selected for this analysis. Toxicity profile (CTCAE 4.0) and the issues related to inclusion criteria for (inserire frequenza e dose es. weekly ….mg ) Durvalumab were explored. The study is still ongoing.

Results: Thirteen patients were treated with CCRT. All patients (60 Gy/2fr), 11 with concomitant and 2 with sequential platinum-based chemotherapy. Treatment and patients characteristics are summarized in Table 1. The response assessment with CT scan was done after a median time of 41,5 days (range 29-47) from RT. All patients had partial response. Six patients are still having Durvalumab. Three pts were ineligible to Durvalumab because PDL1 unknown (2) or <1% (1). Two patients are still on CCRT treatment and two are waiting for restaging. None patients met the other exclusion criteria: disease progression, radiation pneumonitis and active or previous autoimmune disease. After a median number of 5 (range 1-17) post CCRT Durvalumab, only one patient had an oligo-progression (after 16 cycles). G2 hypothyrodism events (12° and 13° Durvalumab) were registered.

Conclusions: The consolidation immunotherapy has changed the prospective of survival for pts with unresectable, stage III, NSCLC treated with the radical CCRT. Durvalumab is the first immune checkpoint inhibitor demonstrating a positive impact on PFS and OS in this clinical setting. Further investigations should show the possible interaction between immunotherapy and CCRT in terms of safety and tolerability. These preliminary results underline the role of PDL1 status as main limit to Durvalumab program recruiting. Even if these preliminary results seem positive, longer follow up is necessary to better define the safety profile and to collect much more real life data.

## PO203

### RELAPSED GLIOBLASTOMA, STORY OF AN ALMOST 10 YEARS LONG TREATMENT. A CASE REPORT

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Aims: Although glioblastoma multiforme (GBM) is the most common malignant primay brain tumor in adults, it is still associated with a poor prognosis and few patients are still alive 5 years after the diagnosis. The optimal therapeutic strategy for those cases is unclear.

Methods: We described the case of a 62 years old female that in September 2010 had several days of simil-flu sintoms and then accessed the ED for a syncopal episode. Emergency CT showed the presence of an hemorrhagic lesion of the right temporal hemisphere. A right temporal, intra assial, subcortical Glioblastoma

multiforme (GBM, IV WHO, IDH1 and IDH 2 wild tipe, MGMT- unmethylated, 1p/19q non codeleted) was diagnosed in October 2010 and treated with surgical debulking plus radiotherapy (60 Gy in 30 fr) and chemotherapy (Temozolomide 75 mg/m$^2$/day) between January and February 2011. The treatment with temozolomide was not well tollerated during radiotherapy for the apparence of piastrinopenia G4. The patient didn't assume sequential temozolomide in the following months because of hematologic toxicity. GBM relapsed in July 2011; the patient underwent a new surgery followed by chemotherapy. We used fotemustine and bevacizumab (50 mg/m$^2$ + 7,5 mg/m$^2$ Q14) from July 2011 to 2014, when we stopped fotemustine for hematologic toxicity. From 2014 until the present we decided to use bevacizumab as single agent (7,5 mg/m$^2$ Q21).

Results: The patient survived 8 years after the relapsed of the desease with 100% KPS and stable trimestral MRI.

Conclusion: We report on the successful long term treatment on a relapsed GBM, IV WHO, IDH1 and IDH 2 wild tipe, MGMT- unmethylated, with 8 years story of bevacizumab therapy, with and without fotemustine. The therapy of relapsed glioblastoma is still unclear: a good use of bevacizumab could be linked to the research of appropriate candidates, maybe through the identification of specific GBM characterisation and biomarkers

**PO204**

## DURVALUMAB AFTER CHEMORADIOTHERAPY WITH VMAT TECNOLOGY IN LOCALLY ADVANCED NSCLC (BASED ON PACIFIC STUDY CRITERIA): FEASIBILITY AND OUR INITIAL EXPERIENCE

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Aims: The standard of care for patients with a good performance status and unresectable stage III non-small-cell lung cancer (NSCLC) is chemoradiotherapy (CTRT). Most patients with locally advanced NSCLC, unresectable, have disease progression despite definitive CTRT. However, the median PFS among patients who have received CTRT is poor (approximately 8 months), and only 15% of patients are alive at 5 years. Pacific trial, phase 3 study, has shown a PFS benefit with use of anti-PDL1 antibody durvalumab as consolidation therapy in patients with stage III NSCLC who did not have disease progression after CTRT. Durvalumab is a selective, high-affinity, human IgG1 monoclonal antibody that blocks PDL1 binding to programmed death 1 and CD80, allowing T cells to recognize and kill tumor cells.

Methods: Eligible patients had histologically or cytologically documented locally advanced, unresectable NSCLC according to the Staging Manual in Thoracic Oncology, v7, of the International Association for the Study of Lung Cancer. Recently in our center 2 male patients respectively of 45 and 61 years had received two cycles cisplatin (days 1 8 29 36) and etoposide (days 1-5 and 29-33) at a dose of 50 mg/m$^2$ both drugs, concurrently with definitive radiation therapy. 60 Gy in 30 fractions with volumetric modulated arc therapy VMAT in which the mean dose to the lung was less than 20 Gy, V20 was less than 35%, or both. CBCT according to the practical guidelines for the use of IGRT by AIRO Piedmont-Liguria. At the onset of durvalumab both patients had no grade 2 or higher unresolved toxic effects (according to Common Terminology Criteria for Adverse Events [CTCAE]); and grade 2 or higher pneumonia from the previous chemoradiotherapy. Patients started durvalumab at a dose of 10 mg per kilogram of intravenous body weight every 2 weeks as consolidation therapy for up to 12 months. Another male patient aged 69 started durvalumab but for age and PS was sent for sequential CTRT treatment with cisplatin (35 mg/m$^2$) – vinorelbine 25 mg/m$^2$ and subsequent radiotherapy at the same dose and criteria of concomitant treatment. Results In our initial experience we can see a good tolerance and feasibility of using durvalumab after CTRT for advanced NSCLC. For our patients then it will be important to evaluate DFS and OS over time and surely enlist new cases.

Conclusions: This is a new standard of care for unresectable local-regionally advanced NSCLC. Durvalumab has been shown to increase survival in locally advanced NSCLC and well tolerated. Certainly the use of technologies such as VMAT and IGRT allow to contain side effects and complete integrated treatments.

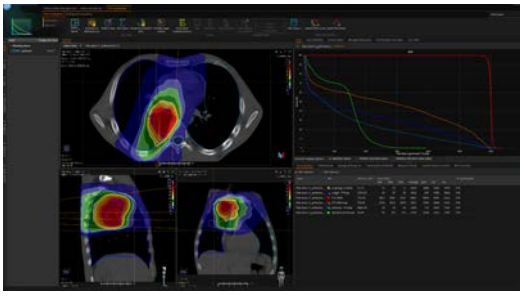

**Figure 1.**

PO205

## GERIATRIC-ONCOLOGY ASSESSMENT FOR COMPLEX CANCER PATIENTS MANAGEMENT IN RADIATION ONCOLOGY UNIT

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Aims: As result of an increasing life expectancy, the incidence of cancer cases diagnosed in the older population is rising. By 2030 approximately 70% of all cancer will diagnosed in people older than 65 years. New technologies associated with aging related changes and patients' needs have led to a new scenario in front of which we move on. On this basis in 2017, the Gemelli-ART (Advanced Radiation Therapy) Center of the A. Gemelli IRCCS, started a cahoots with a onco-geriatrician. The aim of this study is to evaluate the impact of geriatric forma mentis in the management of complex patients admitted to a Radiation Oncology Unit.

Methods: This is an observational study of complex patients admitted to Radiation Oncology Unit between April 2016 and December 2018. The complex patient was defined as the aged >80, and/or affected by multiple comorbidities, polypharmacy and severe toxicity, or younger admitted through the ER for severe toxicity, sepsis, severe acute events. All patients were assessed by a geriatric assessment, followed by an onco-geriatrician during their treatment and their therapies were tailored and drawn on their features. The complex patients admitted between April 2016 and December 31st 2016 were considered as comparing sample. The patients admitted from January 1st 2017 and December 31st 2018 were intervention sample.

Results: The complex patients admitted to the Radiation Oncology Unit raised from 93 in 2016 to 228 in 2018 (+145%). The total average Unit length of stay was slightly decreased: 5,6 days in 2016, 5,5 days in 2017 and 2018. The average unplanned complex Unit length stay was substantial reduced: 20,6 days in 2016 to 13,2 days in 2018 (36% less). 66,16% of the complex patients underwent to treatment. Among all the patients admitted, the treatment suspension rate was the 17,91%. The suspension rate was 3% in the 80s planned admitted patient (FIT) versus 47% in the unplanned admitted patients. Mortality ratio and reason for hospitalization were considered in the data analysis.

Conclusions: Our data suggest the utility of the geriatrician's expertise in a Radiation Oncology Unit to personalise the patient's treatment. The multidimensional approach allowed to treat an increasing number of complex patients with standard treatment: 66,16% of the complex patients underwent to treatment, with a curative goal in the 45% cases, to avoid undertreatment of fit but complex patients and overtreatment of younger unfit and frail patients.

PO206

## LUNG ABSCOPAL EFFECT AFTER RADIATION THERAPY (RT) FOR BRAIN METASTASES OF NON-SMALL CELLS LUNG CANCER (NSCLC): OUR EXPERIENCE

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Aims: In recent years, immunotherapy and target therapy have become an integral part of the treatment of many cancers, including non-small cell lung cancer (NSCLC), though unfortunately not all patients treated have durable clinical responses. The aim of this study is to evaluate the lung abscopal effect of immunotherapy and target therapy combined with whole-brain radiotherapy (WBRT) and/or stereotactic radiotherapy (SRT) in patients with brain metastases from NSCLC.

Methods: A total of 12 patients treated in 2018 were included, 2 of which received WBRT, 9 SRT and 1 SRT followed by WBRT. All received radiation therapy (RT) to the brain combined with immunotherapy and target therapy consisting of monoclonal antibodies directed against the programmed death protein-1 (PD-1)/programmed death ligand-1 (PD-L1) immune checkpoint (Nivolumab and Pembrolizumab) and epidermal growth factor (EGFR) tyrosine kinase inhibitors (Afatinib and Gefitinib) also in T790M-mutated (Osimertinib); 5 of them received chemotherapy too. Possible abscopal responses were evaluated in terms of radiographic regression of the lung tumor burden, in particular through a chest computed tomography (CT) 45/60 days after RT, whereas the brain metastases were monitored through a brain MRI at the same time of follow-up. The tumor responses were assessed by the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines and classified into the complete response (CR), partial response (PR), stable disease (SD) and progression of disease (PD).

Results: Regarding the lung disease, 6 patients had a PD, 5 patients a SD and only one patient experienced an apparent abscopal response demonstrated by a CR at the chest-CT. On the other hand, as regards brain metastases response, a PR and a SD were registered among 5 and 6 patients respectively, with a PD occurred only in one patient. The only patient who experienced an apparent abscopal effect received both WBRT and SRT, suggesting that maybe the underlying mechanism is influenced by the RT techniques.

Conclusions: As it is not definite that these observations truly represent the abscopal effect of radiation, further studies with larger cohorts of patients and stricter criteria to control potential confounding factors should be fostered in order to better investigate this

issue, especially to understand how and how much the timing of immunotherapy with respect to RT and the RT technique choice may influence the abscopal effect.

## PO207

### FRACTIONATED BRAIN STEREOTACTIC RADIOTHERAPY WITH CONCURRENT IMMUNOTHERAPY OR TARGET THERAPY: ONGOING RESULTS

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Aims: To evaluate cerebral toxicity and outcomes in patients with brain metastases undergoing concomitant fractionated stereotactic radiotherapy (FSRT) and immunotherapy or target therapy.

Methods: Between January 2018 and March 2019, 28 patients were treated at our center with FSRT for 32 brain metastases. All patients received immunotherapy or target therapy concomitantly to FSRT as follows: 18 (56%) lesions were treated during immunotherapy (Nivolumab, Pembrolizumab, Ipilimumab), 8 (25%) with anti HER2 drugs (Pertuzumab, Trastuzumab, Lapatinib) , 4 with anti EGFR (Iressa, Tarceva) (13%), 2 with antiangiogenetics agents (Bevacizumab)(6%). We considered concomitant treatment all cases where time between radiation and medical therapy was inferior than 15 days. FSRT with volumetric modulated arc therapy (Rapid Arc) was adopted. The treatment occurred after the packaging of a repositionable stereotactic mask and the treatment plan was performed merging CT / RM images. The mean measure of lesion size was 11mm (range 5-32 mm). Gross Tumor Volume (GTV) was expanded of 2 mm to create the Planning Target Volume (PTV). The mean volume of PTV was 7.44 cc (range 0.75-13.41 cc). The total dose to PTV ranged from 24 to 27 Gy in 3-5 consecutive fractions of 5-8-9 Gy each one. All patients underwent a Magnetic Resonance Imaging (MRI) with a contrast enhanced within 4-6 weeks after the end of the treatment and sunsequently every 3 months. Response to treatmente was intended as a reduction or stability in size of the treated lesion. Toxicity was represented by the percentage of perilesional oedema or radiation necrosis induced.

Results: 14/32 lesions showed a complete response, 15 / 32 a partial response to treatment and 3/32 had stable disease. MRI toxicity's evaluation showed reduction of perilesional oedema in all lesions treated and one patient developed radiation necrosis from 12 months to treatment. Three patients died before the first follow up due to systemic disease progression. 1 patient showed relapse of disease who reqested reirradiation.

Conclusions: Our preliminar data confirm efficacy of FSRT and new therapy. FSRT appears to be associated with lower toxicity in this patient setting. Longer follow up and larger series are needed in order to eventually confirm these data.

## PO208

### RADIATION THERAPY TO CHEST-WALL AND SUPRA-INFRACLAVICULAR NODES FOLLOWED BY STEREOTACTIC BOOST TO A RETRO-CLAVICULAR CT-PET POSITIVE NODE, WITH CONCURRENT TRASTUZUMAB-BASED IMMUNOTHERAPY IN A YOUNG WOMAN AFFECTED BY LOCALLY ADVANCED BREAST CANCER: A CASE REPORT

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Aims: Evaluate clinical response and safety of a stereotactic boost to a CT-PET positive retro-clavicular node following locoregional radiotherapy concurrent to a Trastuzumab-based immunotherapy, after mastectomy and nodal axillary dissection and adjuvant chemo-immunotherapy in a young woman affected by a locally advanced (IIIC stage) breast cancer.

Methods: A 41-years old woman affected by a poorly differentiated right breast infiltrating ductal carcinoma (pT2 pN3a Mx stage, HER2-like phenotype), undergone to adjuvant chemotherapy with epirubicin and cyclophosphamide (4 cycles) followed by Paclitaxel and Trastuzumab (12 weeks), was submitted at the end of chemo-immunotherapy to a CT-PET scan, to assess the suspected presence of liver metastases: the examination has excluded liver metastases, but it has showed an intense uptake of a right retro-clavicular node. Therefore, she has continued the Trastuzumab administration and underwent to concomitant locoregional radiotherapy (right chest wall and supra-infraclavicular ipsilateral nodes) to a total dose of 50 Gy (2 Gy/fx., 5 days a week), followed by a 10 Gy stereotactic boost on CT-PET uptake (GTV), added by a 3 mm isotropic margin The treatment has been performed by LINAC Sinergy Elekta Medical System, with photon beams single isocenter technique; the boost was administered by 10 MV photon beam stereotactic technique (9 coplanar fields). The treatment plan has been developed by Oncentra Masterplan TPS, performing image fusion between CT-simulator scan (volumetric scan of 5 mm thickness) and CT PET. The treatment plan respected entirely the OAR dose constraints provided at our institution. The setup verification has been performed by CBCT daily during the first 3 days, then weekly, whereas, during the boost administration, the verification has been day-to-day. The patient has been assessed by clinical exam and blood count, recording in medical file the RTOG toxicity degree. Following the radiation

therapy, the patient has continued Trastuzumab administration to the planned end (12 months).

Results: The radiation treatment has been completed at the prescribed dose, without interruption. Only G2 supraclavicular skin toxicity was recorded, quickly and completely resolved with the appropriated local and systemic therapy. There was no hematological toxicity. The patient has been re-assessed with clinical and instrumental examination at 3, 6 and 9 months from the end of radiation therapy. A CT-scan performed at 3 months did not show the retro-clavicular node. A CT-PET scan done at 6 months has evidenced the complete disappearance of retro-clavicular uptake; nevertheless, it showed pulmonary and skeletal progression. Thereby the patient, following a medical oncology assessment, has been subjected to a TDM-1 based treatment and radiotherapy on a skeletal critical lesion. A new CT-PET scan performed at 9 months from the end of locoregional radiation therapy remained negative on chest wall and supraclavicular region but showed further pulmonary and mediastinal progressive disease. No radio-induced late toxicity is demonstrated to date.

Conclusions: The locoregional radiation therapy followed by stereotactic boost on CT-PET uptake was shown be effective, determining the complete and durable response of retro-clavicular node. It has been showed safe and well tolerated, and near one year after did not result, to date, in any late collateral effects.

**PO209**

## STEREOTACTIC RADIOSURGERY PLUS IMMUNOTHERAPY OR TARGETED THERAPY FOR BRAIN METASTASES FROM NSCLC

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Aims: Data regarding the interactions between Immunotherapy (IT) or Targeted Therapy (TT) and Radiosurgery (RS) for the treatment of brain metastases (BM) are not available. Aim of the present study is to evaluate the efficacy and safety of RS delivered in association to IT or TT for BM from NSCLC.

Methods: We retrospectively analysed data from NSCLC patients with BM treated with RS plus IT or TT. The systemic treatments were administered within the 4 weeks before or after brain RS. During follow-up, all the patients underwent contrast-enhanced brain MRI every 3 months for the first year after RS and every 4 months thereafter. Clinical toxicity was reported according to CTCAE v.4. We analysed outcomes in terms of Local progression-free survival (L-PFS), distant-PFS (D-PFS) and Overall Survival (OS).

Results: We selected 30 patients treated at our centre from 2011 to 2018: 16 women (53%) and 14 men (47%) with a median age of 63 years (range 51-82). All patients were affected by adenocarcinoma; twelve of them (40%) were metastatic at diagnosis and among these 10 patients (33%) had BM. The median number of treated lesions was 3 (range 1-11). All patients were treated in a single fraction: 21 patients (70%) with a total dose of 24 Gy, the others with a total dose of 18 or 21 Gy. The most used drugs were Pembrolizumab (13.4%), Erlotinib (36.6%) and Gefitinib (13.4%). We also stratified patients according to timing: 10 patients underwent RS before starting IT or TT, while 20 after they have already started a systemic treatment. After amedian follow-up of 12 months no symptomatic radionecrosis or G3/G4 toxicity were observed. Median L-PFS and D-PFS rate at 1 year were 82% and 44%, respectively. According to timing patients who underwent RS before starting IT or TT showed a better L-PFS [HR 0.5 (CI 95% 0.06-3.8)] and D-PFS [HR: 0.97 (CI 95% 0.76-8.06)] but a worse OS [HR 1.29 (CI 95% 0.32-5.12)]. Unfortunately these results were not statistically significant.

Conclusions: RS for BM may be safely associated with IT or TT in patients with NSCLC. Prospective studies are needed to confirm our results.

**PO210**

## REAL-LIFE CLINICAL EVIDENCES IN IRRADIATED ADVANCED OR METASTATIC NSCLC TREATED WITH PD-1/PD-L1 INHIBITORS

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Aims: Immunotherapy (IT) with immune checkpoint inhibitors (ICIs) revolutionized outcomes in advanced and metastatic non-small-cell lung cancer (NSCLC). Aim of this study is to sum up the therapeutic effect and safety of PD-1/PD-L1 inhibitors in patients with advanced or metastatic NSCLC in a real-life setting, including patients underwent radiotherapy (RT) before or during the ICIs.

Methods: Consecutive patients with advanced or metastatic NSCLC treated with anti PD-1/PD-L1 between May 2017 and January 2019 were included. Patient demographics, clinical indicators, treatment modalities, adverse event and RT data were collected. Toxicity was evaluated according to the common terminology criteria for adverse events (CTCAE) version 4.0. The efficacy evaluation was divided in: complete

response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). Objective response rate (ORR) was defined as the percentage of patients with CR+PR among the patients, and the disease control rate (DCR) was defined as the percentage of patients with CR+PR+SD among all patients.

Results: Thirty-four patients were treated, median age was 66 years (range: 48-82), mostly male (64.7%), current or former smokers (88.2%) with Eastern Cooperative Oncology Group (ECOG) Performance Status score <2 (82.3%). Eighteen (53%) patients had stage IV disease. Sixteen (17.6%) patients received IT as first-line treatment, 20 (58.8%) as second-line and 8 (2.5%) as third-line and above. About the type of drug used, 21(61.7%) patients were treated with nivolumab, 12(35.3%) with pembrolizumab and 1(2.9%) with atezolizumab. Mean number of IT cycles was 15 (range: 1-44; for a total number of 511 administration performed) with ORR of 28.2% and DCR of 69.2%. Radiotherapy was performed in 26/34 (76.5%) patients on thoracic disease or metastatic sites. Among all patients, we observed 1/34 (2.9%) G3 hepatic toxicity, 2/34 (5.8% ) G2/G3 colitis and 1/34 (2.9%) G3 renal toxicity. Among the 26 patients who received any RT, we observed 3/26 (11.5%) G2/G3 pneumonitis and 1/26 (3.8%) G4 pneumonitis.

Conclusions: In a real-world setting, including irradiated patients, the therapeutic effect and tolerance of PD-1/PD-L1 inhibitors are considerable. Therefore, some criteria should be identified to correlate with time of specific toxicities occurrence, to better predict treatment outcomes in a scenario of personalized medicine.

## PO211

## TAILORED TREATMENT OF EARLY BREAST CANCER IN ELDERLY PATIENTS: A SYSTEMATIC REVIEW

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Aims: To depict the management of elderly patients with early stage breast cancer , focusing on the role of systemic therapies (endocrine therapy-ET, chemotherapy, novel agents) and radiation therapy (RT), through a review of the available literature.

Materials: The review was conducted by searching English medical papers in 1990-Apr 2019. Key words were: elderly, breast cancer, chemotherapy, radiation, adjuvant. A total of 580 articles were initially recluted but 66 papers were selected.

Results: Several studies have evaluated the possibility of omitting the RT (see Table 1) but higher LR rates without impact on OS were observed in all studies when RT was excluded. Technological improvements (IMRT, VMAT, HDBT) are very useful in order to reduce cosmetic outcome and improve quality of life of frail patients. The optimal sequence of ET, concomitant or sequential to RT, is under investigation, and it is questioned the possible choice of prolonged therapy after standard 5 years. Data regarding chemotherapy suggesting better outcomes in endocrine non responsive breast cancer. CMF regimen is considered the standard protocol, although age related mortality resulted increased. In a large meta analysis (limited data in elderly) taxane and/or anthracycline-based regimens reduced breast cancer mortality by about one-third. In neoadjuvantsetting, chemotherapy showed a lower ratio of pathological complete response in elderly vs youngers, but triple negative breast cancer patients showed a good prognosis regarding OS, comparable to younger patients. The risk of cardiotoxicity seems to be age related so the use of trastuzumab is very debated. Currently, other anti-HER2 agents (pertuzumab, lapatinib) are used in neoadjuvant setting, but the data on elderly are still premature. Novel molecules are rapidly changing the clinical management of breast cancer patients but are tested especially in locally advanced and metastatic setting. Among these, particulary interesting are inhibitors of CDK4 and 6, Alpelisib (PI3K enzymes mutations), immune checkpoint (PD1, PDL1, CTLA4) inhibitors, atezolizumab. Elderly patients are under-represented in clinical trials, although ageing can be frequently correlated with a decrease in the effectiveness of the immune system.

Conclusions: For frail elderly women, treatment decisions should be individually decided considering geriatric assessment and limited life expectancy and tumour characteristics.

**Table 1.**

| WBRT vs no RT | | | | | | |
|---|---|---|---|---|---|---|
| *References* | *patients* | *age* | *stage* | *treatment* | *Relapse LR (%)* | *OS (%)* |
| Fyles 2004 | 386 | ≥50y | low risk (T1-2 N0) | WBRT+TMX | 0,5 | |
| | 383 | | | TMX alone | 7,7 | |
| Livi 2005 | 472 | 60-92y | low risk | surgery + RT | 3,4 | |
| | 759 | | | surgery | 10,6 | |
| Livi 2006 | 917 | ≥65y | all | surgery + RT | 9,7 | 65,4 |
| | 583 | | | surgery | | 72,4 |
| Troung 2006 | 4836 | 50-89y | T1-2, N0-1, M0 | surgery + RT | 3 | 72 |
| | | | | surgery | 9 | 90 |
| Potter (ABCSG) 2007 | 414 | 66 | low risk | WBstboost | 0,6 | 97,9 |
| | 417 | | | no RT | 7,7 | 94,5 |
| Hughes (CALGB) 2004-201 | 636 | ≥70y | stage I | WBRT | 2 | 67 10yy |
| | | | | no RT | 9 | 66 10yy |
| Kunkler (Prime II) 2015 pt | 658 | ≥65y | low risk | WBRT | 1,3 | 93,9% 5y |
| | 668 | | | no RT | 4,1 | |
| Nagar 2017 | 4460 | ≥70y | early | WBRT | | 71.5% 100 mth |
| | 1910 | | | no RT | | 51.3% 100 mth |
| Herskovic 2018 | 51635 | ≥65y | T1-T2N0M0 Her neg | RT (WBRT, SBRT...) | | 93.0% 5y |
| | 9760 | | | no RT | | 83.6% 5y |
| Goldberg 2019 | 1964 | ≥65y | stage I | surgery+RT | 0,9 | 99 |
| | 1325 | | | surgery+RT+ET | 1,4 | 98 |
| | 719 | | | surgery+ET | 3,1 | 97 |
| | 1068 | | | surgery | 9,4 | 89 |

**PO212**

## ASSOCIATION BETWEEN IMMUNOTHERAPY CONCOMITANTLY WITH PALLIATIVE RADIOTHERAPY IN METASTATIC PATIENTS: REAL-LIFE REPORT OF TOXICITY IN A MONOISTITUTIONAL CASE SERIES

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Aim: To assess the safety of the association of radiotherapy (RT) and systemic treatments with immunotherapy drugs to treat cancer patients in palliative setting.

Methods: A retrospective analysis included consecutive patients treated with palliative RT, and at least one line of immunotherapy treatment between June 2017 and December 2018 was performed. Immunotherapy treatments were defined concomitant when the systemic drug was not suspended during radiotherapy or shifted less than 2 weeks.

Results: 42 patients were included. They had 44 palliative RT treatments. RT was delivered with a different fractionation schedules (10 patients 4Gy x 5; 12 patients 3Gy x10; 11 patients 8Gy x 3; 7 patients 5Gy x 3; 4 patients 8Gy x 1) concomitantly with different immunotherapy drugs (anti PD-1; PDL-1; CTLA-4; anti-IOS). The majority of patients were affected by metastatic NSCLC (20 cases – 47%) and most frequent palliative site of RT treatment was bone (29 patients – 69%). No acute grade ≥3 toxicity was reported in the whole cohort. Late grade ≥3 toxicities only occurred with 2 cases of pneumonitis in nivolumab patients.

Conclusion: In our experience, concomitant association of immunotherapy drugs and palliative RT did not seem to increase toxicity expected from separate treatments. Prospective studies are needed to better characterize the toxicity of each association.

**PO213**

## PROTON BEAM THERAPY FOR PEDIATRIC CNS TUMORS: AN OVERVIEW OF ONGOING TRIALS

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Aims: Radiotherapy (RT) represents a fundamental approach in the multimodal management of pediatric central nervous system (CNS) tumors and modern technologies are improving the dose-sparing of developing normal tissues with the aim to reduce the risk of late toxicities and secondary malignancies.Proton Beam Therapy (PBT) could lead to achieve these results due to the physical characteristics of protons.In this work we provide an overview of the ongoing trials which are evaluating the role of PBT in this setting.

Methods: On 6th May 2019 we searched on clinicaltrials.gov website the following keywords: "Pediatric CNS tumors" and "Proton beam therapy".We specifically included studies enrolling only pediatric patients and we excluded studies in suspended,terminated,withdrawn or unknown status.

Results: Our search provided nine trials.Among them, three were in recruiting status and six were active but not recruiting.Centers in the United States were the major investigators.Two studies had Results: the NCT00105560 trial confirmed that PBT for medulloblastoma had similar survival outcomes compared to conventional RT, with acceptable toxicity; the NCT00602667 study – which is evaluating a risk-adapted approach to reduce radiation exposure in young children with medulloblastoma – suspended the option of consolidative PBT in intermediate-risk patients and continued focal photon-RT. The NCT01180881 and the NCT02559752 trials are assessing neurobehavioral functioning and neurocognitive performance after PBT, respectively.Information on patients' quality of life after PBT (also for pediatric non-CNS tumors) are being collected in the NCT01115777 study.The NCT03281889 trial is studying bone spine-sparing PBT in pediatric craniospinal radiation with the aim to reduce the growth-decline.Acute and late toxicities of PBT craniospinal irradiation, as well as survival outcomes and treatment efficiency, are also being evaluating in the NCT01063114 trial.Similarly, the NCT01067196 trial is studying late effects and survival outcomes of PBT for CNS tumors.Finally, the NCT03696355 trial is assessing the antitumor activity of GDC-0084 in patients with diffuse pontine/midline gliomas and its combined effects with PBT/RT.

Conclusions: Preliminary results suggest that PBT may represent an alternative to photon-treatments for pediatric CNS tumors, especially for medulloblastoma.Confirms from ongoing prospective studies are necessary to clearly define PBT effectiveness and safety.

## PO214

### CAVEOLIN-1 SUSTAINS HUMAN EMBRYONAL RHABDOMYOSARCOMA RADIORESISTANCE BY RESTRAINING RADIATION-INDUCED ROS ACCUMULATION, G2/M SYNCHRONIZATION AND IMPROVING DOUBLE STRAND BREAKS REPAIR

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Aims: Resistance to ionizing radiation (IR) used by radiotherapy (RT) characterizes rhabdomyosarcoma (RMS), the most common soft tissue sarcoma in children, mainly classified in two major subtypes, embryonal (ERMS) and alveolar (ARMS). The accumulation of Caveolin-1 phosphorylated on tyrosine 14 (pCav-1) improves ERMS aggressiveness and its role in determining radioresistance has been herein investigated.

Methods: Radiations were delivered using an x-6 MV photon linear accelerator and their effects were assessed by performing some analysis.

Results: RD-pCav-1-expressing-cells (RDFO) resulted more radioresistant, as suggested by clonogenic assay and the reduced levels of phosphorylated H2A histone family member X (γ-H2AX), a biomarker of Double Strand Break DNA damage (DSBs), in RT-treated RDFO cells. pCav-1 improved the ability of RD to activate an antioxidant response as indicated by the reduce reactive oxygen species (ROS) accumulation and the increased expression of Nrf2 and related antioxidant enzymes and miRNAs downstream targets. IR did not synchronize RDF0 cells in the most radiosensitive G2/M phase that resulted in arrested in the most radioresistant G1/S phase of the cells cycle. This restrained the activation of intrinsic apoptosis- and senescence-pathway mediated cell death induced by subsequent IR, disposing of cells in a state of reversible cell growth arrest that also improved the activation of the homologous repair (HR) and non-homologous-end-joining (NHEJ) DNA repair pathways and radioresistance-related signaling.

Conclusions: The identification of molecular mechanisms that affect radioresistance may provide insights into therapeutic targets for combating RMS and collectively, these data provide new insights into Cav-1-driven radioresistance of RMS.

## PO215

### MONOINSTITUTIONAL EXPERIENCE ON THE USE OF VOLUMETRIC ARC THERAPY (VMAT) COMPARED TO 3D CONFORMAL RADIOTHERAPY (3D-CRT) IN A PEDIATRIC POPULATION TREATED FOR HODGKIN'S LYMPHOMA

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Purpose: To retrospectively compare the dose distribution to non-targeted tissues in pediatric patients treated for mediastinal Hodgkin's lymphoma (HL) using 3D Conformal Radiotherapy (3D-CRT) and Volumetric Arc Therapy (VMAT).

Methods: Datasets of 52 patients (27 females and 25 males) with median age of 15 years (range 6 -17) were obtained. Thirty and twenty-two patients were treated with 3D-CRT and VMAT, respectively. Low dose (14.4-25.6 Gy) involved field radiotherapy following chemotherapy (COPP/ABV) was delivered to the mediastinum according to AIEOP 2004 HD study protocol. Heart, thyroid, breast, lungs and spinal cord were identified as organs at risk (OARs). Provided that the dose distribution in the target volume was similar between the two treatments, dose-volume histograms (DVHs) were evaluated and compared for OARs.

Results: Mean dose to the heart was 3.12 Gy (3D-CRT) and 2.72 Gy (VMAT) (p=0.33), respectively; the same feature for thyroid was 10.84 Gy (3D-CRT) and 8.75 Gy (VMAT) (p=0.07), respectively; among the female population, VMAT resulted in a better sparing of breast volumes receiving intermediate or high doses compared to 3D-CRT (3D-CRT Dmax left and right breast: 16.31 Gy and 15.21 Gy versus VMAT Dmax left and right breast: 10.46 Gy and 10.28 Gy, p=0.03). No significant difference between the two techniques was observed in terms of mean dose received to both the breasts and the lungs. Dmax for spinal cord was 18.04 Gy (3D-CRT) and 13.29 Gy (VMAT), respectively (p= 0.0005).

Conclusions: VMAT resulted in a substantial sparing of thyroid and spinal cord. Mean doses to heart, breasts and lungs did not significantly differ between the two techniques, while VMAT allowed a better sparing of breast volumes receiving intermediate/ high

doses potentially involved in the risk of second malignancies.

## PO216

### REPORT OF OUR EXPERIENCE OF A PEDIATRIC PATIENT WITH EWING'S SARCOMA

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Aims: Ewing's sarcoma is a rare tumor that typically affects young age and that for its complexity requires a multi-disciplinary approach. It is a radio-sensitive tumor for which radiation therapy (RT) can either be used as adjuvant therapy following surgery or as the only radical therapy in non operable patients. In this case report we talk of our experience with a paediatric patient that we treated in 2015, focusing on the curative and functional results we obtained and on the late effects of the treatment.

Methods: A 6 years old girl with Ewing's sarcoma to the left popliteal fossa underwent a large surgical excision in January 2015, to which followed in June 2015 adjuvant chemotherapy with IVADo protocol (Isofosfamide, Vincristina, Actinomicina d, Doxirubicina) and then, another surgical excision of the residual disease in July 2015. In October 2015 the patient came to our clinic and accordingly to AIOM guidelines and in consideration of her young age, the tumor dimension and the surgical treatment, it was decided to carry out adjuvant RT with a 10 MeV electron beam. RT was performed in a prone position with the aid of a pneumatic pillow, with a total fractionation dose (TFD) of 41,4 Gy in 1,8 Gy fractions. All along the therapy, weekly clinical examinations evaluated the patient's well being and provided support therapy to acute radiation toxicity and to the mild anaemia that was diagnosed at the very beginning of the treatment. At the end of RT, the patient was followed with three-months periodical follow-up visits, laboratories tests and MR scans, all of which always turned out to be negative.

Results: Despite patient's young age and the concurrence of anaemia, there was no need to interrupt RT. The patient underwent all the RT sessions, reporting skin toxicity of first degree in the RTOG toxicity scale at most. 4 years after treatment, she's still alive with no progression of the disease, she's regained limb mobility and her quality of life is greatly improved.

Conclusions: This case is a clear example of how radiation therapy, in association with other therapeutic strategies, can offer good clinical outcome and local management of the disease.

## PO217

### LATE TOXICITY OF TOTAL BODY IRRADIATION IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Aims: Total Body Irradiation (TBI) represent one important component of pre-transplantation of bone marrow in pediatric patients with Acute Lymphoblastic Leukemia (ALL). The increased overall survival pays more attention to the evaluation of side effects and quality of life. In this work we analysed the acute and late toxicities (according to CTCAE 5.0 scale) of patients treated with myeloablative TBI.

Methods: From 2005 to 2017, 29 TBI treatments were performed in our center in patients aged 2-18 years with ALL. the dose delivered to all patients was 12 Gy in double daily administration of 2 Gy.

Results: in the acute phase we found episodes of G1 nausea and vomiting in 58% of patients, G2 headache in 29% and episodes of generalized pruritus (G2) in 13%. To date 15 of 29 transplantated patients result in complete remission, 14 died. With a median follow-up of 5 years (range 1-13 years) 66% of patients presented bilateral surgically corrected cataract, 40% endocrinological dysfunction (reduction of GH with consequent delay in body growth, hypothyroidism and delay in pubertal development), 6% esophageal stenosis. Documented deaths refer to: complications related to transplantation in 33%, disease progression in 58%, veno-occlusive disease in 3% and 6% died before transplant.

Conclusions: in the examined TBI population, as regard late side effects, we observed that endocrinological problems and cataract are frequent with a moderate impact on quality of life.

## PO218

### CRANIO-SPINAL IRRADIATION FOR LOW/INTERMEDIATE RISK PEDIATRIC MEDULLOBLASTOMA ACCORDING TO PNET V MB INTERNATIONAL PROTOCOL: A NEW STATIC IMRT TECHNIQUE WITH JAGGED-JUNCTIONS

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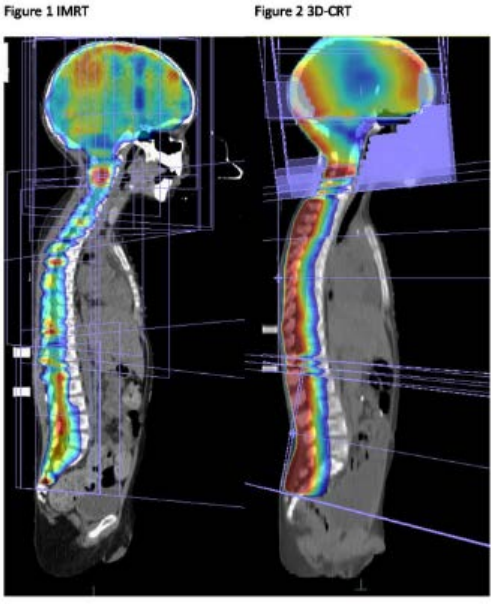
Aims: Pediatric medulloblastoma at low/intermediate risk is conventionally treated with craniospinal irradiation (CSI). Since 2015 at University of Catania the international Protocol PNET V MB has been adopted,with the aim of reducing the dose of irradiation on the craniospinal axis (CSA) to 18-23,4 Gy,while main-

taining the dose administered to the tumor bed at 54Gy. There is currently no therapeutic standard for the RT technique to be adopted and the problems relating to the junctions between the target volumes and the inhomogeneity of dose distribution with 3D-CRT,especially to the spinal cord,are well known. Our aim is to evaluate the feasibility and dosimetric benefit of a new static IMRT technique with jagged-junctions.

Methods: We developed a dosimetric comparison between conventional 3D-CRT and static step-and-shot jagged-junctions IMRT (IMRT-JJ) on 5 patients,age 2-18years,with craniocaudal volumes between 54,3 and 86,1cm. Dose prescribed to CSA was 18-23,4Gy. 3D-CRT used conventionally couch rotation,junction shifts during treatment,2-3isocenters at different depth. IMRT-JJ plan used 3field sets,each with a unique isocenter:1field set with 7beams treated the cranium, 2field sets treated the spine,each set using 3fields. Isocenters were at the same depth. Fields from adjacent sets were overlapped and the optimization process softly combined the dose inside the overlapped junction.




**Figures 1 and 2.**

Results: Both 3D-CRT and IMRT-JJ allowed to respect the OARs dose constraints. Dosimetric aims,defined as 95% of prescribed dose to 95% of PTV and 107% of prescribed dose to ≤5% of PTV(both cranial and spinal volumes),were also respected with both methods. 3D-CRT better covered PTV Brain than IMRT-JJ(95% isodose surface covered 95,7-100%vs96,5-96,8% of volume). IMRT-JJ (Figure 1) has the advantage of reducing inhomogeneities, avoiding hot and cold areas and having the 107% isodose surface in the PTV Spine lower than 3D-CRT (Figure 2):5,1-6,3%vs17-23,8%. IMRT-JJ permits to avoid junction shifts during RT, allowing a faster treatment delivery,thanks to the identification of several isocenters on the same longitudinal axis,without couch rotation.

Conclusions: The results of the IMRT-JJ are equal or higher than conventional 3D-CRT technique. The IMRT-JJ allows obtaining a better homogeneity of the dose distribution to the spinal volume. Another advantage is represented by the notable shortening of the processing times of the treatment not having to verify the joints and not having to rotate the couch.

## PO219

## RADIATION INDUCED HYPOTHYROIDISM IN PEDIATRIC TUMORS OF CENTRAL NERVOUS SYSTEM: LONG TERM RESULTS OF MONOINSTITUTIONAL EXPERIENCE

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Aims: To investigate primary and secondary hypothyroidism in pediatric patients affected by central nervous system (CNS) tumors.

Methods: From January 1999 to April 2016 we retrospectively analyzed 65 patients who had been treated with three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated radiotherapy schedule (IMRT). We recorded all clinical characteristics and median dose to pituitary gland and thyroid. Primary endpoints were to determine a dose constraints for central and peripheral hypothyroidism. Categorical variables have been summarized with absolute and percentage count; continuous ones with mean and Standard Deviation (SD). A curve Receiver Operating Characteristic (ROC) has been developed to find the optimum dose cutoff to maximize predictive accuracy 10 years after the end of radiotherapy. To estimate the probability of events over time a Cox model was used, adjusted by age at the end of therapy, sex and indication to surgery. Tumor type characteristics are assumed not to be directly associated with the outcome.

Results: Median follow up was 135 months (range:27-236). Clinical characteristics of all patients and those compared to the pituitary dose groups are shown in the Table 1. 18 pts out of 65 were excluded from analysis as they had thyroid and/or pituitary damage prior radiotherapy, 15 of 47 pts underwent Involved Field RT and 32 pts craniospinal irradiation. 16/47

(34%) pts had central damage, only 4/32 (12.5%) had a peripheral damage. We detected an association between pituitary mean dose and central hypothyroidism. The optimum radiation cutoff identified is 30.5 Gy. Five years after radiotherapy about 13% of patients who received a pituitary mean dose under 30.5 Gy developed a central hypotirodism against about 41% of those who received 30.5 Gy or more, HR 4.87 (95% CI 1.09-21.71); Adjusted Cox p = 0038. On the other side, no significant associations between thyroid mean dose and peripheral hypothyroidism (adj Cox, p=0.725) have been found, because of the small sample that doesn't allow a robust analysis.

Conclusions: Our data confirm the relationship between central hypothyroidism and pituitary mean dose in pediatric patients; relationship between dose delivered – damage thyroid is ongoing, because it is necessary to enlarge the sample and to study the damage that has occurred since the introduction of IMRT as a key technique of pediatric radiotherapy.

**Table 1.**

| | Overall | Pituitary Dose < 30.5 Gy | Pituitary Dose ≥ 30.5 Gy | p |
|---|---|---|---|---|
| n | 47 | 15 | 32 | |
| Age at Diagnosis (mean (SD)) | 7.73 (3.79) | 8.20 (5.19) | 7.51 (3.01) | 0.566 |
| Age Stop RT (mean (SD)) | 8.98 (3.66) | 9.11 (4.85) | 8.92 (3.03) | 0.872 |
| Sex = M (%) | 34 ( 72.3) | 10 ( 66.7) | 24 ( 75.0) | 0.806 |
| Radiotherapy = 1 (%) | 47 (100.0) | 15 (100.0) | 32 (100.0) | - |
| Chemotherapy = 1 (%) | 45 ( 95.7) | 14 ( 93.3) | 31 ( 96.9) | 1 |
| Surgery = 1 (%) | 31 ( 66.0) | 13 ( 86.7) | 18 ( 56.2) | 0.085' |
| technique = 3D (%) | 45 ( 95.7) | 14 ( 93.3) | 31 ( 96.9) | 1 |
| type (%) | | | | 0.523 |
| Astrocitoma | 7 ( 14.9) | 2 ( 13.3) | 5 ( 15.6) | |
| Ependimoma | 3 ( 6.4) | 2 ( 13.3) | 1 ( 3.1) | |
| Germinoma | 6 ( 12.8) | 1 ( 6.7) | 5 ( 15.6) | |
| Glioma | 4 ( 8.5) | 1 ( 6.7) | 3 ( 9.4) | |
| Medulloblastoma | 24 ( 51.1) | 9 ( 60.0) | 15 ( 46.9) | |
| Other | 3 ( 6.4) | 0 ( 0.0) | 3 ( 9.4) | |

## PO220

### FRACTIONATED STEREOTACTIC RADIOTHERAPY IN LOW GRADE GLIOMAS IN CHILDHOOD: LONG-TERM TOXICITY EVALUATION IN THE SIOP LGG1-LGG2 PROTOCOLS

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Among the multiple Radiotherapy technical options in pediatric neurooncology, Fractioned Stereotactic Radiotherapy (FSRT) permits the complete coverage of the target with the best surrounding healthy tissue sparing. The aim of this retrospective study is to evaluate the long-term toxicity in patients treated with FSRT for Low Grade Glioma (LGG). Our serie consists of 31 children, 19 males and 12 females, median age 7 years, range 3-16, treated at the Radiotherapy Unit of the Istituto Oncologico Veneto in Padua, enrolled between 1996 and 2005 in the two consecutive SIOP protocols LGG-1 1996 and LGG-2 2003. The diagnosis of LGG has been histologically proven in 14 pts.; 17, NF1 positive, according to the protocols, underwent FSRT after radiological diagnosis of optical pathway mass. Children with a mass up to 5 cm of diameter, regardless primary site, were eligible to a 54 Gy/27F FSRT on a target volume defined by pre and postoperative T1 and T2- weighted MRI with contrast, fused with the set up CT scan, plus 1-2 mm margin. All pts. have been treated with the Radionics X knife System; after this serie we moved to the BrainLab Exactrac. At a median follow-up of 17 years, range 13-21, all patients are alive: 5 in complete radiological response and 22 with a stable, asymptomatic disease; in 4 NF-1 cases, the lesion grew dimensionally after FSRT, being asymptomatic, they continued the planned follow-up. One out of the 5 pts. now in clinical complete remission has been reoperated for local relapse and 1 of the stable disease pts. has been reirradiated on a spinal metachronous lesion. In our experience, the significant margin reduction allowed by FSRT did not jeopardize outcome: local control has been superior than that reported for the cohort treated with 3DCRT in the same protocols. No SFRT-related adverse effects have been recorded, particularly at neurologic and endocrinologic examination. In our population, now with a median age of 25 years, range 18-39, the quality of life evaluated by visual and hearing function assessment and social integration evaluation is almost overlapping to that of the healthy peers. Personal experience and scientific literature confirmed not only the actual worth of FSRT for tumors of any anatomical site, but also its excellent tolerability.

## PO221

### TOTAL BODY IRRADIATION AND REGULATORY/CONVENTIONAL T-CELL ADOPTIVE IMMUNOTHERAPY IN PEDIATRIC HLA-HAPLOIDENTICAL TRANSPLANTATION FOR HIGH-RISK ACUTE LEUKEMIA

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Aims: Hematopoietic stem-cell transplantation (HSCT) is the standard treatment for pediatric patients with high-risk acute lymphoid leukemia (ALL) . As the best donor, the matched sibling, is not always available, the 1-haplotype mismatched relative (haploidentical) is a valid alternative. In conditioning to T-depleted haploidentical HSCT, total body irradiation (TBI) is essential. In this setting we designed an inoculum which included a megadose of CD34+ cells and adoptive immunotherapy with conventional T cells and thymic-derived CD4+/CD25+ FoxP3 regulatory T cells (Tregs). Our aim was to separate the Graft versus Leukemia (GvL) effect from Graft versus Host Disease (GvHD) and thus reduce the incidence of post-transplant relapse.

Methods: From January 2017 to Decembre 2018, 11 children with ALL (9 male, 3 female, median age 9 years, range 5-19, 6 in 1st complete remission (CR), 2 in 2nd and 3 in 3rd) underwent haploidentical HSCT. TBI total dose was 13.5 Gy delivered in 9 fractions twice a day (lung dose was 9 Gy) from days –15 to –11 in 9 patients. In 3 children who required general anesthesia the TBI dose was 9.9 Gy (lung dose 6 Gy) delivered in 3 daily fractions from days –12 to - 10. Chemotherapy included thiotepa 5 mg/kg on days -10 and -9; fludarabine 50 mg/m$^2$ from days -10 to -6; cyclophosphamide 15 mg/kg on days -8 and -7. Haploidentical grafts consisted of 2x10$^6$/kg Tregs, 1x10$^6$/kg Tcons and 10x10$^6$/kg purified CD34+cells. On day -2 Rituximab 200 mg/mq was administered as PTLD prophylaxis. No post-transplant immunosuppression was given.

Results: TBI-related acute toxicity was G1 in 11 patients. All patients achieved sustained full donor engraftment. Immune reconstitution was good, with peripheral blood T cells rapidly increasing. Grade II-IV acute GvHD developed in 2 patients (18%) and chronic GvHD in none. 2 patients died (18%), 1 of invasive aspergillosis, 1 of grade IV aGVHD). Another patient relapsed and died after a second transplant. At a median follow up of 24 months (range 1-28), 8 (73%) patients are alive in remission without cGVHD.

Conclusions: This transplant strategy was successful in haploidentical transplantation for children with high-risk ALL. The conditioning regimen was associated with low toxicity and relapse rates. The appropriate Tcon/Treg ratio was confirmed to exert a powerful T-cell dependent GvL effect with a low incidence of aGvHD.

**PO222**

## TARGET OPTIMIZATION IN CRANIO-SPINAL TREATMENTS PERFORMED IN VMAT TECHNIQUE IN PEDIATRIC PATIENTS

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Aims: Medulloblastoma is the most common malignant brain tumor in childhood. The radiation therapy as cranio-spinal axis irradiation with boost on the site of the primary tumor allows to reduce recurrences. The target definition needs of the registration of simulation CT with pre-and post-surgical magnetic resonance imaging (MRI); but the visualization of images registration shows that there is a no optimal correspondence at subaracnoid space level (partial volume artifacts). The aims of this analysis was to understand whether the optimized treatment in VMAT may represent a risk with respect to the dose distributed to leptomeninges and encephalic parenchyma as a consequence of the definition of volumes influenced by partial volume artifacts.

Methods: Pediatric patients affected by medulloblastoma were considered to perform craniospinal treatment plans. The coverage dosimetric data were compared by optimizing a first treatment plan only on Planning target volume (PTV) of Brain (Brain+ 0.5cm), PTV Spine (Spine+0.5cm) at PTV Brain + Spine (CSA), and a second treatment plan adding PTV leptomeninges (0.4 external and 0.3 inner margins from PTV Brain and Spine) (CSA leptomeninges) in such a way as to favor a better coverage of the leptomeninges district.

Results: Overall 42 treatment plans of 21 patients were compared. The V95% distribution with respect to the volume of interest PTV leptomeninges showed, in the cases of V95% <95%, a lower average value in the case of a non-optimized plan for leptomeninges (SCA) compared to the optimized plans (CSA leptomeninges): 84% vs 86.4%. Considering the PTV Brain Meninges in ACS plan the V95% was lower than the optimized plans (CSA leptomeninges): 90% vs 93%. (Figure 1). The optimization allows the dose to be increased at this level as it can help reduce potential cold spots in which a possible relapse could occur. In the case of non-optimized treatments, in 4 cases out of 21, V95% is less than 85%, which is not the case in optimized. The absence of a significance in the overall value of the PTV leptomeninges denotes instead the absence of significant changes with the method at the level of the medullary canal itself. The difference in terms of V105% instead is significant but against the optimized procedure.

Conclusions: This dosimetric analysis suggest that the definition of subarachnoid space in target delineation allows to improve the dose distribution in this locations, critical for disease recurrence.

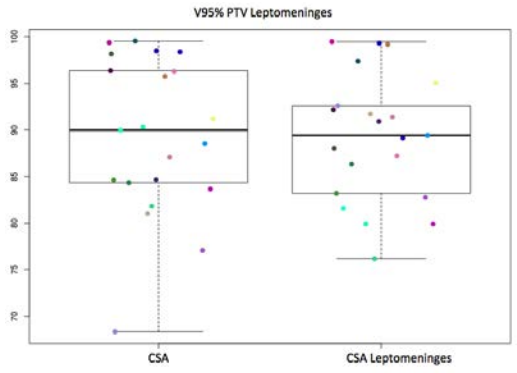


**Figure 1.**

**PO223**

## THE DOSIMETRIC IMPACT OF THE BLADDER VOLUME VARIATIONS ON THE DOSE TO ORGANS AT RISK (OAR) DURING HDR BRACHYTHERAPY ENDOMETRIAL CANCER

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Aims: The purpose of this study was to establish a dosimetric correlation between the bladder volume and the dose received by the organs at risk (OARs) (bladder, rectum and urethra) in computed tomography-guided High-Dose-Rate (HDR) brachytherapy in endometrial cancer , and to define an optimal bladder volume to limit the dose to OARs.

Methods: In a retrospective study, 21 endometrial carcinoma patients (101 intracavitary applications) treated at our institute with CT-based HDR brachytherapy (vaginal cylinder) between 2016 and 2018 were included. At each fraction, all patients had a urinary catheter for bladder filling with physiological solution (150cc), rectal emptying and vaginal applicators (2,5 cm diameters) before CT scan. The brachytherapy plan was generated on the Oncentra treatment planning system (Oncentra® Brachy v4.5.3), a geometrical optimization was used to calculate treatment plans. The dose-volume histograms (DVHs) of the OARs were generated. The bladder volume was computed and the following parameters were calculated from DVHs: dose to D2cc for rectum, D2cc and D0,1cc for bladder and urethra. The bladder volume values ranged from 146 cc to 560 cc (mean 217,2 cc and standard deviation 33,5cc). Patients were classified into five groups depending on the bladder volume: up to 150cc, 150-200 cc, 200-250cc, 250-300 cc and > 300 cc.

Results: The D2cc to bladder and D0,1cc urethra increases as a function of the increasing bladder volume, while the D2cc to rectum decreases if bladder volume increases (Figure 1).

ConclusionsWe found a relationship between bladder volume and OARs doses. According to our results, a bladder volume between 200 cc and 250cc determines a dose (D2cc) to the rectum lower than the prescribed dose and seems that this bladder volume allows to contain the dose to the urethra below 105% of the prescribed dose. The dose to bladder was always less than 80% of the prescribed dose.

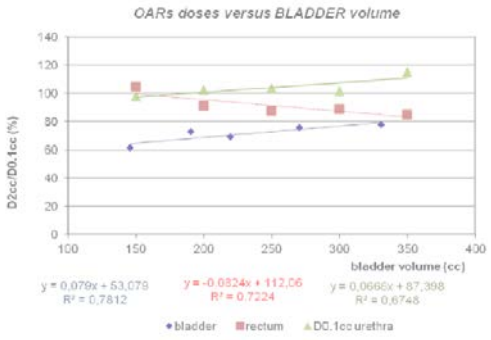


Figure 1.

**PO224**

## INTRA-CAVITARY BRACHYTHERAPY AND IMRT COMBINED WITH CHEMOTHERAPY FOR GYNAECOLOGICAL CANCER

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Aim: Brachytherapy is well-established as an integral component in the standard of care for treatment of patients receiving primary radiotherapy for gynaecological cancer. A decline in brachytherapy has been associated with negative impacts on survival in the era of modern EBRT techniques. This study to investigate the treatment effects and toxicities of IMRT and intra-cavitary brachytherapy combined with chemotherapy for gynaecological cancer.

Methods: 15 gynaecologic cancer patients were performed adjuvant chemotherapy with paclitaxel and carboplatin administrated for two cycles before radiation therapy. All patients received intra-cavitary brachytherapy and finally the IMRT.

Results: All patient also received a high-dose-rate intra-cavitary brachytherapy at the point ""A"" dose of 20.0-30.0 Gy in 6.0 Gy per fraction. All patients received IMRT to 50 Gy (2 Gy per fraction). No significant differences found regards to acute and chronic radiation toxicities, including myelosuppression, dermatitis, enterocolitis, proctitis and cystitis. The only toxicity recorded by chemotherapy.

Conclusion: Intra-cavitary brachytherapy and IMRT combined with chemotherapy is safe and effective for gynaecological cancer. Conformal external beam therapies such intensity modulated radiation therapy (IMRT) or stereotactic body radiation therapy (SBRT) should not be used as alternatives to brachytherapy in patients undergoing primary curative-intent radiation therapy for cervical cancer. Computed tomography or magnetic resonance image-guided adaptive brachytherapy is evolving as the preferred brachytherapy method. With careful care coordination brachytherapy can be successfully delivered at different treatment centers without compromising treatment time.

## PO225

### CLINICAL OUTCOMES FOR CT-GUIDED HIGHDOSE-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 52 patients with LACC (range 30-85 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. 38/52 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 46/52 and all patients received intracavitary brachytherapy (dose range 10-28 Gy). We recorded 48/52 complete response. Three/52 showed a not respondent disease. We observed 8/52 relapses (one local and 7 sistemic) after a median time of 7 months (range 1-24 months) with a median DFS of 28 months (range 2-93 months). After a median follow up of 32 months (range 20-62 months ). 32/52 patients were alive without disease. Fifteen patients were dead (10 for disease and 5 for other causes in absence of cervical cancer). The evaluation of the toxicity according to RTOG scale showed G1 genitourinary complications in 20/52 patients and G2 in 5/52, while only one patient complained of G3 toxicity. Gastrointestinal toxicity occurred in 11/52 patients for G1 grade and in 6/52 patients for G2 grade. 8/52 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.

## PO226

### ONE-WEEK VAGINAL BRACHYTHERAPY (VBT) SCHEDULE AS EXCLUSIVE ADJUVANT POSTOPERATIVE TREATMENT IN INTERMEDIATE AND HIGH-INTERMEDIATE RISK (HIR) ENDOMETRIAL CANCER PATIENTS

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Aim: Vaginal HDR brachytherapy as exclusive adjuvant treatment in postoperative HIR endometrial cancer patients is considered as standard approach. However, total dose, fractionations and overall treatment time have not been homogeneously delivered up to now. Aim of our study was to report survival outcomes and toxicities incidence by using a one-week short vaginal Brachytherapy schedule.

Methods: Eighty consecutive patients with endometrial adenocarcinoma had been treated at our Department between September 2007 to September 2017 with exclusive high dose rate (HDR) brachytherapy short schedule (7 Gy/fraction/every other day/1 week). The dose was prescribed at 5 mm of applicator surface. Disease stage was assigned according to the FIGO surgical staging 2009. The stage distribution was as follows: IA (37 pts) IB (43 pts). Acute and late rectal, urinary and toxicity was recorded according to Radiation Therapy Oncology Group scores and LENTSOMA for acute and late vaginal toxicity.

Results: Median follow was 48 months(range 15-119 months) and 5-year DFS and CSS were 89.2% and 95.4% respectively. Overall recurrence rate was 7.5%. Six/80 patients relapsed after a median time of 18 months ( range 5-51 months) : 1 (1.2%) at vaginal vault and pelvic lymph nodes, 1 patients ( 1.2%) at pelvic lymph nodes, 1 (1.2%) at vaginal vault, pelvic lymph nodes and distant site and 3 (3.75%) as only metastatic disease. Death has occurred in 5 patients. Three patients died for intercurrent causes without evidence of disease. Acute bladder toxicity G1- G2 was reported in 5 (6.25%) patients, vaginal toxicity G1-G2 in 10 (8%) and none gastrointestinal toxicity. Late Bladder and gastrointestinal G1 toxicities were reported in 4 (5%) patients and late vaginal toxicity in 18 (22.5%) patients, most of them with G1-2 toxicity. There was no evidence of grade 3-4 toxicity.

Conclusions: Exclusive short course adjuvant VBT is an effective treatment in patients with early stage endometrial cancer and provides good outcomes in terms of disease local control and disease-free survivalwith low rates of toxicity profile.

## PO227

### UVEAL MELANOMA THICK BETWEEN 4 AND 6 MM AND TREATED WITH 2 DIFFERENT RADIOISOTOPES (I-125 OR RU-106): SINGLE INSTITUTION EXPERIENCE

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Aims: Goal of our work was to evaluate if a disease thickness cut-off of 5 mm may be considered the best choice to choose gamma emitter sources, as I-125, for the treatment of uveal melanomas.

Methods: The data of patients affected by primary uveal melanoma and treated in our institutional IOC (Interventional Oncology Center) since December 2006 to December 2016 were retrospectively reviewed. Uveal Melanoma presenting a ≤ 5 mm thickness are generally treated with Ru-106 plaques, while I-125 seeds are used for thicker disease presentations. For these reasons, only patients with a disease thickness between 4 mm and 6 mm treated with Ru-106 or I-125 plaque were included in our analysis.

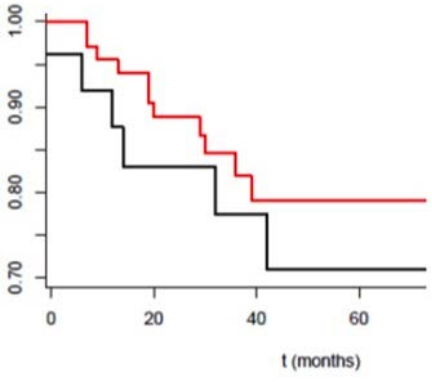


**Figure 1.**

Results: 107 patients were considered for this analysis (81 treated with Ru-106 and 26 treated using I-125). Nine patients developed local recurrence instead 7 had distant metastases. Even though no statistically significant difference (p=0.36) was observed between the two groups (I-125 versus Ru-106) in terms of Disease Free Survival a statistical trend in favour of the group treated with I-125 was found as shown in figure 1, although the patients' prognosis should be worse because of a higher thickness of the lesion. Five patients treated with I-125 (19.2%) experienced radiation maculopathy; this finding is important because such adverse event was experienced by 21 patients treated with Ru-106 (25.9%).

Conclusions: We report that using I-125 seeds for Uveal Melanoma with thickness between 5mm and 6mm is not associated with a statistically significant increased risk of radiation maculopathy. We believe that further multicentric investigations may help to confirm the results of this study.

## PO228

### CAN RADIOTHERAPY BE COMBINED WITH RADIOFREQUENCY ABLATION IN THE MANAGEMENT OF SYMPTOMATIC OSTEOLYTIC SKELETAL METASTASIS?

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Aims: To evaluate the feasibility and effectiveness of combining radiofrequency (RF), cementoplasty (CP) and Radiotherapy (RT) for pain treatment of bone metastasis (mts) in oligo-metastatic patients (pts).

Methods: From April 2015 to December 2018 twenty-six pts. (16 men, 10 women; median age 64 years) with 28 injuries to bones (vertebral column n = 24; femur, n = 2; sacrum, n = 4) were treated. Diagnosis of bone mts and then its treatment should be based on the combination of different elements: clinical evaluation, CT, MRI and nuclear medicine patterns. The mini-invasive treatment of oligo-metastatic pts aims pain relief that improving the quality of life; treat biomechanical stability of the spine; and an antineoplastic effect - cytoreductive. RF ablation was performed with the pts under sedation a CT - guidance, and was followed by cement injection. Pain relief was valuated with visual analogue scale (VAS) score. After 10 days on average, the patient was subjected to Stereotactic-RT or Volumetric Modulated Arc Therapy (VMAT) technique and a total dose of 20-30 Gy.

Results: Technical success and pain relief was archived in all pts. Pain rating with the VAS decrease from a mean of 9 to a mean of 4, and after 3 month was detected a mayor decrease (2,5). We recorded an overall improvement in the quality of life measured with a suitable test There was no particular toxicity. At present 17 patient died for progression of disease. The evolution of the disease will be evaluated with the use of MRI.

Conclusion: Our data showing the importance of a multi-disciplinary approach oligo-metastatic patients. RF with CP and RT carried out by experts is effective for pain relief and functional recovery in patients with painful bone metastases and can significantly improve quality of life.

## PO229

### ISIORT POOLED ANALYSIS 2019: CHARACTERISTICS OF INTRAOPERATIVE RADIOTHERAPY IN 12.680 PATIENTS

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Aims: Data from centres performing intraoperative radiotherapy (IORT) was collected within the International Society of Intraoperative Radiotherapy (ISIORT) program. The purpose of the present analysis is to analyse and report the main clinical and technical variables of the IORT procedures performed by the participating centres.

Materials and Methods: In 2007, the ISIORT-Europe centres were invited to record anonymized demographic, clinical and technical information related to their IORT procedures in a shared online database.

Results: The number of centres increased from 3 centres in 2007 to 45 centres in the current year. A total of 12.680 IORT procedures have been recorded up until March 2019. The number of procedures performed with electrons was 11.100 (87.5%), while 978 (7.7%) treatments were performed with x-rays. The median age of treated patients was 61 years (range: 1 month – 94 years). Gender was female in 10.606 (83.6%) of cases and male in 1.589 (12.5%). The indication for treatment was curative in the majority of individuals (11.810 cases, 93.1%). The number of patients included in study protocols was 3.196 (25.2%). The most frequent tumour type was breast cancer with 9.897 cases (78%) followed by rectal cancer with 938 cases (7.4%), soft tissue and bone sarcomas with 699 cases (5.5%), prostate cancer with 191 cases (1.5%), pancreatic cancer with 131 cases (1%) and gastric cancer with 30 cases (0.2%). Detailed data in terms of clinical and technical patient characteristics are available.

Conclusions: Data on treatment chronology shows how the number of IORT recorded cases increased in parallel with the interest in ISIORT project. The survey provides an overview of use of IORT worldwide, including patient selection criteria and treatment modalities, and could represent the basis for designing future clinical trials.

## PO230

### HIGH DOSE RATE INTRAVAGINAL BRACHYTHERAPY +/- EBRT AS A VALID ADJUVANT TREATMENT FOR ENDOMETRIAL CARCINOMA: A FIVE-YEAR EXPERIENCE

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Introduction and aims: Standard therapy for endometrial cancer is abdominal hysterectomy with bilateral salpingo-oophorectomy followed by chemotherapy, external beam radiotherapy (EBRT), high dose rate (HDR) brachytherapy or the combination of these treatments depending on clinical and pathologic characteristics. This study aims to evaluate efficacy and toxicity of adjuvant HDR brachytherapy +/- EBRT in patients with endometrial cancer.

Methods: From 2014 to 2018, sixty patients with endometrioid endometrial cancer were treated at Radiotherapy Department in Taranto with adjuvant HDR brachytherapy +/- EBRT. Mean age was 66 years (range between 43 and 84 years). All patients were treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy. Lymphadenectomy was administered for 83.3% of patients with a mean of 22 removed nodes. The FIGO stage was: I (56.6%), II (23.3%), III (20.1%) while histological grades were G1 in 15%, G2 in 68.4% and G3 in 16.6%. Twenty-six percent (26.6%)

of patients received also adjuvant chemotherapy while twenty-four women were also treated with EBRT. Pelvic external radiotherapy was administered with a total dose of 45 Gy (1.8 Gy/die) and HDR brachytherapy was administered with a total dose of 15 Gy (5 Gy per fraction) after EBRT and with a total dose of 25 Gy (5 Gy per fraction) without EBRT. For each fraction, Computed Tomography scans of the whole pelvis were obtained in order to contour Clinical Target Volume, Planning Target Volume and organs at risk. Rate of recurrence, rate of metastasis and Overall Survival (OS) were calculated. The acute and late gastrointestinal (GI) and genitourinary (GU) toxicities were scored according to the EORTC/RTOG scales.

Results: Median follow-up was 27 months (1-57 months). Acute GI and GU toxicity was G1 for 5% and 15% of patients, respectively. No late GI toxicity was observed, and late GU toxicity was G1 for 11.6% and G2 for 1.7% of patients. No other toxicities were observed in our experience. The 5-year overall survival was 94%. Vaginal recurrence occurred in one patient and one patient experienced nodal recurrence. Five percent (5%) of patients had metastases (two patients to lungs and one patient to bone, liver and lungs).

Conclusions: Our analysis showed that adjuvant HDR brachytherapy for high- and intermediate-risk patients with endometrial carcinoma provides excellent local control and overall survival with very low acute and late toxicity also after EBRT.

## PO231

### INTRAOPERATIVE ELECTRONS BOOST FOLLOWED BY SHORT HYPOFRACTIONATED RADIOTHERAPY TO THE WHOLE BREAST WITH TOMOTHERAPY® HI-ART SYSTEM: PRELIMINARY REPORT FROM PILOT AND PHASE II STUDY

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Aims: To report the clinical outcome of adjuvant breast cancer (BC) radiotherapy including intraoperative electrons (ELIOT) boost to the tumor bed followed by hypofractionated external beam radiotherapy (HEBRT) to the whole breast in postmenopausal patients (pts).

Methods and Materials: 43 postmenopausal BC pts received breast-conserving surgery and 12 Gy intraoperative boost with electrons, followed by 8-fraction HEBRT (4 Gy/fraction, total dose 32 Gy, over 1.5 week) with intensity modulated radiotherapy (IMRT) delivered with TomoTherapy ® Hi-Art System (Tomotherapy Inc., Madison, WI) in Direct modality. Sixteen pts belonged to the pilot trial (5/2012- 10/2013) and the remaining ones to the phase II trial IEO 351 (4/2016-3/2019). Acute toxicity was evaluated at the end of HEBRT (maximum grade) and at 1 month afterward, using the RTOG scale. Late toxicity was recorded at 6 and 12 months of follow-up using Lent/Soma scale. Local control was reported on the base of the last follow-up (FU) visit.

Results: Data on 42/43 pts were reported. One drop-out occurred in the phase II trial. Median age was 64 years (range 51-77). Most BC stages were pT1pN0 (sentinel node biopsy). The maximum acute skin side effects was observed at the end of HEBRT with 33/42 (78%) Grade 1, 3/42 (7.14%) Grade 2, and no Grade 3 toxicity. G2 edema affected the whole breast in 10 cases (23.8%) and tumor bed in 15 cases (35,7%). Late toxicity was available for 25 pts and was described in Table 1. Radiological necrosis was found in 16/42 on the ultrasound images. At the time of this analysis, with a median FU of 23.1 months ( range 1-83.7), all pts were alive. Information on local control was available 39/42 pts: 38 were free from any recurrence, while 1 suffered from skin metastases. One pt developed contralateral BC.

Conclusions: The preliminary results showed that the schedule with ELIOT boost followed by HEBRT was feasible and well tolerated. Longer FU is needed to assess local control and effectiveness.

**Table 1.**

| | Breast (25 pts) | | | | Tumour Bed (25 pts) | | | |
|---|---|---|---|---|---|---|---|---|
| | G0 | G1 | G2 | Not Evaluable | G0 | G1 | G2 | G3 |
| Pain | 21 | 3 | 1 | - | 19 | 5 | 1 | - |
| Atrophy | 25 | - | - | - | 19 | 5 | 1 | - |
| Dry Skin | 20 | 5 | - | - | 21 | 4 | - | - |
| Hyperpigmentation | 22 | 3 | - | - | 20 | 5 | - | - |
| Hyporpigmentation | 21 | 4 | - | - | 25 | - | - | - |
| Fibrosis | 21 | 4 | - | - | 4 | 9 | 10 | 2 |
| Telangiectasia | 25 | - | - | - | 25 | - | - | - |
| Striae (o stretch marks) | 25 | - | - | - | 25 | - | - | - |
| Ulceration | 25 | - | - | - | 25 | - | - | - |
| Oedema | 21 | 2 | 2 | - | | | | |
| Lymphoedema | 25 | - | - | - | | | | |
| Breast Volume Retraction | 9 | 11 | 5 | - | | | | |
| Breast Volume | 6 | 11 | 6 | 2 | | | | |

| Cosmesis (25 pts) | | | | | |
|---|---|---|---|---|---|
| | Excellent | Good | Mediocre | Poor | Not Evaluable |
| Patient | 5 | 11 | 3 | 3 | 3 |
| Physician | 4 | 10 | 7 | 0 | 4 |

## PO232

### LONG-TERM OUTCOME OF IORT ASSOCIATED WITH CONSERVATIVE BREAST SURGERY

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Objective. Intraoperative radiotherapy (IORT) consists in a single-dose partial breast irradiation performed immediately after breast conservative surgery. The

objective of our study is to evaluate the long-term outcome of patients who underwent IORT in terms of overall and disease-free survival.

Materials and methods. We retrospectively analysed data on all patients operated of breast conservative surgery from 2005 to 2014 at the Clinic of Surgery of Udine, taking into consideration the characteristics of the patients, of the tumours and the treatments performed. The patients were then subdivided according to the execution of IORT or traditional external whole breast irradiation (EBRT), and then stratified by age (≥48 or <48). Data were analysed by R (version 3.5.0), considering significant $p<0.05$.

Results. In the selected period, we operated 1246 patients with conservative breast surgery. Among them, 105 received IORT. At a median follow-up of 8.5 years, we observed 6 local recurrences (5.7%) that were all successfully removed. We observed no distant recurrence and no cancer-related mortality. In 4 cases, the patients were subsequently operated for a contralateral breast cancer (3.8%), and in 21 we found at least one second tumour other than breast cancer during postoperative follow up (20%).

Conclusions. The prevalence of local recurrences after IORT is similar to that of patients undergoing traditional EBRT. Local recurrences after IORT were observed at a distance of at least 5 years from the procedure, but did not adversely affect overall survival. Therefore, we believe a prolonged follow-up in this type of patient is adequate

## PO233

### SMELL PROTOCOL: STUDY FOR FUNCTIONAL MULTIPARAMETRIC EVALUATION OF EXCLUSIVE INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) IN THE TREATMENT OF NASAL VESTIBULE CARCINOMAS

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Aim: Squamous cell carcinoma (SCC) of the nasal vestibule (NV) is a relatively rare condition, accounts about 1% of all head and neck malignancies. Gold standard of treatment for nose vestibule SCCs remain surgery, external beam radiotherapy (EBRT) and interventional radiotherapy (IRT, BrachyTherapy BT). Functional preservation is taken currently into increasing consideration. The present work evaluated nose functional parameters comparing patients underwent interstitial IRT vs healthy controls and patients treated with intensity modulated (IMRT)-EBRT.

Methods: We evaluated 10 consecutive previously untreated patients (group 1), affected by NV-SCC treated with interstitial IRT between 2012 and 2017, using an anatomy friendly implantation technique. The tumours were classified in 3 groups, according to the subsite of origin, namely "ala/limen nasi", "columella/septum", "inferior border/superior lip". Patient and tumor characteristics are summarized in table I. This cohort was compared to 8 patients treated by IMRT-EBRT (group 2) because of NV-SCC and both groups were compared to 10 sex and age matcheable healthy subjects, with no history of rhinosinusitis or nasal symptoms (Healthy controls). All patients accepted the performance of the tests, which included clinical evaluation (with the NOSE scale score), rhinomanometry, olphactory testing, nasal citology and evaluation of mucociliary clearance through saccharine test.

Results: 5-year disease specific survival of the patients with NV-SCC primarily treated by interstitial IRT was 92.3%. No late skin or cartilaginous toxicity are observed in the IMRT-EBRT and IRT groups. Particularly, no chondrites, chondronecrosis nor septal/alar perforations were reported in the IRT group, probably because of the anatomy friendly implantation technique. The most significant differences between the groups of IMRT-EBRT and IRT as well the healthy controls emerged for the mucociliary clearance ($p<0.001$ at ANOVA and Student's T test), with a doubled mean time for the transportation of the stained marker in the patients treated by EBRT than in those treated with IRT.

Conclusions: the results of the present study demonstrated the efficacy and the safety of IRT for the treatment of patients with early nose vestibule cancer. Probably, this technique could be the new standard for the treatment of the primary lesion in cT1 and cT2 (according to the Wang staging) NV SCCs.

## PO234

### A METHOD TO VERIFY INTERFRACTIONS DISPLACEMENT OF APPLICATOR DURING HIGH-DOSE-RATE BRACHYTHERAPY (HDR-BT) FOR CERVICAL CANCER

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Aims: To evaluate displacement of applicators during each fraction of cervical HDR-BT and the effect of displacement on the dose to the organs at risk (OAR) when plan of first treatment day was used at subsequent fractions.

Material and Methods: Patients with locally advanced cervical cancer were treated with HDR-BT as boost on primary tumor after radio-chemotherapy treatment. Computed tomography (CT)-based planning was performed using a single uterine Fletcher's applicator and two vaginal ovoids, then a CT was done each fraction to verify appropriateness of replacement. Changes in position of Flethcher's applicator were evaluated at each image set in relation with fixed bony landmarks (i.e., pubic bone) in all directions measuring maximal dose (Dmax) to rectum and bladder. Also rectum and bladder volume variations were evaluated. Common Terminology Criteria for Adverse Events version 4.03 was used to grade toxicity.

Results: Twelve patients with squamous cell carcinoma of the cervix were recruited from September 2017 to April 2019. Median age was 60 years and median Karnofsky performance status 100%. Median dose of HDR-BT was 3x7Gy (range, 2-4x7Gy) The median applicator translational variations were: 5 mm, 2 mm, 3 mm in cranio-caudal, lateral and antero-posterior (A/P) direction, respectively. Overall A/P applicator translation is related to the rectal and bladder dose. A displacement ≥ 5 mm in A/P direction determines a +/- 35% of Dmax to both rectum and bladder resulting 3x4.5Gy (-35%) and 3x9.5Gy (+35%) of prescribed dose. On the contrary, at subsequent fractions, rectum and bladder volumes remained substantially equal with respect to those contoured at first CT. Acute G2 rectal and bladder toxicities were in 3/12(25%) and 2/12 (16%) patients, respectively. No >G1 late toxicity was registered.

Conclusions: The geometric relationships between HDR-BT applicator, rectum and bladder can vary during the course of HDR-BT fractions. Based on our preliminary results we decided to replan HDR-BT when there was an A/P displacement of Fletcher's applicator ≥ of 5 mm. Anyway, the study is ongoing.

## PO235

### REIRRADIATION WITH INTRAOPERATIVE RADIOTHERAPY (IORT) FOR PATIENTS AFFECTED BY BREAST CANCER AFTER PRIOR THORACIC RADIOTHERAPY: ACUTE TOLERANCE AND LATE TOXICITY

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Aims: Mastectomy is recommended for patients (pts) suffering of new or recurrent breast cancer after prior thoracic radiation. The normal tissue tolerance does not permit a second full-dose course of whole breast irradiation after a second breast-conserving surgery (BCS). IORT could be an option as re-irradiation in selected pts. We retrospectively investigated the feasibility of a second BCS followed by IORT for selected pts with localized breast cancer and prior thoracic radiation.

Methods: Thirty-three pts, who declined salvage mastectomy for their breast cancer after prior thoracic radiation, were treated with BCS and IORT between 2009 and 2019. Twenty-five pts (76%) presented breast cancer local relapse after whole breast irradiation, 8 (24%) previously received mantle field irradiation for lymphoma. IORT was delivered with the low energy X-rays IntrabeamTM device (Carl Zeiss Meditec AG, Oberkochen, Germany), using a single dose of 20-21Gy at applicator surface. Acute surgical complications and late toxicity were registered and scored by CTCAE version 5.0. Unaesthetic results were reported. Local control (LC) and overall survival (OS) were estimated by Kaplan-Meier method.

Results: The median time from prior thoracic radiation to breast cancer presentation was 13 years (range 6-34). All pts underwent BCS and partial breast reirradiation with IORT and only 5 pts (15%) required more than 3 days of hospitalization. Three pts presented seroma and 2 patients hematoma that needed drainage. The distance between skin and applicator was minimum 10 mm and no skin changes were detected. For late toxicity analysis we included 26 pts with a mean follow up of 62 months (6-123). No cases of late Grade ≥3 toxicity were registered. Only 10 pts (38%) had Grade 1-2 late toxicity. Subcutaneous fibrosis was seen in 6 cases (23%), fat necrosis in 4 (15%), chronic breast pain in 2 (8%) and persistent seroma in 2 (8%). Unaesthetic outcome due to fibrosis with skin retraction occurred in 2 pts and was corrected with lip-filling. Three pts with local recurrence underwent salvage mastectomy. 5ys-LC and 5ys-OS were 94.7% and 94.4% respectively.

Conclusions: BCS with IORT is a feasible option for breast preservation in pts with localized breast cancer after prior thoracic radiation. Acute tolerance was excellent and late toxicity was acceptable, without cases of Grade≥3 late toxicity. Prospective trials are required to confirm these preliminary findings

## PO236

### 18F[FDG] PET-GUIDED BRACHYTHERAPY FOR CARCINOMA OF UTERINE CERVIX :LONG-TERM RESULTS

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Aims: Concomitant chemo-radiation and intracavitary brachytherapy (BT) is the standard treatment for locally advanced cervical carcinoma. In our previous experience for the first time in Italy we reported the feasibility of [18F]FDG-PET in the BT treatment planning as functional imaging technique able to visualize neoplastic tissue. Long term results were evaluated in terms of overall survival (OS) and late toxicity. The site of recurrence was analysed and compared if it was PET positive during BT.

Methods: From June 2007 to May 2010, thirteen women with locally advanced cervical carcinoma were

enrolled into the study. All patients underwent external beam radiation therapy (EBRT) to whole pelvis (box technique to a total dose of 50.4 Gy) with weekly concomitant cisplatinum chemotherapy. HDR BT was performed weekly (5 Gy per fraction; 5 to 6 fractions). All BT fractions were planned by CT scan and, in the first and in the fourth fraction, 18 [FDG] PET/CT was also employed. Local control rate, progression free survival (PFS), overall survival (OS) and treatment related toxicities under RTOG criteria were evaluated.

Results: With a median follow-up period of 102 months (range: 4-144), the 8-years overall survival (OS) and 8-years progression-free survival (PFS) were 76.9% and 61.5% respectively. Three patients (23%) died for progression disease. Only for one patient was recorded a grade 3 genitourinary toxicity. Only one patient had a local relapse corresponding to a PET positive area in BT guided planning (Figure 1).

Conclusions: FDG-PET/CT-guided Intracavitary Brachitherapy for patients with locally advanced cervical cancer resulted feasible and safe, with an optimal clinical outcomes in term of OS and PFS. The recognition of local relapse in PET positive area could suggest the opportunity of dose escalation.

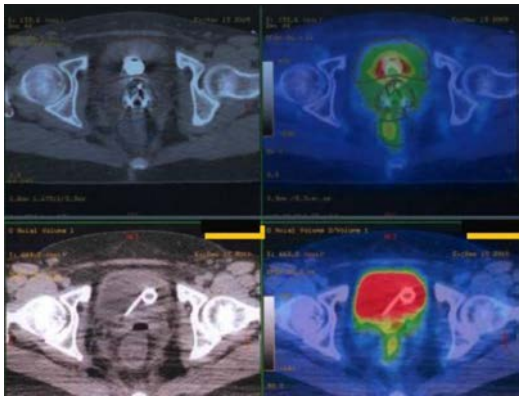

**Figure 1.**

## P0237

## DOSIMETRIC COMPARISON OF TWO DIFFERENT TREATMENT PLANNING OPTIMIZATION METHODS FOR VAGINAL CUFF HDR BRACHYTHERAPY WITH MULTICHANNEL APPLICATORS FOR ENDOMETRIAL CANCER: A PRELIMINARY INSTITUTIONAL EXPERIENCE

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Aims: To compare dosimetric parameters of Hybrid Inverse Planning Optimization (HIPO) versus HIPO plus manual optimization method in vaginal cuff adjuvant brachytherapy (VBT) for endometrial cancer with multi-channel vaginal cylinders (MVCs).

Methods: We reviewed CT data sets from 8 patients affected by endometrial cancer (FIGO Stage IA G2-3, IB G2) treated with 3 fractions (7 Gy/fr) of intracavitary Hight Dose Rate (HDR) VBT using MCVs. The diameter of the applicators ranged from 2.5 to 3.5cm. The CTV was defined as the upper third of the vagina and included the vaginal mucosa to a maximal distance of 5mm from the applicator. No margin was added to the CTV to define the PTV. Bladder and rectum were contoured as organ at risks (OARs). For each patient a first treatment plan (HIPOplan) was generated in the TPS (Oncentra Brachy vr 4.5.3). The HIPO method was initially used to calculate the optimal dwell positions and times. The optimization continued until the planning goals were satisfied. Starting from the HIPOplan, a second manually modified plan (HIPO-Manualplan) was generated with the aim to improve PTV coverage but not exceeding the OARs constraints. Target coverage was evaluated calculating the minimum dose to 90 and 98% of the PTV (DPTV90, DPTV98) and the percentage of PTV receiving ≥90, 98 and 100% of the prescribed dose (VPTV90, VPTV98, VPTV100). Hot spots to the PTV were defined as VPTV150 and VPTV200. Dose homogeneity index (DHI) and Simplified Conformal Index (COIN) were finally calculated for each plan.

**Table 1. Dosimetric parameters (average ± SD) calculated in $HIPO_{plan}$ and $HIPO\text{-}manual_{plan}$.**

| Parameter (%) | Optimization method | | | |
|---|---|---|---|---|
| | HIPOplan | | $HIPO\text{-}Manual_{plan}$ | |
| V90 | 91,86 | ± 6,49 | 99,99 | ± 0,29 |
| V98 | 80,45 | ± 9,43 | 98,93 | ± 1,03 |
| V100 | 77,48 | ± 10,66 | 98,54 | ± 1,40 |
| V150 | 16,41 | ± 8,59 | 37,20 | ± 6,28 |
| V200 | 27,11 | ± 3,03 | 6,88 | ± 2,64 |
| D90 | 93,82 | ± 4,36 | 109,31 | ± 5,00 |
| D98 | 85,67 | ± 6,86 | 100,92 | ± 3,29 |
| $D_{rectum\ 2cc}$ | 56,83 | ± 7,13 | 71,51 | ± 7,06 |
| $D_{bladder\ 2cc}$ | 57,52 | ± 8,47 | 71,69 | ± 9,99 |

Results: Target coverage expressed by V90, V98, V100, D90 and D98 was higher in $HIPO\text{-}Manual_{plans}$ than in $HIPO_{plans}$. V150 was higher in $HIPO\text{-}Manual_{plans}$ but V200 was lower. Doses to OARs were higher in $HIPO_{plans}$ DHI and COIN were better in $HIPO\text{-}Manual_{plans}$ (Plan parameters shown in Table 1).

Conclusions: Hybrid HIPO-Manual optimization method showed a better coverage of the PTV without of a clinically significant increasing of hotspots to the target volume (V200) and a better DHI and COIN. Our experience suggests that dosimetric results of HIPO are strongly dependent to dose constraints and weights used in the optimization and to the PTV delineation. A subsequent HIPO-Manual can improve PTV coverage,

DHI and COIN. The next step will be to validate a new algorithm to evaluate and compare these different optimization methods.

## PO238

### INTRA-OPERATIVE RADIOTHERAPY (IORT) FOR TREATMENT OF LOCALLY ADVANCED ESOPHAGEAL CANCER: PRELIMINARY RESULTS IN A SERIES OF 17 PATIENTS

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Aims: To assess feasibility and efficacy of intraoperative radiotherapy (IORT) as a boost after preoperative chemo-radiotherapy (RT) in patients with locally advanced esophageal cancer.

Methods: From 2007 to 2016, 17 patients (pts), median age 61 years, with locally advanced esophageal cancer were enrolled in our institutional protocol and underwent pre-operative chemo-radiation therapy followed by surgery with IORT boost. Tumor locations were: 2 in upper, 11 in middle and 4 in lower esophageal third. Pathology was squamous cell carcinoma in 15 cases and adenocarcinoma in 2 cases. Clinical stages were: 2 pts stage II, 13 pts stage III and 2 pts stage IV. Pre-operative radiotherapy was prescribed with conformal technique by using 6-15 MeV X-rays to a total dose of 44 Gy in 22 fractions (2 Gy/fr) and one patient to total dose of 41,4 Gy in 23 fractions (1,8 Gy/ fr). Chemotherapy was given concomitantly to radiotherapy with cisplatin and 5-FU and in one case with carboplatin and taxol. IORT was performed after surgical resection to the tumor bed and/or regional lymph nodal areas by a dedicated linear accelerator (Mobetron, Intraop, Sunnyvale, CA, USA). A single dose of high-energy electrons (6, 9 or 12 MeV) of 10-15 Gy was delivered by collimator (3-5.5 cm) with bevel 0°-30°. Procedure timing was 20-25 minutes.

Results: One of 17 pts received only preoperative RT for severe renal failure and one patient required one week later surgery for mediastinitis. 4 pts developed chemo-related toxicity. Surgery consisted of total or sub-total esophagectomy with lymphadenectomy. One patient died during surgery for massive bleeding; 2 pts died one month after surgery for pulmonary embolism and gastric necrosis. Postoperative complications occurred in 7/14 cases and consisted of pulmonary embolism, gastro-tracheal fistula, respiratory distress. After median follow-up of 33 months (range 1-127 months), we observed overall survival at 1, 2, 5 years of 71%, 50% and 40%, respectively. Causes of death were: 1 pulmonary embolism, 1 pulmonary distress,1 cardiac failure and 10 progression disease with distant relapse only 2 of them (20%) showing also regional recurrences after 11 and 21 months from surgery.

Conclusions: IORT during surgery for esophageal cancer seems to be a feasible procedure combined with preoperative chemo-RT, although the risk of toxicity and complications is not negligible. Larger number of pts and longer follow-up are needed to assess the efficacy of this approach.

## PO239

### PREOPERATIVE SELECTION CRITERIA FOR INTRAOPERATIVE FULL DOSE RADIOTHERAPY (IORT) IN PATIENTS WITH EARLY BREAST CANCER

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Introduction: Breast conserving surgery (BCS) followed by whole breast radiotherapy is the standard of care for most of patients with early breast cancer . As alternative, IORT is an attractive option that shows the advantages in delineating precisely the tumor bed under visual control, performing an immediate oncoplastic breast surgery, decreasing normal tissue toxicity and reducing treatment duration. In a previous publication our institution highlighted preoperative selection criteria (age >50, the absence of lobular histology, tumor size ≤ 20 mm, pN0 or pNmic, G1-G2, ki67 ≤ 20%, non triple negative status) for patients suitable for BCS and IORT 21 Gy. These criteria are slightly different and more conservative than ASTRO or ESTRO guidelines.

Methods: We retrospectively reviewed 870 patients who underwent BCS and IORT full dose 21 Gy from January 2006 to October 2018 at Papa Giovanni XXIII Hospital, Bergamo. All patients were classified as "fulfilled" or "unfulfilled" according to our preoperative criteria as previously published; Relapse Free Survival (RFS), Metastases Free Survival (MFS) and Overall Survival (OS) have been evaluated testing the inference by long-rank test.

**Table 1.**

| | RFS % | | MTS % | | OS % | |
|---|---|---|---|---|---|---|
| | 5 years | 10 years | 5 years | 1 0 years | 5 years | 10 years |
| Aggregated data | 93.1 | 85.2 | 95.5 | 90 | 94.4 | 88.3 |
| Fulfilled | 98.5 | 93.0 | 99.4 | 93.8 | 98.3 | 94.6 |
| Unfulfilled | 92.9 | 83.1 | 94.4 | 89.9 | 93.5 | 86.6 |
| p (log-rank) | p = 0,002 | | p = 0,004 | | p = 0,020 | |

Results: Median age was 65 (range 35.8-85 years). Median follow-up was 6.4 years (range 0- 13 years) The Table 1 (1) reports RFS, MFS, OS at 5 and 10 years and

the respective p values calculated by log-rank test for all patients and the two subgroups.

Conclusions: Given the statistically significant difference between the two groups for all the examined end points we confirm and strongly recommend to be very conservative in preoperative selection criteria. Following these criteria, IORT has a recurrence rate similar to that of patients treated with adjuvant whole breast radiotherapy and breast toxicity not exceeding grade 1 RTOG toxicity scale.

## PO240

### TOXICITY ASSESSMENT OF WOMEN TREATED WITH HIGH-DOSE-RATE VAGINAL BRACHYTHERAPY IN STAGE I OF ENDOMETRIAL CANCER: COMPARISON OF TWO DIFFERENT SCHEDULES

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Aims: To compare acute and late toxicity in women with I stage endometrial cancer (EC) receiving adjuvant high-dose-rate (HDR) vaginal brachytherapy (VBT) with two different prescriptions of dose.

Materials and Methods: The record of 78 patients treated with adjuvant HDR VBT were analyzed. The two VBT schedules were: 21 Gy in 3 fractions (25 pts., Group I) and 22 Gy in 4 fractions (53 pts., Group II) delivered every two days. The acute and late genitourinary (GU) and gastrointestinal (GI) toxicity was rated according to RTOG and vaginal toxicity according to LENT–SOMA. Differences in toxicities were compared using Fisher exact test and significance was defined as a two tailed p-value <0.05.

Results: G1 acute GU toxicity was observed in 6 patients in the Group I (24%) and in 19 patients in the Group II (35%) (p=0,43). One patient in the Group I suffered from acute G2 GU toxicity (4%) (p=0,32). G1 acute GI toxicity was observed in 1 patient (4%) of the Group I and in 5 patients (9,4%) of the Group II (p=0,65). G2 acute GI toxicity was observed in 2 women of the Group II (3,7%) (p=1). Four patients in the Group I (16%) and 6 patients in the Group II (11,3%) suffered from acute vaginal G1 toxicity(p=0,71). At a mean follow-up of 37.5 months (95%CI 32,4-42,3), late G1 GU toxicity was observed in 6 women of the Group I (24%) and in 2 (3,8%) of the Group II (p=0.01). One woman in the Group I (4%) suffered from late G2 GU toxicity (p=0,3). Late G2 GI toxicity was observed in 1 woman in the Group I (4%) and in 2 women with in the Group II (3,8%) (p=1). In the Group I, late vaginal G1 and G2 toxicity was observed in 16% (4 pts.) and in 4% (1 pt.), respectively. In the Group II 5 women with late G1 (9,4%) (p=0,45), 3 women with late G2 (5,7%) (p=1) and 1 woman with late G3 (1,9%) (p=1) were observed. At a mean follow-up of 37.5 months (95%CI 32,4-42,3), in the group of women treated with four fractions (22Gy), vaginal recurrence and distant metastases was reported in one patient (1,9%) after 30 months and in one woman (1,9%) after 15 months, respectively.

Conclusions: Our evidence seems to indicate that vaginal HDR brachytherapy, delivered in three (21 Gy) or four fractions (22 Gy), is similarly effective and associated with a low rate of relevant late GU, GI and vaginal toxicity.

## PO241

### THE ROLE OF INTERVENTIONAL RADIOTHERAPY (BRACHITHERAPY) FOR NOSE VESTIBULE CANCER: SINGLE INSTITUTION EXPERIENCE.

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Aims: The purpose of this study was to evaluates treatment outcomes following Interventional Radiotherapy (IRT) for nose vestibule cancer.

Methods: A multidisciplinary tumor board, which provides therapeutic recommendations following histological diagnosis and staging according to the WANG and TNM classification, evaluates all patients (pts) in Fondazione Policlinico Agostino Gemelli IRCSS with nose-vestibule cancer. For the reported patients the multidisciplinary team indicated an exclusive IRT. Plastic tubes were always placed with interstitial approach, in the operating room in the presence of the surgeons and radiation oncologists with expertise in IRT. The exact configuration and the number of catheters was always tailored to the extent, depth and shape of the target volume. The dose was prescribed to encompass the complete clinical target volume (CTV) and spare as much of the surrounding healthy structures as possible. Pts received a total dose of 44 Gy in 14 fractions, 3 Gy per fraction, except the first and last fraction (4Gy), 2 fractions per day (b.i.d.) 5 days per week. Only one pts received a total dose of 42 Gy in 12 fractions, 3 Gy per 6 fractions and 4 Gy per 6 fractions. We measured as outcome Local Control (LC) and a patients-reported outcome to assess the pts satisfaction.

Results: 16 consecutive pts were involved in this analysis, 11 (68,8%) male and 5 (31,2%) female. The median age was 67,5 (range 46-83), the median follow

up was 45,5 months (range 5-84). All pts (100%) were affected by nose vestibule cancer. Two (12%) tumors were Basal cell Carcinomas (BCC) while 15 (88%) tumors were Squamous cell carcinomas (SCC). In the 100% of pts IRT was delivered as a definitive treatment for primary disease. Nine pts (90%) expressed a degree of satisfaction between enough and a lot and only one pts (2%) was not very satisfied. The LC at 12 and 24 months was 87,5%. No interruptions of the IRT schedule for acute toxicity were recorded.

Conclusion: This study confirms that IRT could be considered as a definitive treatment in nose vestibule cancer with excellent esthetic outcome.

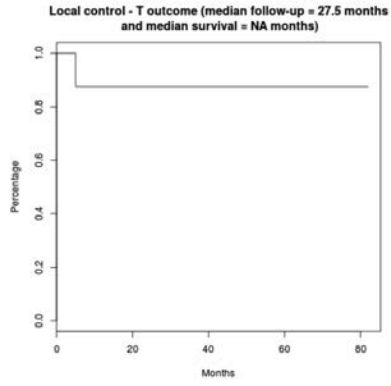


**Figure 1.**

## PO242

### LATE ASSESSMENT OF GENITOURINARY, GASTROINTESTINAL AND VAGINAL TOXICITY IN WOMEN TREATED WITH ADJUVANT VAGINAL BRACHYTHERAPY OR PELVIC EXTERNAL-BEAM RADIOTHERAPY PLUS VAGINAL BRACHYTHERAPY IN STAGE I OF ENDOMETRIAL CANCER

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Aims: To study late toxicity in women receiving adjuvant vaginal brachytherapy (VB) versus pelvic external-beam radiotherapy plus vaginal brachytherapy (EBRT-VB) in Stage I endometrial cancer (EC).

Materials and Methods: The records of 191 women with postoperative Stage I EC and subsequently treated with vaginal brachytherapy (21Gy/3 fractions or 22Gy/4 fractions) (71 pts.) or pelvic external-beam radiotherapy (45 to 50.4 Gy over 5 weeks) plus vaginal brachytherapy (10Gy/2 fractions) (120 pts.) were analyzed. All brachytherapy treatments were delivered every other days. Tolerance to treatment was graded according to RTOG scale, for late genitourinary (GU) and gastrointestinal (GI) toxicity, and according to LENT–SOMA for late vaginal toxicity. Differences in toxicities were compared using Fisher exact test. Significance was defined as two tailed p-value <0.05.

Results: Nine patients (7,5%) in the group treated with EBRT-VB [mean follow-up: 45, 9 months (95%CI 44,1-54.7)] and 1 patient (1,4%) in the group treated with VB [mean follow-up: 36,9 months (95%CI 31,9-41,9)] suffered from G2 or higher late GI toxicity (p=0,42). Grade 3 (0,8%) and grade 4 (3,3%) late GI toxicity was only observed in the group treated with EBRT-VB. Four patients (3,3%) in the group treated with EBRT-VB and 1 patient (1,4%) in the group treated with VB suffered from G2 or higher late GU toxicity (p=0,65). Similarly to the late GI toxicity, grade 3 (0,8%) but not grade 4 late GU toxicity was only observed in the group treated with EBRT-VB. Thirteen patients (10,8%) in the group treated with EBRT-VB and 5 patient (7,2%) in the group treated with VB suffered from G2 or higher vaginal toxicity (p=0,45). Grade 3 late vaginal toxicity was observed in 7 out of 120 (5,8%) patients treated with EBRT-VB and in 1 patient treated with VB, respectively (p=0,26). Vaginal recurrence and distant metastasis rate was 2,8% for both indicators [mean follow-up of 36,9 months (95%CI 31,9-41,9)] in the group treated with VB and 2,5% and 3,3% in the group treated with EBRT-VB [mean follow-up: 45,9 months (95%CI 44,1-54.7)].

Conclusions: the low rate of relevant late GI, GU and vaginal toxicity seems to indicate that the combined use of pelvic external-beam radiotherapy with VB is well tolerated. Superiority of EBRT-VB compared with VB was not demonstrated. VB alone remains an appropriate adjuvant treatment in stage I EC.

## PO243

### HDR BT TREATMENT OF NON-MELANOMA SKIN CANCER: OUTCOME AND FEASIBILITY IN A RETROSPECTIVE ANALYSIS

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Aim: To evaluate tumour control and toxicity in elderly patients treated with HDR-BRT.

Methods: A total of 55 patients underwent skin HDR-BRT from October 2007 to July 2018 with Iridium-192 source. 34 lesions in 31 patients affected by NMSC were enrolled; lymphopoietic, breast and benign histology (keloids) were excluded from the analysis. The median age at diagnosis was 79,6 years [48,5-102,4]. A surface flap was customized to the size of each target lesion and the catheters were embedded; every treatment was optimized with 3D planning using

CT imaging. Different prescribed doses and fractionation have been chosen: 24- 31.5 Gy in 8-12 fractions for palliative treatment (5 cases, 15%), 34-52 Gy in 10-20 fractions for adjuvant treatment (20 cases, 59%) and 36,75-60 Gy in 7-30 fractions for radical treatment (9 cases, 26%); the average biological effective dose (BED) was 35.7, 51 and 60.9, respectively. The treatment was mostly delivered with daily fraction and some schedules were accelerated with 2 fractions a day. Acute and late toxicity has been recorded according to CTCAE 4.0.

Results: At a median follow-up of 12 months (range 3-77,2 months), local control was 97%; in particular no patient treated with an adjuvant BRT HDR after radical surgery had local recurrence and 7 of the 9 lesions (78%) who received a radical dose showed a complete response. In only 4 lesions a partial response was observed, mostly in the palliative group, and just 1 case developed a progression. No severe acute toxicity was recorded; just 32% of the cases presented G2 acute toxicity, recovered within 2 months from the end of BRT. Late G1 toxicity was showed in almost a quarter of the lesions; no G2 or greater late toxicity was recorded. 62% lesions showed an excellent cosmetic impact and just 2 cases resulted in a fair cosmetic outcome.

Conclusion: HDR-BRT represents an effective and safe solution for the treatment of NMSC, even in elderly population, with excellent clinical outcome and very low toxicity. More data with a longer follow-up are necessary.

**PO244**

## INTERMEDIATE AND HIGH-RISK PROSTATE CANCER TREATED WITH PERMANENT INTERSTITIAL BRACHYTHERAPY AND EXTERNAL BEAM RADIOTHERAPY. A MONOISTITUTIONAL EXPERIENCE

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Aims: A combination of brachytherapy with supplemental external beam radiation therapy (EBRT) and androgen deprivation therapy results in excellent biochemical control and cause-specific survival in the most unfavorable subset of intermediate and high-risk prostate cancer patients. Moreover the technique is associated with very low rates of acute and late toxicity.

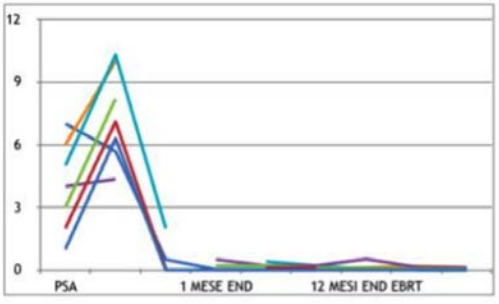
Methods: We retrospectively analyzed 7 patients with diagnosis of intermediate-high risk of prostate cancer, treated from December 2010 to August 2017 with I 125 BT LDR and successive EBRT +\- androgen deprivation therapy (ADT). Toxicity were scored according to CTCAE scale at the end of treatment, one month later, and subsequently 3-6-12 months after EBRT. PSA progressions were scored before BT LDR, at the end of treatment, one month later, and subsequently 3-6-12 months after EBRT.

Results: Pts treatments schedule were the following: I 125 BT LDR (110 Gy with a D90 ≥160 Gy in literature D90>145 Gy ) and external beam radiotherapy (EBRT) with a total dose 45 Gy in 25 total fraction. Median PSA pre BT LDR was 7,1 ng/ml (range 4,35-10,3). We observe a progressive decreasing PSA trend, which is reported in Figure 1. In Table 1 we reported results of genitor-urinary (GU) and gastro-intestinal (GI) toxicity.

Conclusions: In our experience permanent interstitial brachytherapy usually with supplemental EBRT and androgen deprivation therapy results in excellent biochemical control cancer patients. Symptoms score registered have a decreasing grade trend: GU and GI toxicities are very common 1 months after the end of BT LDR and EBRT (respectively 71% of pts G2 and 57% of G1) but in long term FU the total of patients have a complete response.

**Table 1 and Figure 1.**

| | | POST BT | | 1 MONTH | | 3 MONTHS | | 6 MONTHS | | 12 MONTHS | | 18 MONTHS | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Toxicity | Grade | N | % | N | % | N | % | N | % | N | % | N | % |
| gi | G0 | 6 | 0.86 | 4 | 0.57 | 6 | 0.86 | 4 | 0.57 | 4 | 0.57 | 5 | 0.71 |
| | G1 | 1 | 0.14 | 2 | 0.29 | 1 | 0.14 | 2 | 0.29 | 0 | 0 | 0 | 0 |
| | G2 | 0 | 0 | 1 | 0.14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | missing | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.14 | 3 | 0.43 | 2 | 0.29 |
| gu | G0 | 0 | 0 | 1 | 0.14 | 4 | 0.57 | 5 | 0.71 | 4 | 0.57 | 5 | 0.71 |
| | G1 | 2 | 0.29 | 5 | 0.71 | 3 | 0.43 | 1 | 0.14 | 0 | 0 | 0 | 0 |
| | G2 | 5 | 0.71 | 1 | 0.14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | missing | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.14 | 3 | 0.43 | 2 | 0.29 |



## PO245

### 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.

## PO246

### ABSTRACT WITHDRAWN

## PO247

### PROGNOSTIC ROLE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) AND PATHOLOGICAL RESPONSE (PR) IN LOCALLY ADVANCED RECTAL CANCER (LARC) TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY (CRT)

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Aims: In Italy Colorectal cancer (CRC) is still one of the most common malignancy with 51.000 new cases observed in 2018. About 30% of these new cases are rectal cancers. Preoperative chemoradiotherapy (CRT) is the standard treatment for locally advanced rectal cancer (LARC) before surgery. Few studies have reported data of the prognostic significance of neutrophil-to-lymphocyte ratio (NLR) in patients with rectal cancer. A lot of studies relates the raise of NLR to the poor survival of patients with rectal cancer (RC). Nowadays,the greatest number of scientific publications regards the Asian population. We retrospectively investigated the relationship between NLR and response to neoadjuvant treatment.

Methods: From July 2017 to April 2019 we consecutively treated 39 patients with LARC with capecitabine (825mg/mq/bid) and concomitant RT. Subsequently patients received radicalsurgery. Baseline clinical and radiological staging was T4N0 for one patient; T3N1 for 17 patients, T3N0 for 18 patients, T2N1 1 patient and T2N0 for 2 patients. Before starting CRT (baseline), we collect white blood cell count (WBC), absolute neutrophil count (ANC) and absolute lymphocyte count (ALC). NLR was calculated as ANC/ALC. NLR=3 was defined high. NLR was related to pathological tumor response (sec.AJCC/CAP). We made a comparison between pre-CRT NLR and post-CRT NLR, gathering patients in four subgroups.

Results: At baseline NLR was < 3 in 24/39 (62%) and a NLR=315/39 (38%) respectively. A 0 TRG was recorded for 7 patients with NLR=3 (46%) and for 13 patients with NLR< 3 (54%). The percentage of lymphocytes in the total WBC population was higher in patients with pCR than that without pCR. One patient with NLR=6 showed disease progression, in this case

percentage of lymphocytes was low (13%).

Conclusions: Our data suggest that baseline low NLR could be an indication of a good pathological response but our cohort is too small to have statistical relevance. Other studies with numerous samples are needed to validate the prognostic meaning of NLR as prognostic marker in patients with LARC who received CRT.

## PO248

### MULTICENTER OBSERVATIONAL STUDY ON EFFECTS OF A SPECIFIC DIETARY SUPPLEMENT OF "MASTHIA COMPOSTA" TO MAINTAIN THE NORMAL CONDITIONS OF ORAL MUCOSA AND ESOPHAGUS DURING RADIOTHERAPY OR CHEMO-RADIOTHERAPY

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Aims: We conducted an observational multicenter study to evaluate the capability to maintain the normal conditions of mucous and esophagus of an oral suspension of "Masthia composta"("Mc")(Aloe, Masthia, Hyaluronic Acid, Klamath seaweed and Mallow) in patients (pts.) affected by head and neck or thoracic tumors treated with radiotherapy (RT) or Chemo-RT .

Methods: 74 pts.(63 with Head and Neck cancer, 5 with Pulmonary cancer, 2 with Esophagus cancer, 2 with metastatic neck lymph nodes and 2 with Thymoma) were evaluated. The pts. were treated by hypo or normo-fractionated RT at doses of 50-70 Gy. They took "Mc" 10 ml/3 times a day throughout the whole RT. Characteristics of Head and Neck pts. are reported in Table 1. Mucositis and esophagitis were evaluated before, weekly and at the end of RT by RTOG/CTCAE 4.0 scale. In case of symptoms, pts. were treated by pharmacological supportive care.

Results: Mucositis (evaluated in head and neck pts. alone) was >G1 in 7/63 (11,1%) pts. at second week of therapy, in 9/63 (14,3%) at third week, in 16/63 (25,3%) at fourth week, in 3/63 (4,8%) at fifth week, and in 9/63 (14,3%) at sixth /seventh week. Globally, 44/63 pts. (69,8%) developed mucositis > G1 between second and seventh week of RT. G3 mucositis was present in 9/63 (14,3%) pts. Esophagitis (evaluated in all pts.) was > G1 in 5/74 (6,8%) pts. at second week of therapy, in 4/74 (5,4%) at third week, in 17/74 (23%) at fourth week, in 2/74 (2.7%%) at fifth week, and in 5/74 (6,8%) at sixth /seventh week. Globally, 33/74 pts. (44.6%) developed esophagitis > G1 between second and seventh week of RT. G3 esophagitis was present in 5/74 (6,8%) pts. All pts. evaluated had good compliance to "Mc" without any side effect.

Conclusions: Studies of radical RT or Chemo RT in Head and Neck cancer (Trotti, 2013, Mallick, 2016, Ghi, 2017) reported a mean incidence of mucositis in 80% of pts. and in particular G3 or more in 34-41%. In present study mucositis >G1 appeared in 69.8% of pts. which of G3 in 14.3%. Neck or thoracic radical RT or Chemo-RT can induce esophagitis in about 75% of pts. and the incidence of G3 or more toxicity is usually 20-30% (Wang, 2016, Verma, 2017, Zhao, 2019). We found esophagitis >G1 in 44.6% of pts. which of G3 in 6,8%. Our results, despite on a limited number of pts. and without a control arm, suggest efficacy of the oral suspension of "Mc" to maintain the normal conditions of mucous and esophagus with a good tolerance by patients.

**Table 1. Head and Neck patients' characteristics.**

| | | Patients' number |
|---|---|---|
| Tumor Site | Oropharynx | 20 |
| | Oral Cavity | 12 |
| | Larynx | 12 |
| | Hypopharinx | 10 |
| | Nasopharinx | 8 |
| | Parotid Gland | 1 |
| T Stage | cT1-T2 | 22 |
| | cT3-T4 | 18 |
| | pT1-T2 | 10 |
| | pT3-T4 | 10 |
| | Relapse | 3 |
| N Stage | cN0-N1 | 15 |
| | cN2-N3 | 28 |
| | pN0-N1 | 6 |
| | pN2-N3 | 14 |
| Treatment | RT alone | 28 |
| | Concomitant CT-RT | 27 |
| | Concomitant Cetuximab | 6 |
| | Sequential CT-RT | 2 |

## PO249

### CELLULAR PHONE'S RADIOFREQUENCY EXPOSURE AND INSORGENCE OF GLIOMA: A SISTEMATIC REVIEW AND A METANALISYS

A. Guaineri[1], G. Peretto[1], A. Alghisi[1], D. Tomasini[1], L. Triggiani[1], P. Borghetti[1], M. Maddalo[1], S. Pedretti[1], C. Tomasi[2], S. Catalani[3], L. Spiazzi[4], S.M. Magrini[1], M. Buglione[1]

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Aims: In recent years an increase in the incidence of new glial tumors related to the use of mobile telephony devices has been claimed. The aim of this analysis is to verify the relation between exposure to radio frequencies, emitted by mobile phones, and the glial neoplasms occurrence.

Methods: Data sources: A systematic review and meta-analysis of articles in English, Italian, French and Spanish using EMBASE and PUBMED as search engines has been conducted. The search was conducted

entering the following string: ""cellular phone"" OR ""mobile-phone"" OR ""wireless"" AND ""neoplasms"" OR ""cancer"" OR ""brain-tumor"" OR ""glioma"" OR ""meningioma"" OR ""neurinoma"". No date or publication restrictions were imposed. The last search date is April 2018. -Eligibility Criteria/Study selection/ Study design: 1595 articles were initially selected from PUBMED and 2464 from EMBASE for a total of 3035 articles eliminating the double ones, and those not related to gliomas. The articles were firstly selected by 3 independent authors using the title; then the further selection, by an author, was done reading the abstracts and the last choice was based on the full text. Finally 24 publications on 14 retrospective studies have been identified.

Results: Study evaluation: In the overall analysis the data were extracted and measured in terms of the odds ratio (OR) and 95% confidence interval (CI) using the Fixed model which resulted in a heterogeneity of 88.8%, therefore the Random model was applied, and it was significant for all the publications analyzed.-Data extraction: The combined data showed that an association between mobile phone use and glioma odds ratio (OR) =1.104 (95% confidence interval [CI]: 1.031-1.177, p>0.001) could be present. Since in the Funnel graphical representation relating to the publication bias, a strong publication selection bias is evident, a much more precise pooled analysis regarding the single variables is strongly needed.

Conclusions: Even if this very preliminary analysis might suggest a positive association between exposure to radiofrequencies and glial tumors occurrence, a strong selection bias is evident, hampering the robustness of this conclusion. The results of the pooled analysis have to be awaited before drawing any conclusion.

## PO250

### MONO-INSTITUTIONAL OBSERVATIONAL PROSPECTIVE TRIAL ON THE CLINICAL APPLICATION OF HYBRID 1.5 TESLA MR-LINAC

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Aim: The combination of image-guided radiotherapy (IGRT) and highly conformal technique (i.e. intensity-modulated radiotherapy) can allow an improvement in radiation treatment quality, minimizing normal tissue toxicity. Specifically, cone-beam computed tomography (Cone-beam CT) represents a significant advancement in modern radiotherapy. Nevertheless, Cone-beam CT does not permit, especially in soft tissue, a precise differentiation between disease and surrounding organ at risk, increasing uncertainties during radiotherapy. Novel hybrid Linac systems including Magnetic resonance (MR) on-board could be the step forward in IGRT due to the capability to define anatomy in details in order to daily check, correct and adapt dose distribution. In June 2018, Unity® (ElektaTM, Sweden) Linac with 1.5 Tesla MRI on board received CE marking for clinical use. Herein, we present the design of observational prospective study for the first National clinical implementation of 1.5 Tesla MR-Linac (Unity® (CE, Elekta, Sweden)) in the Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria.

Methods: The current study was approved by local Ethical Committee on the behalf of Rete Oncologica Veneta (ROV). Patients eligible to MR-Linac treatment are as follow: a) diagnosis of low-intermediate risk prostate cancer, b) diagnosis of inoperable or borderline pancreatic cancer, c) presence of oligometastatic disease (≤ 4 metastases) and d) local relapse suitable for re-irradiation.

Results: The study population consists of 230 patients recruited in 12 months. Primary endpoints are: I) to define the optimal MR-Linac workflow and the feasibility of the treatment approach, II) to assess a cost-effectiveness analysis of the new technology in order to define a dedicated reimbursement. Secondary endpoints are to evaluate clinical outcomes and to assess potential radiomic parameters.

Conclusions: The results of this study will assess the role of hybrid system Unity® (ElektaTM, Sweden) Linac with 1.5 Tesla MRI on board in the previously described specific settings. MR-Linac is an innovative system in modern radiotherapy. This prospective study will allow a National implementation in daily clinical practice.

## PO251

### ARISE STUDY: PRELIMINARY RESULTS ON EVALUATION OF ANALGESICS PRESCRIPTION AND ON PAIN MANAGEMENT IN RADIOTHERAPY DEPARTMENTS PATIENTS

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Aim: this is an ongoing observational prospective trial to evaluate the adequacy of analgesics prescrip-

tions in Radiotherapy (RT) Departments (Dept), using the Pain Management Index (PMI). In this preliminary analysis we evaluated the correlation of PMI with intensity of pain and with some possible predictive factors.

**Table 1. Characteristics of patients and pain.**

| Characteristics of patients | | |
|---|---|---|
| | | *N (%)* |
| ***Patients*** | | 626 (100.0) |
| ***Gender*** | M | 271 (43.3) |
| | F | 355 (56.7) |
| ***Age*** | ≤ 70 | 415 (66.3) |
| | 71 – 80 | 159 (25.4) |
| | > 80 | 52 (8.3) |
| ***Aim of RT treatment*** | Curative | 392 (62.6) |
| | Palliative | 234 (37.4) |
| ***ECOG-PS*** | 0 | 148 (23.6) |
| | 1 | 299 (47.8) |
| | 2 | 106 (16.9) |
| | 3 | 58 (9.3) |
| | 4 | 15 (2.4) |
| ***Tumor stage*** | Non metastatic | 370 (59.1) |
| | Metastatic | 256 (40.9) |
| **Characteristics of pain** | | |
| | | *N (%)* |
| ***Patients with pain score and/or analgesic score ≠ 0*** | | 458 (100.0) |
| ***Type of pain*** | Neoplastic | 235 (51.3) |
| | Non neoplastic | 142 (31.0) |
| | Mixed | 81 (17.7) |
| ***NRS*** | 0 | 35 (7.6) |
| | 1 – 4 | 166 (36.2) |
| | 5 – 6 | 141 (30.8) |
| | 7 – 10 | 116 (25.3) |
| ***Analgesic drug*** | No therapy | 113 (24.7) |
| | Nonopioids | 175 (38.2) |
| | Weak opioids | 60 (13.1) |
| | Strong opioids | 110 (24.0) |
| ***PMI**** | – 3 | 16 (3.5) |
| | – 2 | 58 (12.7) |
| | – 1 | 144 (31.4) |
| | Negative | 218 (47.6) |
| | 0 | 147 (32.1) |
| | 1 | 59 (12.9) |
| | 2 | 24 (5.2) |
| | 3 | 10 (2.2) |
| | 0 or positive | 240 (52.4) |

***PMI = Analgesic Score - Pain Score**

**Pain score** is evaluated as: 0= none, 1= mild, 2= moderate, 3= severe
**Analgesic score** is evaluated as: 0= none given, 1= non-opioid drugs, 2= weak opioids, 3= strong opioids

Methods: 2000 consecutive patients (pts) of RT Dept will be enrolled 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, noncancer pain-NCP, mixed pain-MP), prescribed analgesics (analgesic score), aim of RT treatment, ECOG Performance Status (PS) will be collected. Pain score and analgesic score are evaluated as shown in Table 1. 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 626 pts enrolled in 7 RT Dept. Of these, 73.2% (458 pts) had pain: in 51.3% cases it was CP, 31% was NCP, 17.7% was MP. PMI was <0 in 47.6% of pts. MP is related to higher NRS than CP e NCP (p=0.002). NCP is related to lower analgesic score values (50% 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). An increasing in NRS is related to a worse PS in all the pts categories. In pts with CP and NCP a worse PS is related with better PMI value (p<0.001 and p= 0.002, respectively). At the univariate analysis, higher pain intensity measured with NRS is typical of pts with metastatic disease (p=0.002), pts receiving palliative RT treatment (p<0.001), and pts with poor PS (p<0.001). The lower adequacy of analgesic prescription (PMI<0) is typical of women (p=0.006), pts with no metastatic disease (p<0.001), pts receiving curative RT treatment (p<0.001) and pts with good PS (p<0.001).

Discussion: the characteristics of pts receiving the most inadequate analgesics prescription are opposite to those of the pts with the most severe pain, suggesting that a negative PMI is not related to a higher pain score but rather to an inadequate management of pain by the physician, whereas Radiation Oncologists approach when prescribing analgesics should not be negatively influenced by the more favourable characteristics of pts. However, it's remarkable that the pain management in critical pts is accurate.

## PO252

## COMPLEMENTARY MEDICINE CAN REDUCE TOXICITIES TREATMENT RELATED AND MAY IMPROVE PATIENT'S COMPLIANCE. THE COMITY STUDY (COMPLEMENTARY MEDICINE IN RADIO-ONCOLOGY TREATMENT)

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Aims: Complementary Medicine (CM) embrace five categories of therapeutic interventions, including whole medical system (naturopathy), biology-based practices (herbal product, probiotics, vitamins) and manipulative and body-based practices (acupuncture). Studies about the utility of CM in oncological patient have increased in literature, but only few of them are focused on radio-oncology and none on toxicities reduction. Acute toxicity can reduce the effectiveness of cancer treatment. CM has anti-inflammatory and anti-oxidant effects that be able to reduce radiation-induced toxicity. The purpose of this study was to assess the potential benefit of CM to reduce the toxicities treatment related and to improve the patients' compliance and adherence to treatment.

Methods: 84 patients were enrolled in this study, all

patients were undergoing to radio-treatment. 28 were affected by rectal cancer and 56 by uterine cancer. 55 patients (65%) underwent to concomitant chemotherapy. All patient were assessed by a physician with expertise in CM before to start the treatment. A weekly re-assessment was planned until the end of radio and chemo treatment. During the visit were performed validated tool to assess toxicities, compliance and adherence to treatment planned. To assess acute radiation toxicity was performed radiation therapy oncology group (RTOG) scoring system. All patients enrolled in this study were assessed every week, also by a radio-oncologist specialist as standard care.

Results: Of the 84 participants (median age 61 years), 45 (53,5%) complete the 4 scheduled CM assessment visits. 41 (34.4%) followed the specific diet indication, 33 (27.7%) consumed nutritional supplements as prescribed, 36 (30.2%) took the combination of probiotic as set during the first assessment. Only 6 patients (5%) complained nausea G2, 5 (4.2%) diarrhea G2, 7 (5.8%) were affected by cystitis and 9 (7.6%) by proctitis. Fatigue was referred by 24(20.2%) pts at the end of treatment compared to 36 (30.2%) that complain fatigue at the first visit.

Conclusion: Our data have been confirmed the hypothesis that CM reduce the toxicities induced by local and systemic treatments, improve the patients' compliance and adherence to RT-CH treatment. It's possible to observe a compliance reduction to CM treatment during the RT timing. We hypothesized that this data was related to the cost of CM in terms of waiting time and occupancy of the day, and the family support for patients offsite.

## PO253

### EFFICACY OF SUCRALFATE-BASED HYALURONIC ACID MOUSSE - IONIC COLLOIDAL SILVER (HYALFATE CREAM / MOUSSE) IN THE PREVENTION, MANAGEMENT AND TREATMENT OF RADIOTHERAPY SKIN DAMAGE IN PATIENTS DURING HEAD AND NECK RADIOTHERAPY

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Background and Aim: Radiation dermatitis is one of the most common side effects of Radiation Therapy (RT). Skin toxicity can compromise the patient's quality of life, limiting daily activities or leading to interruption of radiotherapy treatment in cases of more severe acute toxicity. At the moment there is no existing consensus on its prevention or management. The aim of this work is to evaluate the effectiveness of a Sucralfate-based hyaluronic acid mousse (HYALFATE©) in the prevention, management and treatment of radiotherapy skin damage in patients during head and neck radiotherapy.

Materials and Methods: In this study we evaluate a small cohort of patients who underwent post operative or curative radiotherapy (who were advised to apply HYALFATE mousse twice a day), assessing radiation skin reactions (according to RTOG scale) before starting RT, every four weeks for a period of 16 weeks and compliance to the mousse (allergic reactions and satisfaction with the product).

Results: 2 patients had worsening of general conditions and interrupted RT; 2 patients continued medical checks in their cities; 5 patients stopped use of Hyalfate for acute skin toxicity and they started to use corticosteroid cream. 12 patients used Hyalfate for the whole radiotherapy treatment and in the following weeks. We observed an improvement of local toxicity in all the patients and a good tolerance to the product. None of the patients developed allergic reactions to the product in exam and all the patients were satisfied with Hyalfate.

Conclusion: Radiotherapy skin toxicity, particularly in the head and neck patients, represents a very frequent and often debilitating complication for the patient undergoing radiotherapy treatment. It is very important to better manage this complication to allow the patient to better adhere to the therapy; therefore the adoption of adequate medical devices is absolutely necessary before, during and after radiotherapy treatment

## PO254

### COMPLEMENTARY MEDICINE: MANAGEMENT OF FATIGUE DURING RADIOTHERAPY - ROLE OF KINESIOLOGY EVALUATION WITH LOW DOSE MEDICINE AND PHYTOTHERAPY

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Background and Aims: Radiotherapy is a worldwide modality for cancer treatment burdened by several side effects, both local and systemic, most common of these is Fatigue. Optimal management of side effects can be achieved with different methods. Aim of this study was to identify an asthenic "geopathic person" and select the most suitable remedies for the single person according to a standard kinesiologic method.

Material, Methods and Design: We determined the grade of symptoms (VAS score) and identified a geopathic positivity with a kinesiologic test. In the condition of geopathic positivity we tested phytotherapic and homotoxic remedies with a kinesiologic evaluation and we revaluated regularly the grade of symptoms d during and after the completion of radiotherapy. 79 patients were evaluate and 61 of these were identified as "geopathic" with important initial fatigue (median VAS 9). We have identified the best of four remedies for this symptomatology.

Results: We observed a median VAS score of 0 after

supportive therapy; only 3 patients (5%) we considered not responder because decrease of VAS score < 3.

Conclusions: We can deal with the problem of fatigue with targeted remedies and with a prediction of high percentage of benefit level of 95% using complementary medicine.

## PO255

### FATIGUE IN RADIOTHERAPY AND ACUPUNCTURE (FAIR-AC): A PROSPECTIVE RANDOMIZED PHASE II TRIAL

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Aims: To investigate the actual incidence of fatigue (F) in Italian patients (pts) treated with radiotherapy (RT) for breast (BC) or prostate cancer (PC), and assess the activity of a complementary therapy (acupuncture, (A)) in alleviating F in cancer pts.

Methods: A prospective randomized phase II trial will enroll 400 consecutive pts affected with BC both after breast conservative surgery or mastectomy who will be referred for postoperative RT, and 200 consecutive pts affected with PC, referred for definitive or postoperative RT to three Radiotherapy Centres (in Arezzo, Grosseto and Siena), integrated in the Area Vasta Sud Est RT Network (AVSERTN). Beyond demographic and clinical characteristics, other risk factor for F will be registered (smoking habit, Body Mass Index, time to reach Radiotherapy Facility, hormonal status, qualification, planned RT volume, type of surgery, economic status). After the enrollment in the clinical trial, BC patients will be stratified according to adjuvant and neo-adjuvant chemotherapy (CT) (yes/no), and PC patients according to concomitant androgen deprivation therapy (ADT) (yes/no), because both CT and ADT may cause F before the start of RT. Randomization in the 2 arms protocol (ratio 2:1) will be used. In Arm 1 they will be treated with "standard care" (400 pts), in Arm 2 with "standard care+A" (200 pts), in order to evaluate the improvement due to A respect to standard care alone. Data collection will be made by specific questionnaires investigating F and QoL.

Results: The expected results will be the assessment not only of the actual incidence of F in Italian BC and PC pts treated with RT, but also the evaluation of the activity of A in prevention and alleviation of F (by comparison of results in terms of incidence and severity of F in Arm 1 and Arm 2).

Conclusions: If A will show activity in RT-related F, a phase III trial investigating efficacy of A in RT-related F will be subsequently planned within the AVSERTN.

## PO256

### NEW RADIOTHERAPY APPROACHES FOR STAGE IIIA-IIIB NSCLC COMBINING HYPOFRACTIONATED RT WITH CHEMOTHERAPY: PROPOSAL FOR A NEW CLINICAL TRIAL

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Aim: The common therapeutic strategy for locally advanced lung cancer is based on the use of chemotherapy (CHT) concurrent with conventional radiotherapy. In this study, we evaluated hypofractionated radiotherapy with different temporal association with CHT and analyzed the results in terms of local control (LC), overall survival (OS) and toxicities.

Methods: Between November 2011 and June 2017, 67 pts were treated with Stereotactic Hypofractionated Radiotherapy for locally advanced lung tumor NSCLC stage IIIa-IIIb. Median age was 68.4 ys, KPS >70, 25 pts (37,3%) underwent sequential SBRT after CHT, 22 pts (22,8%) SBRT was delivered between one cycle and another, in 9 pts (13,4%) SBRT before CHT, and 11 pts (16.4%) underwent only SBRT. Histology was Adenocarcinoma and Squamous cell carcinoma in 60% and 40% cases respectively. In pts who have integrated treatment, SBRT was performed no earlier than two weeks before or after CHT. In 26 pts target was contoured on plan CT- PET fusion. Median volume GTV was 82,6 cc (36 -192 cc). Median delivered dose was 40 Gy/5fx (median BED 10 =100 Gy) prescribed to 80% isodose line. Dose Constraints used are reported in AAPM TG 101.VMAT - SBRT was delivered by 6MV beam modulator Linac, in 28 pts breath hold technique was used. Toxicities were assessed by CTCAE 4.3 criteria and the results were evaluated two months after SBRT and every four month successively.

Results: Median follow-up was 16 months (3– 8 mo). 59.7% pts show complete response and 32,8% pts partial response. LC was 90% at 12 mo and 75% at 18 mo for pts underwent SBRT between or after cycles of CHT, and OS was 86% at 12 mo and 74% at 18 mo. In pts underwent SBRT only or SBRT before CHT, LC was 85% at 12 mo and 72% at 18 mo and OS was 83% at 12 mo and 70% at 18 mo.10 pts showed G2 disphagia. Late toxicity G3 was observed in3 pts (esophageal stenosis in 1pts and bronco-esophageal fistula in 2 pts), but endoscopy showed local recurrence in all cases.

Conclusion: In our experience hypofractionated RT for locally advanced NSCLC are safe and effective. Treatments with BED10 >100Gy are effective leading to high LC ( 88% at 12mo and 74% at 18mo). SBRT with CHT increases LC and OS with low toxicities. Our results indicate that the better synergistic effect of RT plus CHT appears when hypofractionated RT is located in the rest period between CHT cycles. To assess the best timing of this association specific trials are needed.

PO257

## PREST: PAIN REDUCTION WITH BONE METASTASES STEREOTACTIC RADIOTHERAPY: A PHASE III RANDOMIZED MULTICENTRIC TRIAL

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Aim: Palliative antalgic treatments represent an issue for clinical management and a challenge for scientific research. Radiotherapy (RT) plays a central role. Techniques such as stereotactic body radiotherapy (SBRT) were largely investigated in several phase 2 studies with good symptom response at 3 months, becoming widely adopted.The efficacy of standard RT for pain management is consolidated. Still is lacking evidence from randomized, direct comparison of RT and SBRT.

Method: The PREST trial primarily investigates efficacy of SBRT in pain control versus standard RT. IMRT-Simultaneous Integrated Boost (SIB) approach was adopted. Personalization of treatment is included in pt selection: performed by both prognosis prediction through a clinically validated prognostic score (Mizumoto prognostic score) and adequate spinal stability is defined according to Spine Instability Neoplastic Score (SINS). Mandatory MRI of the spinal tract is required for planning and imaging response, at baseline and 3 month after treatment.

Results: The PREST trial (NCT03597984) was designed as an interventional study without medicinal, randomized 1:1, open-label, multicentric, phase 3. It enrols pt with painful (Numeric Rating Scale -NRS- <4) spinal bone metastases. Pt at expected prognosis superior to 6 months according to the Mizumoto prognostic score, and SINS scores.

Conclusion: The PREST trial will provide insight on efficacy of an hypofractionated SBRT IMRT-SIB in pain control respect to a standard fractionation.

PO258

## MIXED-BEAM APPROACH (CARBON-ION BOOST FOLLOWED BY PHOTON INTENSITY-MODULATED RADIOTHERAPY) VERSUS PHOTON INTENSITY-MODULATED RADIOTHERAPY IN HIGH-RISK PROSTATE CANCER PATIENTS (AIRC-IG14300)

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Aims: To compare dosimetry in two radiotherapy approaches for high-risk prostate cancer (PCa) treatment: carbon ion radiotherapy (CIRT) boost followed by whole-pelvis intensity modulated radiotherapy (IMRT) versus conventional IMRT. We present the preliminary analysis of a phase II randomized clinical trial (NCT02672449, clinicaltrials.gov).

**Table 1. Dosimetric constraints of organs at risk for the 5 patients.**

| Organ at risk | Constraint | Unit of measure | 1 | | 2 | | 3 | | 4 | | 5 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | CIRT+IMRT | IMRT-only | CIRT+IMRT | IMRT-only | CIRT+IMRT | IMRT-only | CIRT+IMRT | IMRT-only | CIRT+IMRT | IMRT-only |
| Rectum | $D_{0.03\,cm3}$ | (%) | 98,5% | 100,6% | 100,2% | 98,1% | 98,5% | 100,6% | 97,5% | 99,7% | 100,0% | 101,8% |
| | $V_{95\,Gy}$ | (%) | 0,8% | 2,4% | 0,6% | 0,8% | 5,3% | 17,6% | 0,1% | 0,6% | 0,2% | 4,4% |
| | $V_{70\,Gy}$ | (%) | 3,4% | 5,5% | 2,8% | 2,6% | 16,7% | 24,4% | 0,5% | 3,2% | 0,6% | 7,6% |
| | $V_{40\,Gy}$ | (%) | 40,0% | 80,0% | 25,7% | 36,4% | 21,0% | 51,7% | 21,0% | 36,7% | 20,3% | 36,2% |
| Urinary bladder | $D_{0.03\,cm3}$ | (%) | 90,8% | 101,9% | 101,3% | 100,8% | 99,4% | 101,3% | 101,8% | 102,8% | 101,3% | 102,7% |
| | $V_{70\,Gy}$ | (%) | 1,8% | 6,0% | 5,5% | 7,5% | 9,0% | 14,6% | 10,6% | 12,3% | 4,4% | 5,7% |
| | $V_{40\,Gy}$ | (%) | 36,0% | 70,0% | 31,5% | 32,5% | 37,0% | 46,4% | 47,5% | 56,2% | 33,0% | 42,2% |
| Femoral heads | $V_{40\,Gy}$ | (%) | 1,8% | 0,9% | 4,1% | 2,9% | 6,5% | 2,0% | 3,5% | 1,9% | 4,0% | 2,8% |
| Peritoneal cavity | $D_{0.03\,cm3}$ | (Gy) | 51,7 | 53,0 | 51,0 | 51,2 | 50,8 | 51,2 | 51,0 | 52,8 | 50,9 | 51,6 |
| | $V_{45\,Gy}$ | ($cm^3$) | 178,5 | 202,0 | 193,4 | 197,7 | 82,0 | 87,0 | 112,0 | 127,4 | 12,0 | 13,7 |
| Anal canal | $D_{mean}$ | (Gy) | 17,6 | 25,9 | 10,9 | 6,9 | 28,8 | 45,0 | 14,5 | 21,3 | 11,7 | 17,2 |
| Penile bulb | $D_{0.03\,cm3}$ | (Gy) | 48,9 | 55,4 | 17,0 | 10,7 | 55,0 | 63,4 | 38,0 | 30,0 | 5,8 | 7,9 |
| | $D_{mean}$ | (Gy) | 11,3 | 15,2 | 7,7 | 8,2 | 22,9 | 36,4 | 10,5 | 11,9 | 3,7 | 5,4 |

*Five patients were treated with C-ion radiotherapy (CIRT) boost followed by whole-pelvis intensity modulated radiotherapy (IMRT). The comparative photon plan was obtained with whole-pelvis IMRT with sequential boost on prostate. For both plans, the primary goal was target coverage; in particular, concerning prostate planning target volume (PTV), we considered dose to 98% of volume ($D_{98\%}$) >95%, dose to 0.03 cm3 of volume ($D_{0.03\,cm3}$) <107%, mean dose ($D_{mean}$) <102% e dose to 2% of volume (D2%) <104%.*

*Table abbreviations: CIRT – carbon-ion radiotherapy; IMRT – intensity modulated radiotherapy; $DX_{cm3}$ – dose to X $cm^3$ of volume; VX Gy – volume receiving X Gy of prescription dose; Dmean – mean dose.*

Methods: Five consecutive high-risk PCa patients were treated with a CIRT boost receiving 16.6Gy [RBE] in 4 fractions (4.15Gy [RBE]/fraction) followed by whole-pelvis IMRT of 50Gy in 25 fractions (2Gy/fraction). Deformable registration of the planning CTs and corresponding dose was used for plan sum. A comparative IMRT photon plan was obtained as whole-

pelvis IMRT of 50Gy in 25 fractions followed by a sequential boost of 28Gy in 14 fractions (both 2Gy/fraction). The adequate target coverage was the primary goal for plan optimization. For dosimetric comparison, CIRT boost was then re-scaled to a conventional 2Gy/fraction scheme. Results: The rectum volume receiving 70Gy and 40Gy (V70Gy and V40Gy) were lower in CIRT+IMRT than IMRT-only plans. Similar results were found for urinary bladder. Conversely, the IMRT-only approach allows for lower dose to femoral heads whereas in CIRT+IMRT plans the mean V40Gy was 3.9% due to CIRT beam entrance direction (Table 1).

Conclusions: Particle therapy allows reaching a higher sparing of organs at risk, which is expected to reduce induced-toxicity, while increasing the efficacy due to the higher RBE of C-ions. The future development of this prospective trial will lead to more mature data concerning the clinical impact of the mixed-beam approach in high-risk PCa treatment.

**PO259**

## IMPACT OF ACUPUNCTURE ON THE INCIDENCE OF ACUTE TOXICITY IN PATIENTS TREATED WITH DEFINITIVE CONCOMITANT RADIO-CHEMOTHERAPY (RCT) FOR LOCALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA (LAHNSCC): A SYSTEMATIC REVIEW AND OUTLINE OF A PHASE II TRIAL

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Aims: Acupuncture is a rising technique in the management of side-effects derived from oncological treatments. The aim of this work was perform a systematic review literature on the impact of acupuncture on acute toxicity and quality of life in patients with LAHNSCC who underwent concomitant RCT as definitive treatment.

Materials and Methods: We searched Pubmed and Embase and conducted a systematic literature review of articles published between 2009 and 2019, in which subjects with LAHNSCC received acupuncture in the frame of RCT. Articles with patients who had undergone surgery were excluded, as well as case reports, systematic reviews and trials with different endpoints. Abstracts and selected articles that met the main research criteria were included.

Results: Our systematic research produced 108 results, that were thoroughly revised according to our criteria (Figure 1). A total of 101 articles were excluded. We found 7 papers (%) regarding the effects of acupuncture in the pre-specified setting: acute xerostomia (defined as the insurgence of xerostomia within 3 months from the start of RCT) was the primary endpoint in 6 articles (of which 2 were retrospective); acute dysphagia was the primary endpoint in one randomized, controlled trial. There were no articles aiming to assess the overall quality of life in this setting of patients.

Conclusions: The role of acupuncture in reducing acute symptoms induced by RCT has been evaluated in a limited number of studies. In particular, there seems to be little evidence regarding the possible benefit of this technique in the prevention of acute dysphagia, which is a crucial side-effect of concomitant RCT with a great impact on quality of life, as it may possibly cause weight loss, malnutrition and dehydration of patients on treatment. On these grounds we designed a phase II, randomized controlled trial with the purpose to evaluate the possible impact of acupuncture on acute dysphagia in patients treated with definitive RCT.

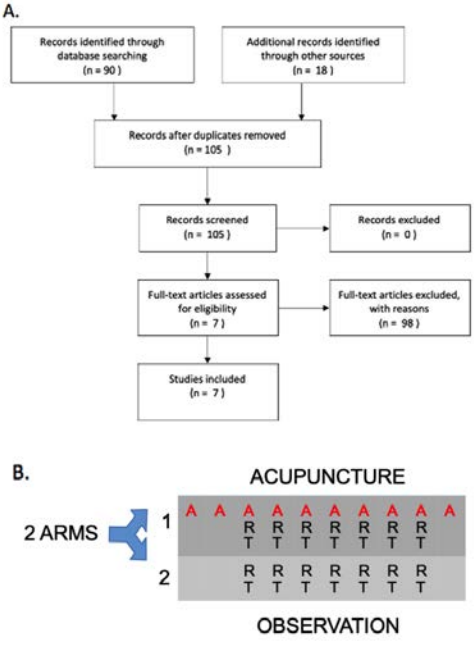


Figure 1.

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## ANTI-EMETIC EFFICACY OF FOSAPREPITANT REGIMEN IN LOCALLY ADVANCED HEAD AND NECK CANCER UNDERGOING CISPLATIN-BASED CHEMO-RADIATION: PILOT COHORT STUDY.

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Aims: Concurrent cisplatin-based chemoradiation (CRT) represents the standard in the curative setting of locally advanced head and neck squamous cell carcinoma (HNSCC). However, it is a highly emetogenic treatment. The aim of our prospective, pilot, single-center experience is to report the efficacy and safety of a Fosaprepitant (FOS)-based regimen in HNSCC patients undergoing standard CRT.

Materials and methods: Patients affected by locally advanced HNSCC candidate to concurrent CRT, administered either as definitive treatment or as adjuvant therapy, were enrolled. Acute toxicity was assessed according to CTCAE v.4.1. To investigate the impact of chemotherapy induced nausea and vomiting (CINV) on patients' quality of life, the Functional Living Index-Emesis (FLIE) and the EORTC QLQ – HN 43 questionnaire were administered at. baseline, T1 (2 weeks) and T2 (5 weeks).

Results: A total of 24 HNSCC's patients, with a median age of 64 years, were enrolled in our study. Only 3 patients (12.5%) had undergone upfront surgery before adjuvant radio-chemotherapy treatment, while, for the other 21 patients, CRT was administered with disease-curative intent. Eleven patients (45.8%) reported G0 as the worst nausea grade during treatment, 8 patients (33.3%) G1 and 5 patients (20.8%) had G2 nausea. The worst vomiting grade was G0 for 18 patients (75%), G1 for 5 patients (21%) and G2 experimented by only one patient (4%). Worst toxicity occurred more frequently in patients treated with the triweekly Cisplatin schedule. Evaluating nausea/vomiting and appetite as single domain in EORTC QLQ-HN 43 questionnaire, we found that T1 mean score was 3.0 and T2 value was 2.4. The mean FLIE baseline value was 123, while mean scores reported at T1 and T2 105.5 and 97.5, respectively. The mean overall FLIE score decrement was 26. At Wilcoxon test, FLIE score was significantly worsened from baseline to T1 (P = 0,0001), but it remained stable at T2. EORTC QLQ HN43 scores was significantly worsened from baseline to T1 (P<0,0001) and from T1 to T2 (P=0,0061).

Conclusions: The use of FOS-regimen in locally advanced head and neck cancer led to similar results in terms of reducing CINV if compared to other antiemetic triplets. Although we reported an improvement on FLIE score, this finding was not consistent when considering EORTC QLQ HN43 scores.

PO261

## REPORT OF OUR EXPERIENCE OF A YOUNG MAN WITH COGNITIVE DEFICIT AND HEAD AND NECK CANCER

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Aims: Radiotherapy (RT) is the mainstay of elective treatment for head and neck carcinomas, due to its healing potential in all non-metastatic stages of the disease. It is strongly suggested to use IMRT not only to minimize late toxicity phenomena, but also for its positive effect on the tumor response. In this case, we report our experience of a young man with cognitive impairment from birth that was diagnosed with a head and neck tumor.

Methods: In April 2015, came to our observation a 25-years-old man with epilepsy and severe cognitive deficit consequential to hypoxic ischemic encephalopathy (HIE) at birth. He had been diagnosed with a craniopharyngeal non-keratinizing squamous cell carcinoma (which the biopsy proved to be of the undifferentiated-lymphoepithelial type) that involved both the nasal fossae, maxillary and sphenoidal sinuses on either side, the left frontal sinus and that eroded the left orbit's roof and the skull base (clivus and the sella turcica), and that had therefore been staged as a IV A tumor. It was then given indication for a neoadjuvant chemotherapy (CT)(cisplatinum, docetaxel and 5FU) followed by concurrent CT cisplatino - based and RT. Concerning the RT, it was used 6 MeV energy IGRT-VMAT, with a dose of 54 Gy (2 Gy per fraction) to the primary tumor and lymphonodal levels from I to IV on either side. It was then administered a boost of 10 Gy (2 Gy per fraction) on the PET positive lesions, for a Total Dose Fractionation (TDF) of 70 Gy. In June 2016 the patient had a intracranial disease progression, so he underwent Stereotactic RT with a dose of 20 Gy (5 Gy per fraction). All along the duration of RT, weekly clinical visits monitored patient's health and provided symptomatic therapy when needed. In February 2018, during the follow up, he was diagnosed a sphenoid mucocele by MRI that caused a progressive vision decrease so he underwent surgery to remove it.

Results: Despite the onset of mucocele, probably as a RT late toxicity, the patient's quality of life and his eyesight improved and, after 4 year, the patient is still alive with a good local control of the disease.

Conclusions: Our case report demonstrated the importance of RT in the multidisciplinary management of head and neck carcinomas in young patients. Furthermore, it confirmed RT potential to produce efficient and superior dose distribution, especially for complex anatomy districts such as in head-and-neck cancer.

## PO262

### EVALUATION OF QUALITY OF LIFE IN PATIENTS WITH RECTAL CANCER AFTER NEOADJUVANT RADIO-CHEMOTHERAPY AND SURGERY

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Aims: To evaluate health-related quality-of-life (QOL) outcomes in patients with age less and more 70 years with rectal cancer after neoadjuvant radiochemotherapy and surgery.

Methods: Widely used colorectal cancer-specific QOL instruments include the Functional Assessment of Cancer Therapy-Colorectal (FACT-C). The FACT-C combines the FACT-G with a with 10-item colorectal cancer subscale (PCS) that addresses lifestyle issues that are related specifically to colorectal cancer such as bowel and stoma management. QOL outcomes were assessed using the FACT-C QOL questionnaire at time-point and subsequently periodically on follow-up. Mean scores of individual domains/scales were compared, between patients with age less and more 70 years, using 't' test.

Results: 37 patients were included in the analysis, with a median age of 67.7 years old (20 pts <70 years and 17 patients > 70 years). Median follow-up was 56,3 months. All patients underwent surgery, only 8.1% of patients underwent abdominal-perineal amputation surgery according to Miles with permanent stoma. At the time of completing the questionnaire 8 patients (21.6%) presented derivative stoma. Several general (emotional functioning, role functioning, social contact) as well as colorectal cancer-specific (bowel function and stoma management) QOL domains were preserved in all patients, only physical weel-being domain was better in young patients (<70 years) con p=0.019. Toxicity profile was similar in two categories of patients.

Conclusions: Neoadjuvant Radio-chemotherapy and surgery for rectal-cancer in elderly patients appeared safe and manageable. Only domain of physical weel-being results is compromised significantly compared to younger patients, without causing treatment interruption.

## PO263

### FERTILITY PRESERVATION IN RADIO-CHEMOTHERAPY FOR RECTAL CANCER: A COMBINED APPROACH

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Aims: Colorectal cancer is the second most frequent form of cancer among women. A combined approach including chemo-radiotherapy (CRT) and surgery is the standard of care for most cases of locally advanced rectal cancer; both radiotherapy and chemotherapy might contribute to impair fecundity and fertility. This is a case report about fertility preservation in a reproductive-aged patient.

Methods: We present the case of a 24-year-old nulligravida woman affected by low rectum adenocarcinoma, staged cT3N1 MRF+ according to TNM system. The suggested treatment was neoadjuvant long course CRT followed by delayed surgery. Before the beginning of treatment, the patient underwent laparoscopic biopsies of the ovarian tissue for cryopreservation purpose and transposition of the left ovary. The patient was also given GnRH agonist leuprorelin for ovarian function suppression before and during neoadiuvant treatment. VMAT radiotherapy was delivered to the pelvis with a total dose of 45 Gy, additional dose up to 55 Gy was administered to the tumour and correspondent mesorectum in 25 fractions with SIB technique; concomitant oral capecitabine administered every day during RT. Uterus, ovaries and vagina were delineated as organs at risk and their position was monitored with daily cone beam-CT.

Results: Treatment plan was optimized in order to minimize the dose to organs at risk, uterus, ovary and vagina in particular (left ovary Dmax=2.1 Gy). CRT was completed within 5 weeks according to the dose prescribed. Ten weeks after completion of the neoadjuvant treatment total mesorectal excision of the rectum was performed and revealed ypT2N0 residual adenocarcinoma. Four months after surgery, clinical and instrumental evaluation showed no signs of residual/recurrent disease. Regular menstrual period was reported from before the surgery and during all the follow-up time.

Conclusions: Ovarian transposition can prevent ovarian insufficiency by placing the organ outside the

radiation field; ovarian cryopreservation followed by auto-transplantation offers the possibility to restore fertility in the case of premature ovarian failure. GnRH analogs administration allowed to diminish the risk of ovarian citotoxicity. IMRT and IGRT can preserve fertility and fecundity in young women who need pelvic radiotherapy for gastro-intestinal malignancies.

**PO264**

## CONTINUOUS POSITIVE AIRWAY PRESSURE (C-PAP) SPARES RADIATION DOSE TO HEART DURING LEFT BREAST CANCER RADIOTHERAPY IN NON-COMPLIANT PATIENT: A CASE REPORT

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Aims: Left breast cancer (LBC) radiation therapy (RT) is widely used to reduce loco-regional recurrences. Deep inspiration breath holding (DIBH) prevents late effects on heart and left anterior descending coronary artery (LAD), but patients need to be fit to this technique. Aim of the study is to demonstrate the efficacy of C-PAP in the treatment of LBC, in reducing toxicity to the LAD and the heart, increasing their distance from the treatment field, also in non-compliant patients.

Methods: C-PAP has long been safely used in patients with respiratory failure and chronic obstructive pulmonary disease to maintain airway patency. It provides a constant stream of pressurized air to the upper airways and lungs. The physiologic effects expected during C-PAP are hyperinflation of the lungs, stabilization and flattening of the diaphragm. We report a clinical case of a 76-year-old woman, with LBC localized to the union of external quadrants, G3, pT1c pN2a, M0, stage IIIa, luminal A. Patient underwent left mastectomy, axillary dissection and standard adjuvant systemic therapy. Patient subsequently received breast RT with VMAT on VersaHD using C-PAP; CT-simulation was performed with Free-Breathing (FB) and then with application of C-PAP. It was prescribed standard radiation treatment.

Results: Even if the machine timing results increased, the patient was compliant and completed entire cycle of radiotherapy without problems. We compared physical changes in FB versus C-PAP, applying C-PAP under 10 cm H2O for 5 minutes, with a pO2 30%, finding out chest expansion and lung volume increase. Left lung volume was 1135.837 $cm^3$ with FB and 1351.780 cm3 with C-PAP (19% increase). The inflated thorax with C-PAP displaced the heart inferiorly and, at the same time, moves it away from left chest wall. Dose volume histogram (DVH) differences between FB and C-PAP: LAD-FB V20=0.2%, LAD-CPAP V20=0%, Left Lung-FB V25=29.66%, Left Lung-C-PAP V25= 24.51%, Heart-FB V25=1.27%, Heart-C-PAP V25=0.86%. V95 (47.5Gy) of PTV was 89% with FB+VMAT vs 94% with C-PAP+VMAT.

Conclusions: RT with C-PAP resulted to be more effective that FB to preserve organs at risk, especially heart, and to increase target coverage in the management of left breast cancer therapy even if we suggest an accurate selection of patient to optimize customized treatment.