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# IL RUOLO DELLA RADIOTERAPIA NELL'ITER TERAPEUTICO DELLA NEOPLASIA DEL CANALE ANALE

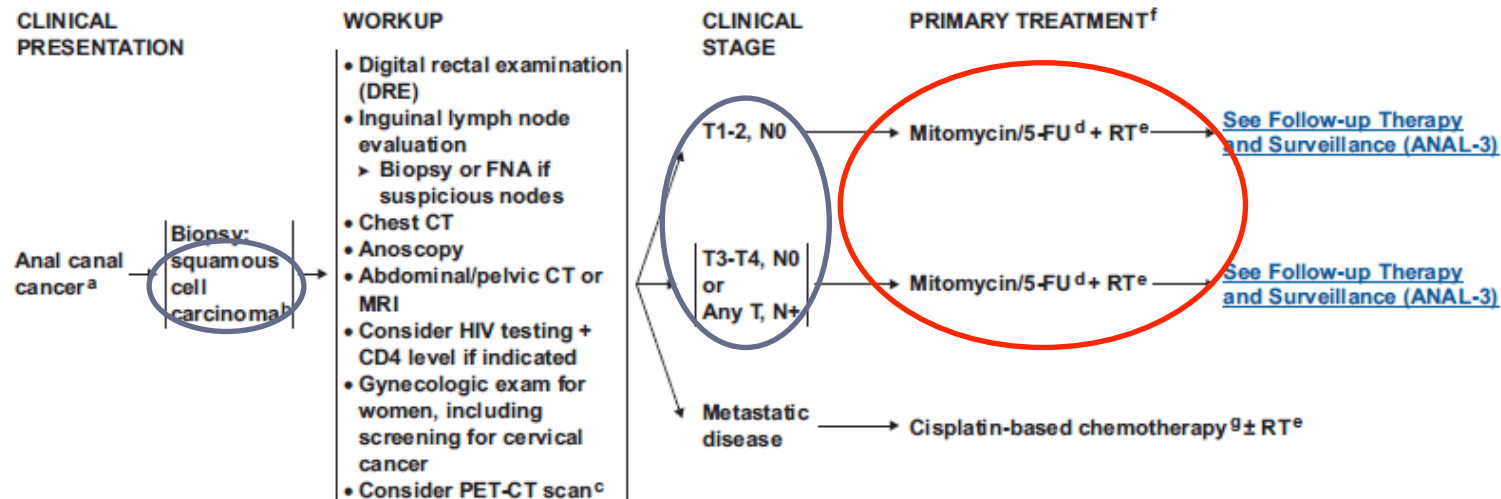


THE LANCET

**Concomitant Radiotherapy and Chemotherapy Is Superior to Radiotherapy Alone in the Treatment of Locally Advanced Anal Cancer: Results of a **Phase III Randomized Trial** of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups**

By H. Bartelink, F. Roelofsen, F. Eschwege, P. Rougier, J.F. Bosset, D. Gonzalez Gonzalez, D. Peiffert, M. van Glabbeke, and M. Pierart

*Journal of Clinical Oncology*, Vol 15, No 5 (May), 1997: pp 2040-2049



<sup>a</sup>The superior border of the functional anal canal, separating it from the rectum, has been defined as the palpable upper border of the anal sphincter and puborectalis muscles of the anorectal ring. It is approximately 3 to 5 cm in length, and its inferior border starts at the anal verge, the lowest edge of the sphincter muscles, corresponding to the introitus of the anal orifice.

<sup>b</sup>For melanoma histology, see the [NCCN Guidelines for Melanoma](#); for adenocarcinoma, see the [NCCN Guidelines for Rectal Cancer](#).

<sup>c</sup>PET-CT scan does not replace a diagnostic CT. The routine use of a PET-CT scan for staging or treatment planning has not been validated.

<sup>d</sup>See [Principles of Chemotherapy \(ANAL-A\)](#).

Ajani JA, Winter KA, Gunderson LL, et al. Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal: a randomized controlled trial. *JAMA* 2008;299:1914. In a randomized trial, the strategy of using neoadjuvant therapy with 5-FU + cisplatin followed by concurrent therapy with 5-FU + cisplatin + RT was not superior to 5-FU + mitomycin + RT.

<sup>e</sup>See [Principles of Radiation Therapy \(ANAL-B\)](#).

<sup>f</sup>Patients with anal cancer as the first manifestation of HIV may be treated with the same regimen as non-HIV patients. Patients with active HIV/AIDS-related complications or a history of complications (eg, malignancies, opportunistic infections) may not tolerate full-dose therapy or may not tolerate mitomycin and require dosage adjustment or treatment without mitomycin.

<sup>g</sup>Cisplatin/5-FU is recommended for metastatic disease. If this regimen fails, no other regimens have been shown to be effective. See [Principles of Chemotherapy \(ANAL-A\)](#). Local control can be achieved with the use of RT.

**Note:** All recommendations are category 2A unless otherwise indicated.  
 Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

# Radioterapia



Report

## Australasian Gastrointestinal Trials Group (AGITG) Contouring Atlas and Planning Guidelines for Intensity- Modulated Radiotherapy in Anal Cancer

Michael Ng, M.B.B.S.(Hons), F.R.A.N.Z.C.R.,\*

Trevor Leong, M.B.B.S., M.D., F.R.A.N.Z.C.R.,<sup>†,||</sup>

Sarat Chander, M.B.B.S., F.R.A.N.Z.C.R.,<sup>†</sup> Julie Chu, M.B.B.S., F.R.A.N.Z.C.R.,<sup>†</sup>

Andrew Kneebone, M.B.B.S., F.R.A.N.Z.C.R.,<sup>‡,\*\*</sup>

Susan Carroll, M.B.B.S., F.R.A.N.Z.C.R.,<sup>§,\*\*</sup> Kirsty Wiltshire, M.B.B.S., F.R.A.N.Z.C.R.,<sup>†</sup>

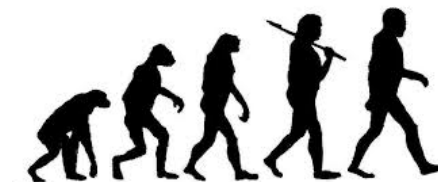
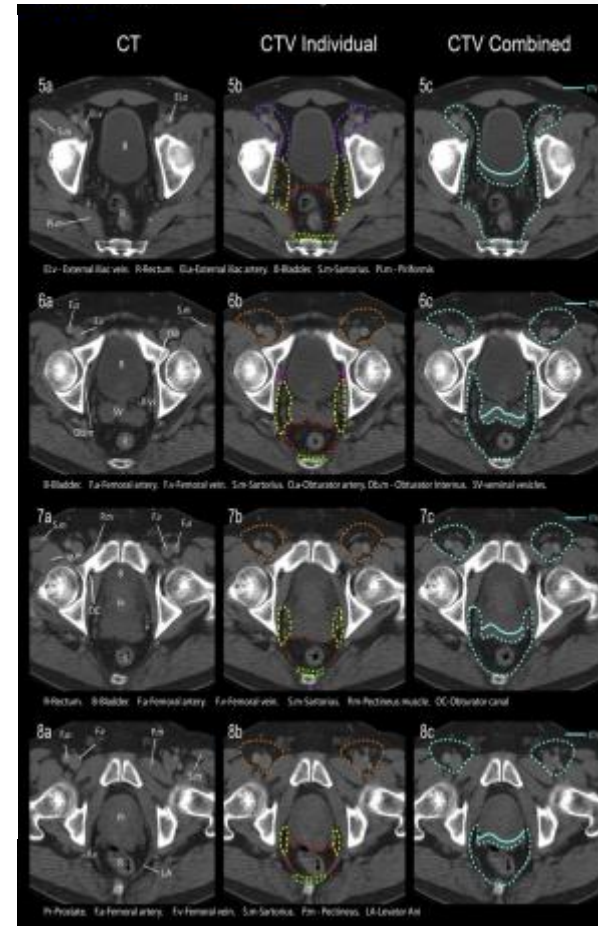
Samuel Ngan, M.B.B.S., F.R.C.S.Ed., F.R.A.N.Z.C.R.,<sup>†,||</sup> and Lisa Kachnic, M.D.<sup>¶</sup>

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<sup>¶</sup>Department of Radiation Oncology, Boston Medical Center, Boston University School of Medicine, Boston, MA;

<sup>||</sup>University of Melbourne, Australia; and <sup>\*\*</sup>University of Sydney, Australia

Int. J. Radiation Oncol Biol  
Phys Vol 83, No 5, pp, 2012



# IMRT



Radiotherapy and Oncology 107 (2013) 189–194

158, 2012  
sevier Inc.

Clinical Investigation: Gastrointestinal Cancer

## RTOG 0529: A Phase 2 Evaluation of Dose-Painted Intensity Modulated Radiation Therapy in Combination With 5-Fluorouracil and Mitomycin-C for the Reduction of Acute Morbidity in Carcinoma of the Anal Canal

Lisa A. Kachnic, MD,<sup>\*</sup> Kathryn Winter, MS,<sup>†</sup> Robert J. Myerson, MD,<sup>‡</sup> Michael D. Goodyear, MD,<sup>§</sup> John Willins, PhD,<sup>\*</sup> Jacqueline Esthappan, PhD,<sup>‡</sup> Michael G. Haddock, MD,<sup>||</sup> Marvin Rotman, MD,<sup>¶</sup> Parag J. Parikh, MD,<sup>‡</sup> Howard Safran, MD,<sup>#</sup> and Christopher G. Willett, MD<sup>\*\*</sup>

L

New York, NY; <sup>\*</sup>Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York; <sup>†</sup>Department of Radiation Oncology, University of Miami, Miami, FL; <sup>‡</sup>Department of Gastrointestinal Oncology, and <sup>§</sup>Department of Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY

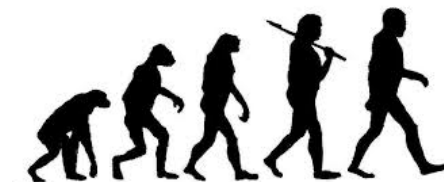
Int J Radiation Oncol Biol Phys, Vol 86 pp 27-33, 2013

JOHN D. WILLINS, PH.D.,<sup>\*†</sup> DAVID P. RYAN, M.D.,<sup>‡</sup> AND THEODORE S. HONG, M.D.<sup>†</sup>

Departments of <sup>\*</sup>Radiation Oncology and <sup>||</sup>Medicine, Boston Medical Center, Boston, MA; <sup>†</sup>Harvard Radiation Oncology Program, Harvard Medical School, Boston, MA; and Departments of <sup>‡</sup>Radiation Oncology and <sup>§</sup>Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

### Summary

RTOG 0529 assessed the utility of dose-painted intensity modulated radiation therapy (DP-IMRT) in reducing the acute morbidity of 5-fluorouracil/mitomycin-C chemoradiation for T2-4N0-3M0 anal cancer. With 52 evaluable patients, the primary endpoint of reducing grade  $\geq 2$  combined gastrointestinal and genitourinary acute adverse events by 15% compared with the RTOG 9811 5-fluorouracil/mitomycin-C arm using standard radiation techniques was not met. However, DP-IMRT yielded significant sparing of acute grade 2+ hematologic, grade 3+ dermatologic, and gastrointestinal toxicity.



# Brachiterapia come boost



anal.pdf (PROTETTO) - Adobe Reader

File Modifica Vista Finestra ?

1 / 32 68,4%

Commento Condividi

brachytherapy

National Comprehensive

clinical practice guidelines *Annals of Oncology* 21 (Supplement 5): v87-v92, 2010  
doi:10.1093/annonc/mdq171

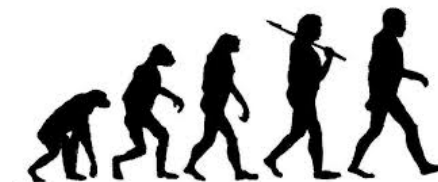
**Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up**

R. Glynne-Jones<sup>1</sup>, J. M. A. Northover<sup>2</sup> & A. Cervantes<sup>3</sup>  
On behalf of the ESMO Guidelines Working Group\*

<sup>1</sup>Mount Vernon Centre for Cancer Treatment, Northwood; <sup>2</sup>St Mark's Hospital, Harrow, UK; <sup>3</sup>Department of Hematology and Medical Oncology, INCLIVA, University of Valencia, Valencia, Spain

Adobe Reader ha completato la ricerca all'interno del documento e non ha trovato alcuna corrispondenza.

Higher doses may be required for more advanced tumours, particularly if a planned gap is used. Currently it is not possible to make a definitive recommendation (based on inter-trial comparisons of differing dose fractionations with or without a gap) on either the requirement for, the form (external beam or brachytherapy) or the appropriate doses for a boost after 50 Gy.



# Boost



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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

## Induction Chemotherapy and Dose Intensification of the Radiation Boost in Locally Advanced Anal Canal Carcinoma: Final Analysis of the Randomized UNICANCER ACCORD 03 Trial

Dider Peiffer, Lucile Toussier-Rangard, Elisabeth Lepret, Thierry Comery, SA 430 Centre, Alain Valleron and Ralfy Trivelpy, Valdoanva-Bouffroy, France; Jean-Pierre Girard, Eric Fournier, Jean-Michel Ravaud, Centre Antoine Lacaze, France; Michel Besson, Institut Curie, France; Valérie, France; Clara Leirenko, Centre Veld, Marseille, Montpellier, France; Marc Gervais, Institut Paul Cabrol, Marseille, France; Frédéric Cuvillier, Hôpital René Hergesson-Jentel, Centre-Saint-Jacques, Paris, France; Xavier Mialhe, Antoine Aldaris, Centre Oscar Lambert, Lille, France; Olivier Beeckel, Robert Dubal, University Hospital, Paris, France; Christine Morin, Centre de Recherche d'Etudes Cliniques en Thérapeutiques, Fédération Française des Centres de Lutte Contre le Cancer, Paris, France; Fawcett Morin, University Hospital, Lyon-Sud, France; Jean-François Sella, Centre

Dider Peiffer, Lucile Toussier-Rangard, Jean-Pierre Gérard, Claire Lemanski, Eric François, Marc Giromandi, Frédérique Cvitkovic, Xavier Mihal, Olivier Bouché, Elisabeth Laperot, Thierry Comroy, Christine Morin-Guilou, Françoise Morin, Antoine Lasinchi, Jean-Michel Hannon-Lévi, Jean-François Sella, Antoine Aldaris, Christophe Hennequin, Bernard Desch, and Michel Durrain

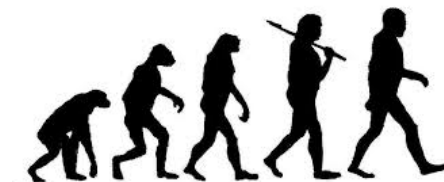
### ABSTRACT

#### Purpose

Concomitant radiochemotherapy (RCT) is the standard for locally advanced anal canal carcinoma (LAACC). Questions regarding the role of induction chemotherapy (ICT) and a higher radiation dose in LAACC are pending. Our trial was designed to determine whether dose escalation of the radiation boost or two cycles of ICT before concomitant RCT lead to an improvement in colostomy-free survival (CFS).

#### Patients and Methods

Patients with tumors  $\geq 40$  mm, or  $< 40$  mm and N1-3M0 were randomly assigned to one of four treatment arms: (A) two ICT cycles (fluorouracil 800 mg/m<sup>2</sup>/d intravenous [IV] infusion, days 1 through 4 and 19 to 22; submitoxan 80 mg/m<sup>2</sup> IV on days 1 and 19; RCT 45 Gy in 15 fractions



# Brachiterapia

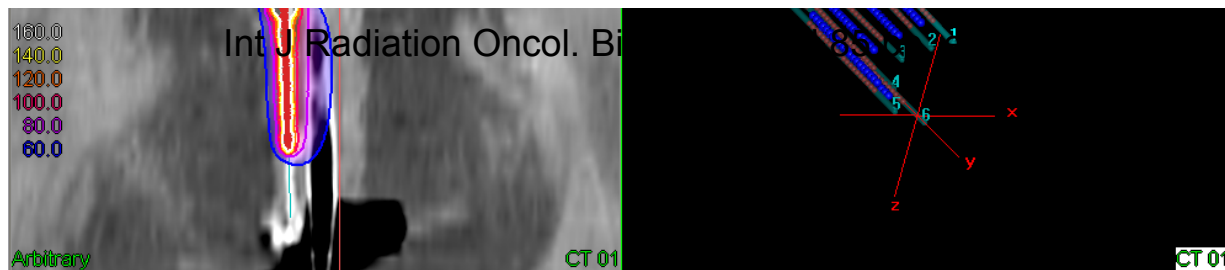


Clinical Investigation: Gastrointestinal Cancer

## Role of Brachytherapy in the Boost Management of Anal Carcinoma With Node Involvement (CORS-03 Study)

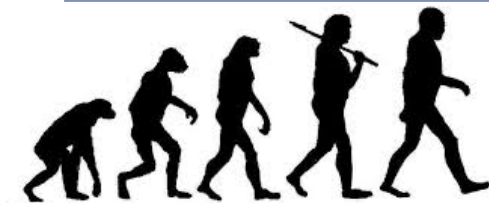
Laurence Moureau-Zabotto, MD,\* Cecile Ortholan, MD, PhD,<sup>†</sup>  
Jean-Michel Hannoun-Levi, MD, PhD,<sup>‡</sup> Eric Teissier, MD,<sup>§</sup> Didier Cowen, MD, PhD,<sup>||,¶</sup>  
Nagi Salem, MD,\* Claire Lemanski, MD,<sup>#</sup> Steve Ellis, MD,\*\* and Michel Resbeut, MD\*,\*\*\*

\*Department of Radiation Therapy, Institut Paoli Calmettes, Marseille, France; <sup>†</sup>Department of Radiation Therapy, Monaco, France; <sup>‡</sup>Department of Radiation Therapy, Antoine Lacassagne Cancer Center, Nice, France; <sup>§</sup>Azurean Cancer Center, Mougins, France; <sup>||</sup>Department of Radiation Therapy, Timone Academic Hospital and North Academic Hospital, Marseille, France; <sup>¶</sup>Department of Radiation Therapy, Val d'Aurelle Cancer Center, Montpellier, France; <sup>#</sup>Catalan Oncology Center, Perpignan, France; and \*\*French Red Cross Center, Toulon, France



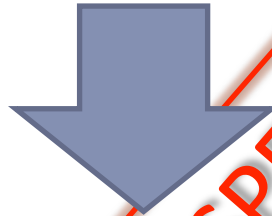
### Summary

The purpose of this study was to assess retrospectively the clinical outcome in anal cancer patients with lymph node involvement, treated with split-course radiation therapy and receiving a boost through external beam radiation therapy or brachytherapy. This study shows that, even in the case of initial perirectal node invasion, brachytherapy boost is superior to external beam radiation therapy boost with regard to the local control rate, without an influence on overall survival, and suggests that N1 status in patients with anal carcinoma should not be a contraindication to use of a brachytherapy boost technique.





## CONFRONTO TRA TECNICHE:



Boost con brachiterapia

V/S

Boost con radioterapia esterna

- ✓ Sopravvivenza globale
- ✓ Fattori prognostici legati alla sopravvivenza

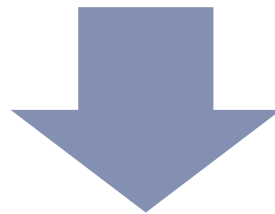
STUDIO RETROSPETTIVO

# Scenario



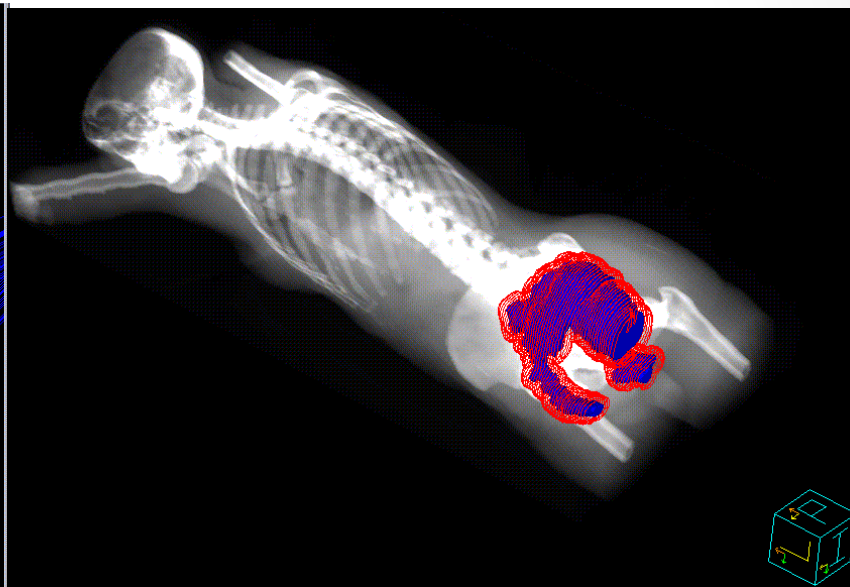
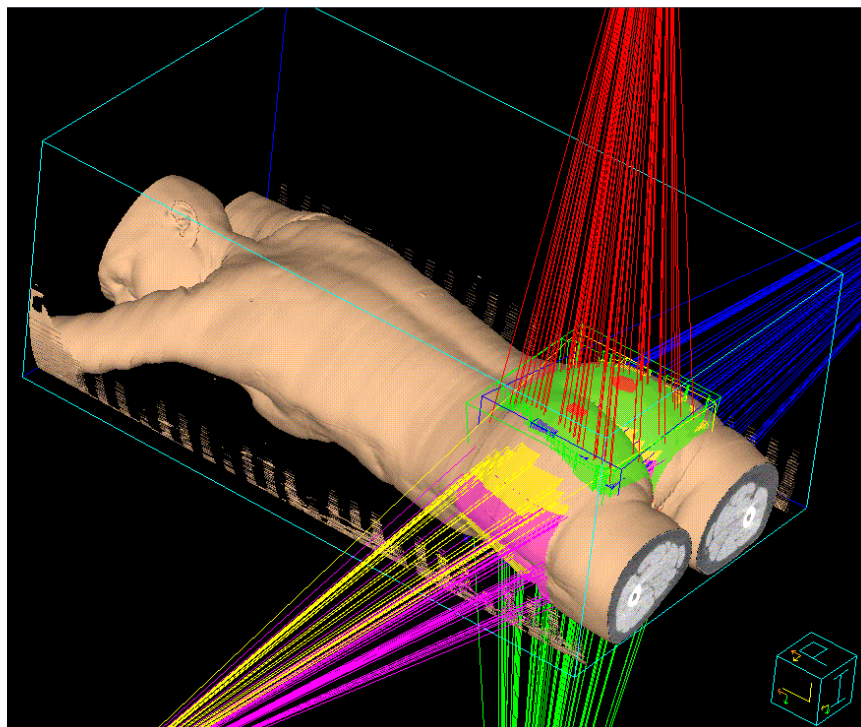
2002-2012: Policlinico  
S.Orsola-Malpighi  
U.O. Radioterapia

185 pazienti con carcinoma del canale anale



125 pazienti arruolati

# Pazienti e metodi



Dose media: 45.3 Gy

Dose media: 18.5 Gy  
Circa 0,8 Gy a pulsata

BOOST :  
BRT-PDR / 3DCRT

Dose media: 16.4 Gy

# Brachiterapia



Projective setup | Applicator Placement | Catheter Reconstruction | Activation | Normalization | Optimization | Prescription | Activity gadget | Notification

160.0  
140.0  
120.0  
100.0  
80.0  
60.0

Arbitrary

CT 01

Structure Set

- Plans
  - Brachy plan
    - AP Applicator
      - Active Dwell Positions
        - #1
        - #2
        - #3
        - #4
        - #5
        - #6
      - Points
        - Basal

Cath.#	Ch.#	Name	Indexer [cm]	Offset [cm]	0.0	1.0	2.0	3.0	4.0	5.0	6.0
1	1	(Manual)	150.00	0.00							
2	2	(Manual)	150.00	0.00							
3	3	(Manual)	150.00	0.00							
4	4	(Manual)	150.00	0.00							
5	5	(Manual)	150.00	0.00							
6	6	(Manual)	150.00	0.00							

# Pazienti e metodi



## Sesso:

Maschi 31 (24.8%)

Femmine 94 (75.2%)

## Istologia:

Squamoso: 100 (80%)

v. Basalioidi: 14 (11.2%)

v. Cloacogenica: 9 (7.2%)

Indifferenziati: 2 (1.6%)

## Età mediana:

61 aa (36-94)

Pazienti > 65 aa:

52 (41.6%)

Pazienti HIV+:

**7 (6%)**

Pazienti HPV+:

2 (1-6%)

	T1 (n=15, 13.5%)	T2 (n=42, 26.2%)	T3 (n=37, 32.5%)	T4 (n=19, 13.4%)
N0 (n=71, 56.3%)	13	34	18	6
N1 (n=29, 23%)	1	7	11	10
N2 (n= 13, 10.3%)	1	1	8	3

(Non erano definibili 14 T e 13 N)

In accordo con AJCC Seventh Edition (2010)

# Risultati



	TOTALE n= 125	BOOST BRT n=100, (80%)	BOOST 3D-CRT n=25, (20%)	p < 0.05
Maschi / Femmine	31 (25%) / 94 (75%)	23 (74%) / 77 (82%)	8 (26%) / 17 (18%)	NS
Età (aa)*	61 (37-94)	61 (37-94)	68 (42-90)	NS
Pz > 65 aa°	52 (42%)	<u>37 (71%)</u>	15 (29%)	0.03
T1	112 (89,6%)	15 (17%)	2 (8%)	0.05
T2		28 (32%)	5 (21%)	
T3		33 (37%)	8 (33%)	
T4		12 (14%)	<u>9 (38%)</u>	
Dose media (Gy)		1525 (800-2250)	1650 (1080-2240)	
Follow-up (mesi)*	43 (1-135)	86 (1-135)	37 (0-118)	<0.001
Pz deceduti°	34 (27%)	25 (25%)	9 (36%)	NS
Recidive°	22 (18%)	13 (13%)	<u>9 (36%)</u>	0.007

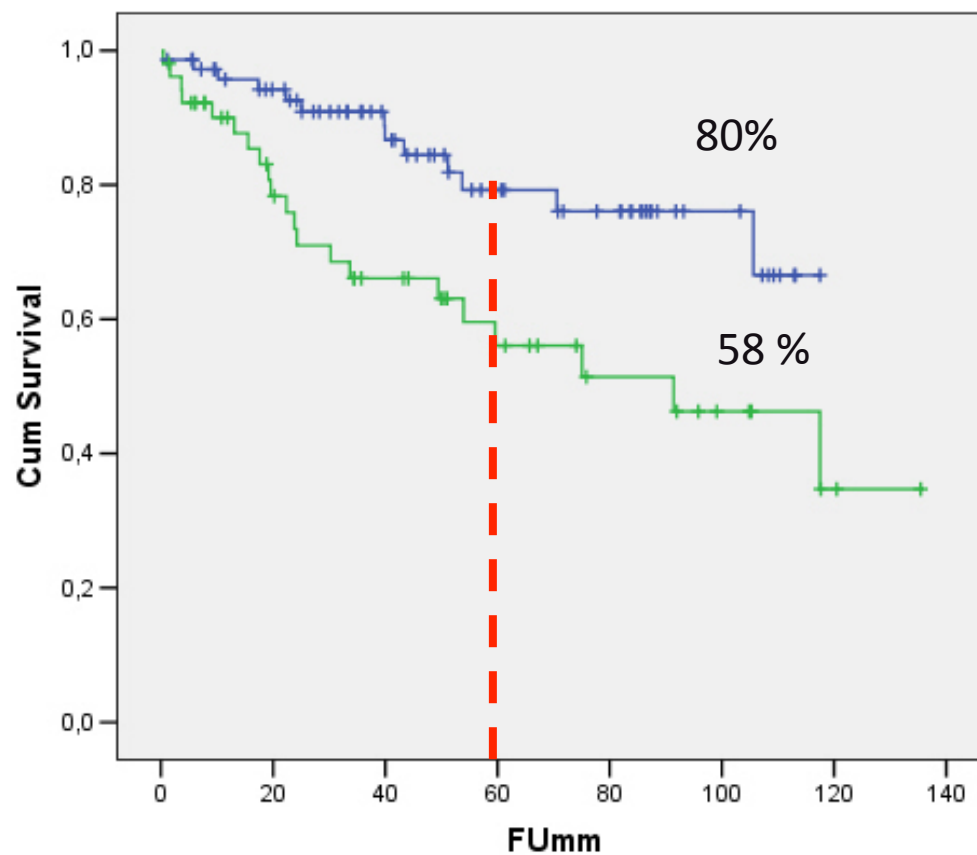
\*Mediana e range

°Valore assoluto e percentuale

# Sopravvivenza per i pz > 65 aa



Survival Functions



— Pz < 65 aa: 80 mesi (63-97)\*  
— Pz > 65aa: 97 mesi (87-107)\*

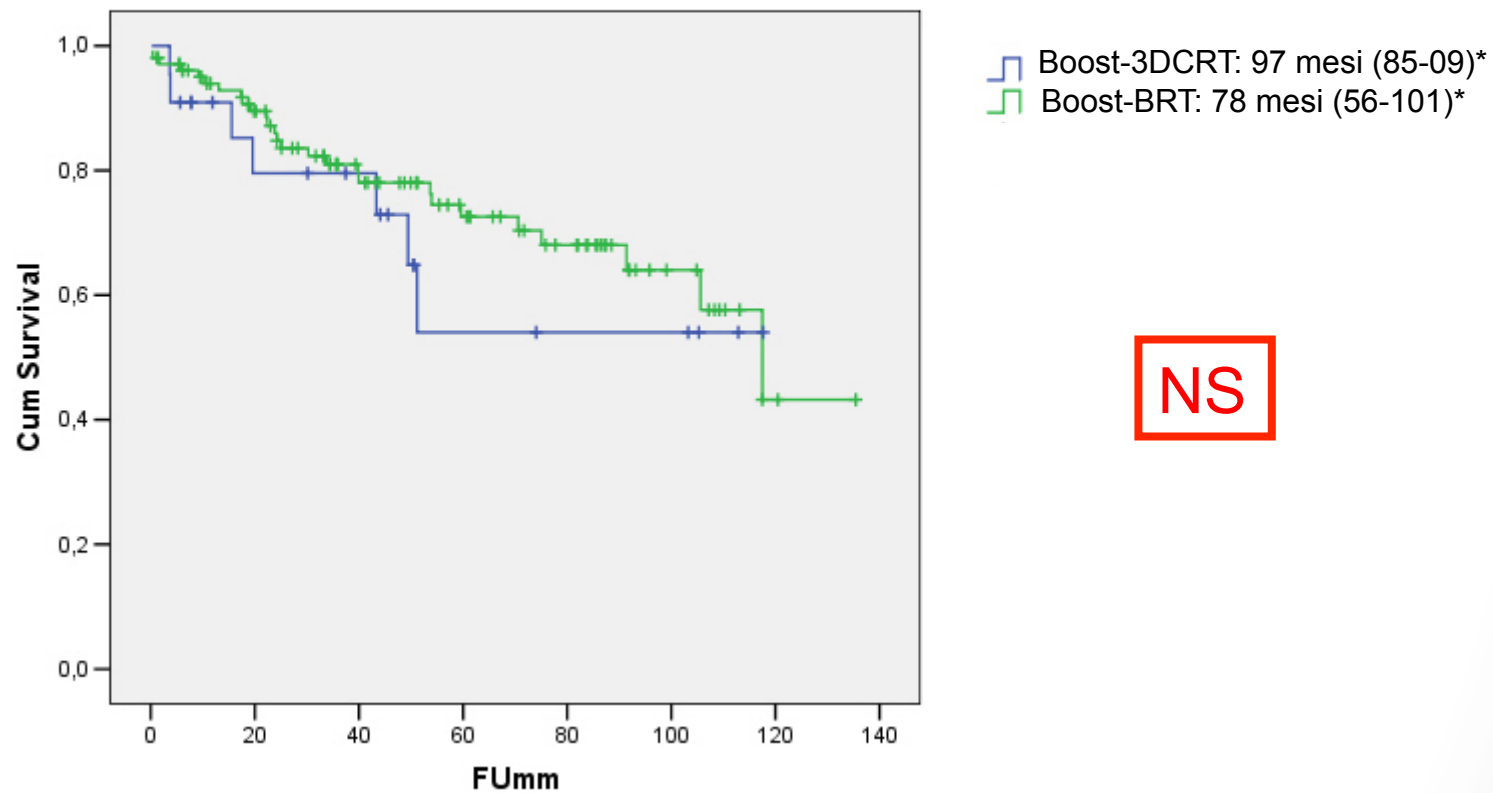
**p= 0,004**

\*: Valore espresso come tempo medio di follow-up e (Intervallo di confidenza al 95° percentile)

# Sopravvivenza per i pazienti sottoposti a boost-BRT o con 3DCRT



Survival Functions



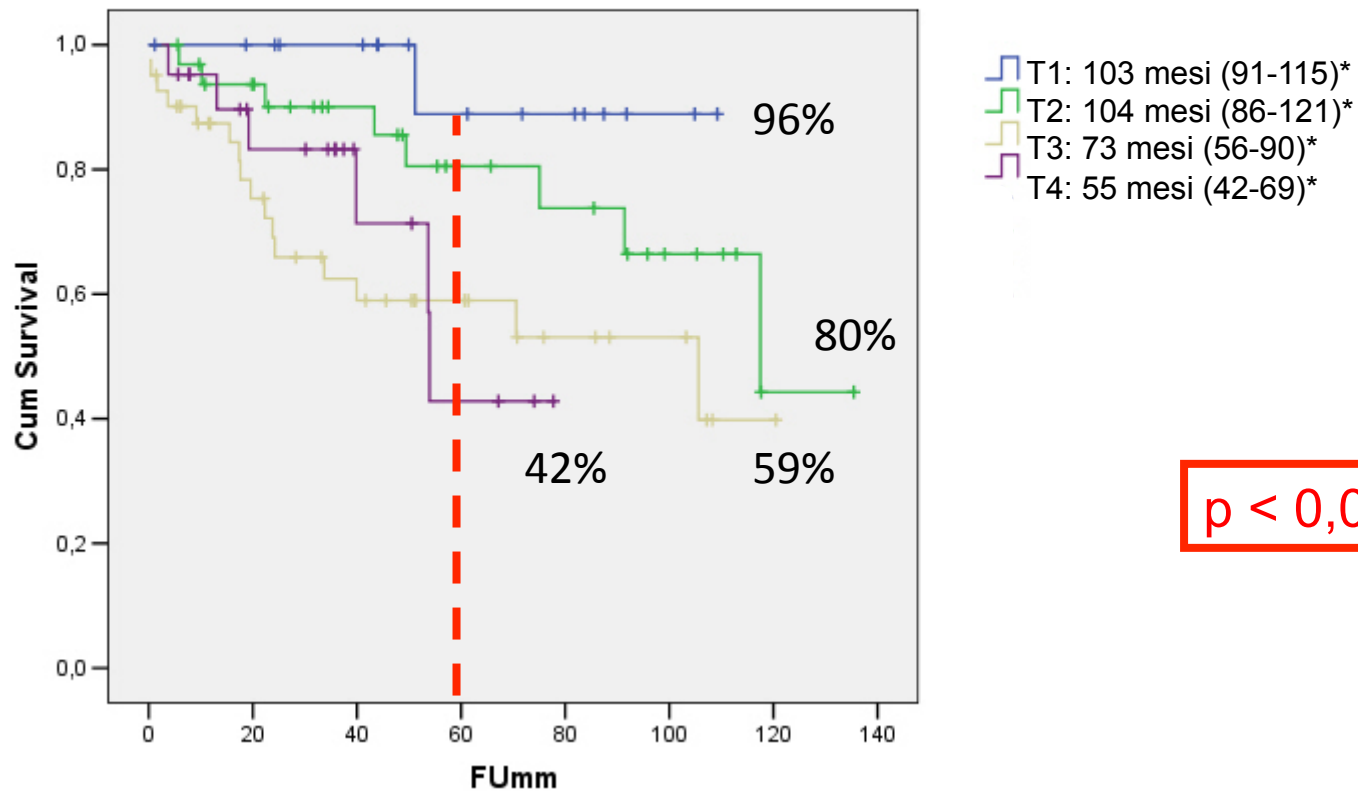
\*: Valore espresso come tempo medio di follow-up e (Intervallo di confidenza al 95° percentile)



# Sopravvivenza in base al T



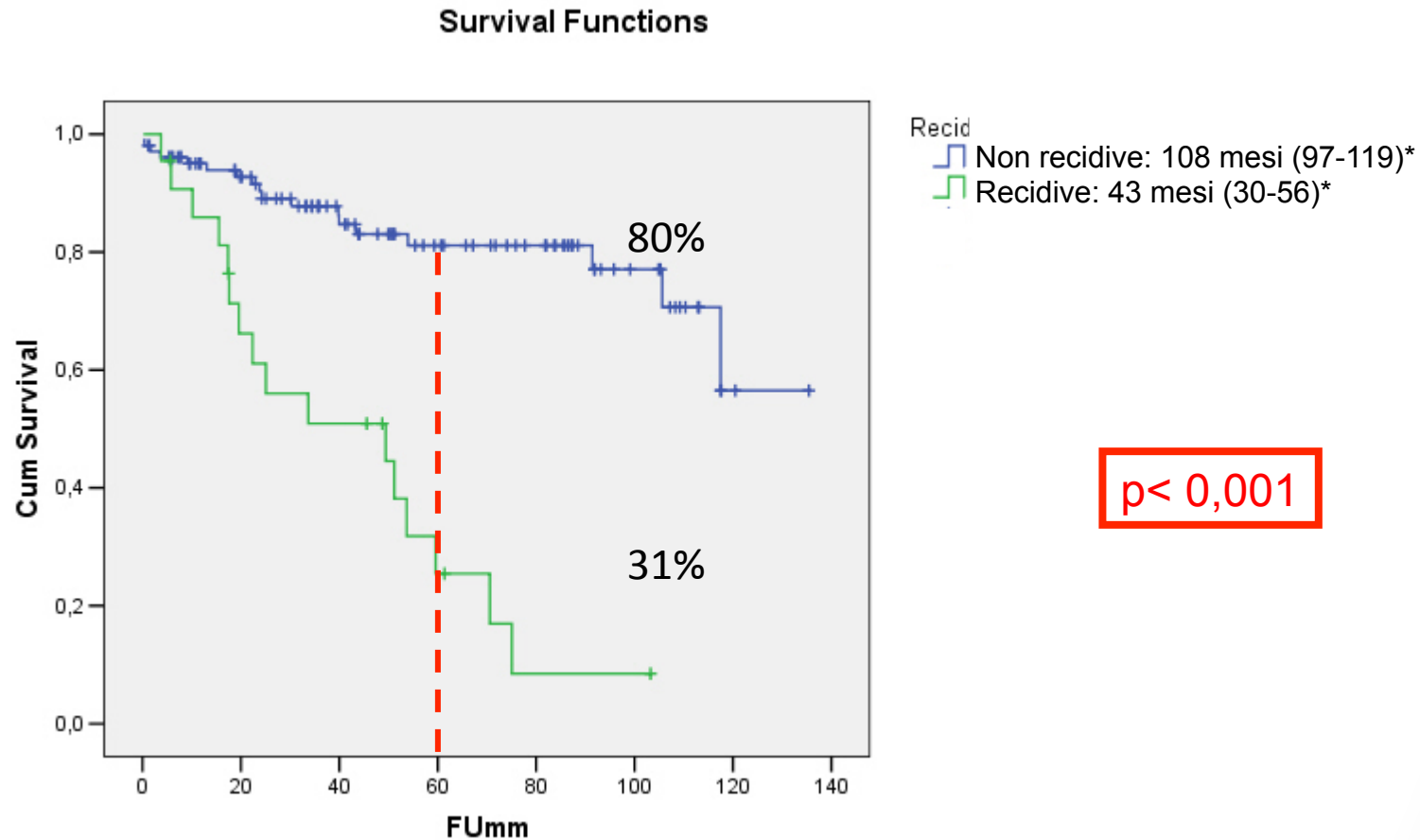
Survival Functions



$p < 0,001$

\*: Valore espresso come tempo medio di follow-up e (Intervallo di confidenza al 95° percentile)

# Sopravvivenza dei pz con recidiva



\*: Valore espresso come tempo medio di follow-up e (Intervallo di confidenza al 95° percentile)

# Modello di Cox per la sopravvivenza



Variabile	X <sup>2</sup>	Significatività (P)	RR	(C.I. 95%)
Recidiva	19.051	< 0.001	5.189	(2.477-10.867)
T	5.962	0.015	1.746	(1.116-2.730)
Età > 65 aa	4.465	0.035	2.217	(1.059-4.641)

# Conclusioni



- Non abbiamo riscontrato una differenza significativa tra le due metodiche anche se la prevalenza di anziani, il T, la presenza di recidive sono leggermente differenti tra le due popolazioni.



Possibile errore: bassa numerosità di alcuni gruppi ?

- L'età maggiore di 65 anni, lo sviluppo di recidiva nel corso della malattia ed il T sono variabili statisticamente significative per predire la mortalità/sopravvivenza.

(Chapet 2005, Int J. Radiation Oncology Biol. Phys)

**TRIAL RANDOMIZZATI**



**Grazie per l'attenzione**