



**“RADIOTERAPIA CON TECNICA AD INTENSITÀ MODULATA (IMRT) NEL TRATTAMENTO DEL CARCINOMA ANALE: STUDIO MULTICENTRICO RETROSPETTIVO OSSERVAZIONALE”**

**RAINSTORM**

**RA**diotherapy with **IN**ten**Si**Ty **mO**dulated (IMRT) techniques in the treatment of anal ca**Rcino**Ma: a multicenter retrospective observation study



Analisi su management della persistenza/ recidiva di malattia loco-regionale dopo RT-CT

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## 987 consecutive non-metastatic AC patients treated within 25 different Italian centers between 2007–2019

**Table 1.** Patient and tumor characteristics.

Patient and Tumor Characteristics		n = 987	%
Age = median 68.5 years (range: 54.00–80.00)			
Gender	Male	281	28.4
	Female	706	71.5
ECOG Performance Status	0	775	78.5
	1	197	19.9
	2	15	1.5
HPV	Negative	210	21.3
	Positive	229	23.2
	NR	548	55.5
HIV	Negative	747	75.7
	Positive	90	9.1
	NR	150	15.2
Tumor site	Anal Canal	879	89.1
	Anal Margin	108	10.9
Histology	Squamous	880	89.1
	Basalioid	84	8.5
	Other	23	2.3
Grading	G1	68	6.9
	G2	328	33.2
	G3	233	23.6
	NR	358	36.3
TNM Stage	T1-T2, N0	330	33.4
	T3-T4, N0	106	10.7
	Any T, N+	551	55.8
Disease extension	Early stage	330	33.4
	LAD	633	64.1
	ED	24	2.4

Legend: ECOG = Eastern Cooperative Oncology Group; HPV = human papilloma virus; HIV = human immunodeficiency virus; NR = non-reported; early disease: T1-T2 tumors; LAD = locally advanced disease (T3-T4 or N+ = node-positive tumors); ED = extended disease (lumbar–aortic and/or common iliac lymph nodes involvement).

330 patients (33.4%) had cT1-2N0 stage, 106 patients (10.6%) had cT3-4N0 stage and 551 (55.8%) had lymph node involvement.

**Overall, 633 patients (64.1%) had locally advanced disease (LAD) at diagnosis.**

Twenty-four patients (2.4%) had a single site of clinical abdominal lymph node involvement (lumbar–aortic and/or common iliac lymph nodes).

*Cancers* 2021, 13, 1902. <https://doi.org/10.3390/cancers13081902>



## Analisi su management della persistenza/ recidiva di malattia loco-regionale dopo RT-CT

### Sede della recidiva:

- GTV T o N
- CTV elettivo
- a distanza
- Iliaci comuni e/o para-aortici
- Inguinali
- Ano
- Pelvi

Imaging (PET-TC, MRI, ...)  
 Biopsia

### Tossicità correlate alla eventuale Re-I

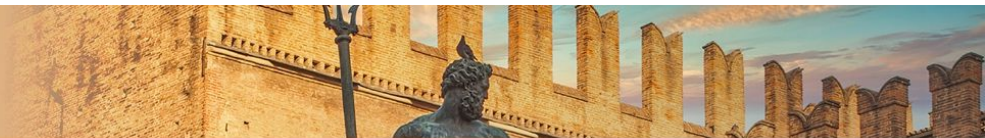
#### Cause della chirurgia:

- 1= persistenza di malattia
- 2= ripresa di malattia
- 3= tossicità

### Complicanze Chirurgiche *Clavien-Dindo classification*

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

\*Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks  
 CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.



Maggio 2022: **Stima preliminare di 176 pz (25 centri)**

Ricevuti 164 pts da 23 centri

Valutabili 139 pts → 25 esclusi per dati insufficienti

**Persistenza di malattia: 94 pts (67.6%)**

**Recidiva: 45 pts (32.4%)**



## Persistenza di malattia: 94 pts (67.6%)

**Intervallo Tempo da inizio RT** = mediana 7 mesi (1-19)

**Sede:**

- **GTV T= 70 (74.5%);** GTV N = 10 (10.7%); CTV elettivo N = 3 (3.2%); multisede = 3 (3.2%); MISSING = 8 (8.5%)
- **Ano =51 (54%);** margine anale =11 (11.7%); pelvi = 13 (13.8%); N inguinali =5 (5.3%); N iliaci comuni/paraortici =2 (2.1%); multisede = 3 (3.2%); MISSING = 10 (10.7%)
- **Conferma bioptica: SI= 50 (53.2%);** NO= 35 (37.2%); MISSING = 9 (9.6%)
- **Resecabilità: SI = 58 (61.7%);** NO = 26 (27.6%); MISSING =10 (10.7%);
- **Chemioterapia mantenimento: SI= 28 (29.8%); NO = 46 (49%); MISSING = 20 (21.2%).**
- **Chirurgia: 64 pts (68%)**
- In 4/64 pts (6.25%) chirurgia effettuata per tossicità
- **Tempo mediano alla chirurgia:** 8 mesi (1-19)
- **Tipo di chirurgia:** Robotica =1(1.5%), Laparoscopica = 18 (28%), MISSING = 45 (70.5%)
- Resezione trans Anale = 3 (4.7%); **Resezione Addomino Perineale = 47 (73.3%),** Resezione multiviscerale = 4 (6.4%), MISSING = 10 (15.6%);
- Ricostruzione anale in 5 (7.8%) con lembo muscolare in 4 (6.4%), con flap peritoneale in 1(1.5%); ricostruzione vaginale in 1(1.5%). MISSING=53 (82.8%)
- **Margini chirurgici: R0 = 35(54.6%); R1 =12(18.75%); R2 =4(6.25%), MISSING =13 (20.4%)**
- **Stage:** pT0 N0= 1 pt; pT1 N0= 6 pts; pT2 N0 = 8 pts; pT3 N0 = 4 pts; pT4 N0 = 12 pts; pN+ = 14 pts; pNx = 2 pts; MISSING = 17 pts

### • Complicanze ferita perineale

Infezioni ferita perineale = 5 (7.8%) ; deiscenza = 4 (6.4%), necessità di VAC therapy = 1(1.5%)

### • Complicanze post-CH (GRADO secondo classificazione Clavien-Dindo)

**G0=19 (29.7%); G1 =7 (10.9%); G2 =7 (10.9%); G3a= 1(15.6%); G3b= 1 (15.6%); G4a=2 (3.7%); G5= 3 (4.7%); MISSING =24 (37.6%)**

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CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

Dindo et al. Annals of Surgery • 2004



## Persistenza di malattia: 94 pts (67.6%)

**Re-I: SI= 10 (10.7%);** N0 = 82 (87.2%); MISSING = 2 (2.1%)

**Re-I:** 2 pts non operati (1= Re-I definitiva; 1= Re-I palliativa);  
8 pts Re-I dopo chirurgia (intervallo: 1-25 mesi)

**Intervallo da RT=** mediana 11.5 mesi (8-29)

**Intento Re-I:** Definitivo= 5pts; palliativo = 5pts

**Tecnica:** 3DCRT= 3 pts; IMRT= 2pts; Tomotherapy=1pt; BRT=  
2 pts; SBRT= 1pt; Protoni= 1 pt

In-field= 2 pts; **out-field= 8 pts**

Ano-retto=3

Pelvi=3

Presacrale =2

N inguinale =1

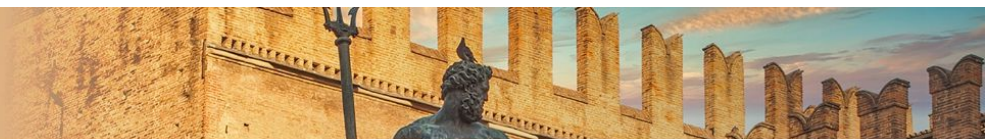
N iliaco interno (dopo miles) =1

**Tossicità acuta post Re-I:** dolore perineale= 2 pts; proctite G3= 2pts;  
disuriaG2= 1 pt; diarreaG1= 1 pt

**Tossicità tardiva:** linfedema 1 pt

**Follow-up mediano=** 19 mesi (1-144)

**Median OS=** 21 mesi (3-146)



## Recidiva: 45 pts (32.4%)

Tempo mediano da inizio RT =14 mesi (7-85)

### Sede:

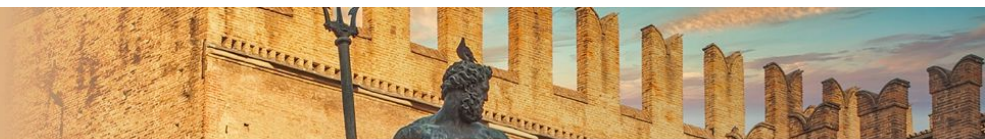
- **GTV T= 38 (84.4%);** GTV N = 3 (6.7%); CTV elettivo N = 2(4.3%); multisede = 1(2.3%); MISSING = 1(2.3%);
- **Ano =32 (71.3%);** margine anale = 2 (4.3%); pelvi = 4 (8.9%); N iliaci comuni/paraortici = 2(4.3%); multisede = 1(2.3%); MISSING = 4 (8.9%)
- **Conferma bioptica: SI= 36 (80%);** NO= 6 (13.3%); MISSING =3 (6.7%);
- **Resecabilità:** SI =31 (68.9%); NO =10 (22.2%); MISSING = 4 (8.9%)
- **Chemioterapia:** SI= 7 (15.5%); NO = 24 (53.3%); MISSING = 14 (31.2%)
- **Chirurgia:** 41 pts (91%)  
In 1/41 pts chirurgia effettuata per tossicità
- **Tempo mediano alla chirurgia:** 14 mesi (7-86)
- **Tipo di chirurgia:** Robotica =3 (7.3%), Laparoscopica =10(24.4%), MISSING =28(68.3%)  
Resezione trans Anale = 2 (4.8%), **Resezione Addomino Perineale = 23 (56.1%),**  
Resezione multiviscerale = 5 (12.2%), MISSING = 11 (26.8%)  
Ricostruzione anale in 3 pts con lembo muscolare; colpoperineoplastica in 1 pt;  
MISSING=37pts
- **Margini chirurgici: R0 = 25 (61%);** R1 =2 (5%); R2 = 0 pts, MISSING = 14 (34%)
- **Stage:** pT0 N0= 1 pt; pT1 N0= 1 pts; pT2 N0 = 11 pts; pT3 N0 = 3 pts; pT4 N0 = 1 pts;  
pN+ = 2 pts; pNx = 3 pts; MISSING = 19 pts

- **Complicanze ferita perineale**  
Deiscenza = 1 pts; necessità di VAC therapy = 1.
- **Complicanze post-CH (GRADO secondo classificazione Clavien-Dindo)**  
G0=20 (48.8%); G1 =2 (4.8%), G2 =1(2.4%); G3a= 1 1(2.4%); G3b= 1  
1(2.4%); G4a= 0pt; G5= 0pt; MISSING = 16 (39.2%)

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Dindo et al. Annals of Surgery • 2004



## Recidiva: 45 pts (32.4%)

**Re-I:** SI= 9 (20%); NO = 36 (80%)

**Re-I:** 4 pts non operati (2 SBRT, 1 pall, 1 BRT); 5 dopo CH  
 (intervallo 2-30 mesi)

**Intervallo da RT=** mediana 23 mesi (14-43)

**Intento Re-I:** Definitivo= 7pts; palliativo = 2pts

**Tecnica:** IMRT/VMAT = 2pts; Tomotherapy=2pt; BRT= 1 pts;  
 SBRT= 4pt

**In-field= 5 pts;** out-field= 4 pts

Canale anale =2

Pelvi=1

Presacrale =2

Paravaginale = 1

Inguine/scroto = 1

N otturatorio=1

N paraortico =1

**Tossicità acuta post Re-I:** proctite G2= 1pts; disuria G1= 1 pt

**Tossicità tardiva:** nessuna

**Follow-up mediano=** 49 mesi (7-144)

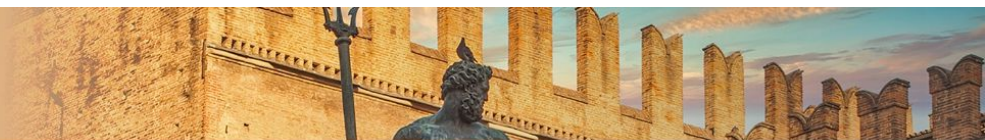
**Median OS=** 50 mesi (14-148)



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## Restiamo in attesa dei dati dei centri mancanti entro fine 2022

