



AIRO-Lazio-Abruzzo-Molise
2° incontro scientifico regionale
Roma, 26 giugno 2012

Target veri o presunti: le neoplasie del retto

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Università Cattolica del Sacro Cuore
Roma



Preop RT-CT & OS

5 randomized European trials

3253 patients

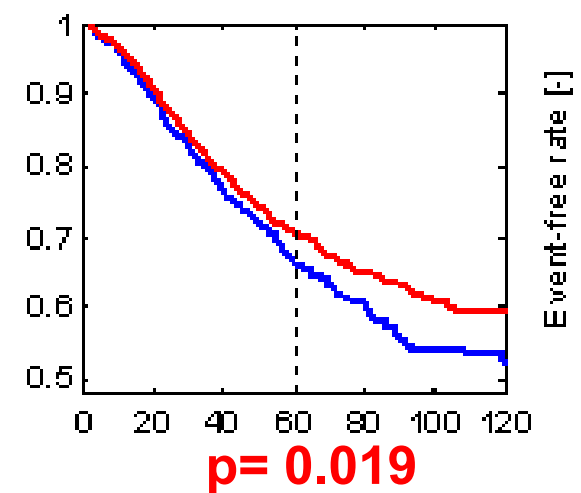
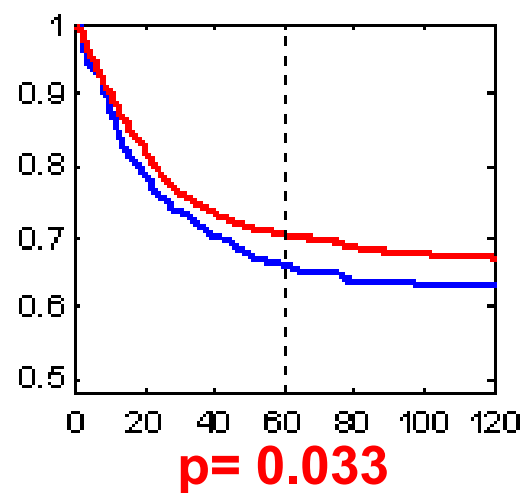
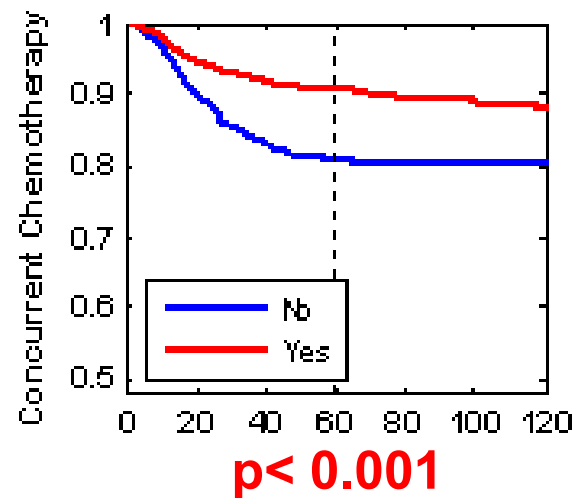
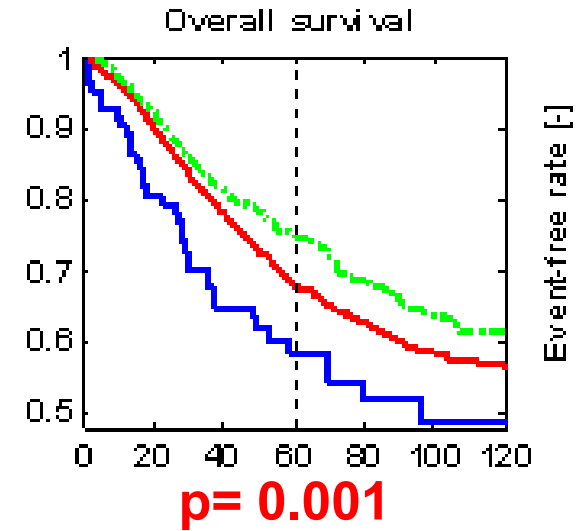
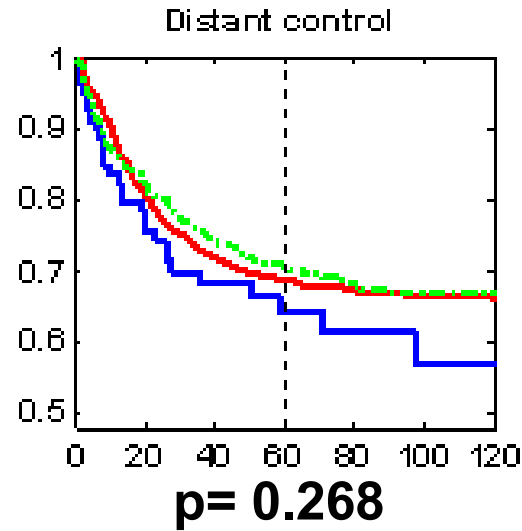
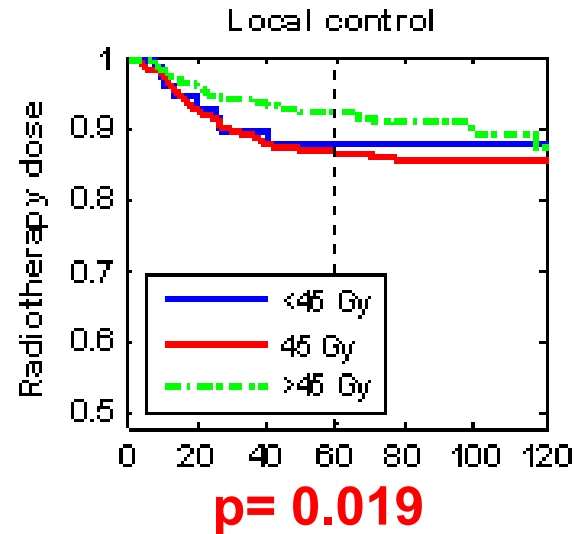
- EORTC trial (Bosset et al, 2006)
- French trial (Gerard et al. 2006)
- German trial (Sauer et al. 2004)
- Polish trial (Bujko et al. 2006)
- Italian CNR trial (Cionini L. et al. in press)



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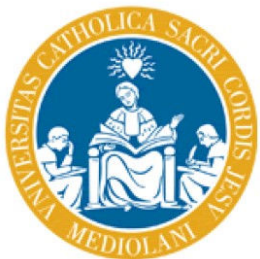
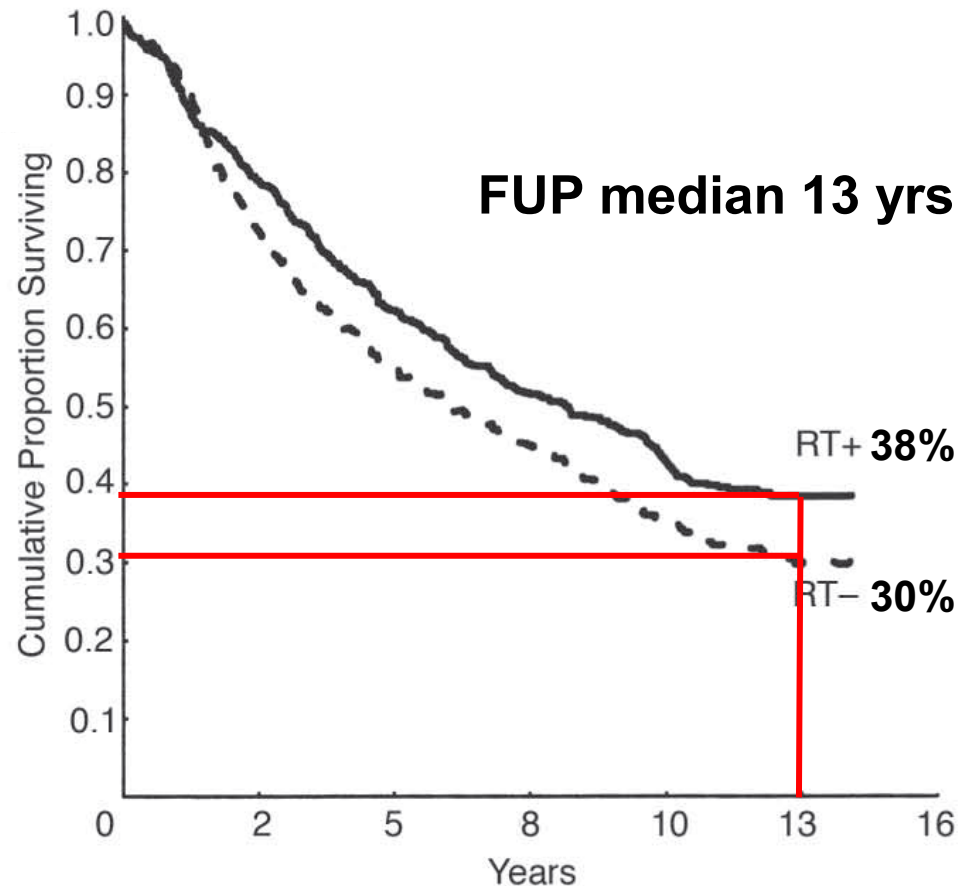
RT-CT analisi monovariata



Preop RT & OS

Sweden trial: 908 R0/1168 pts

Long-term updated outcomes



Folkesson J et al, *JCO* 2005

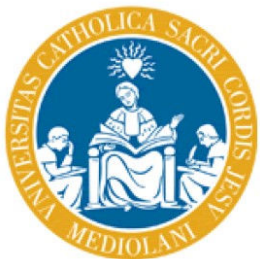
Preop RT & SVV



1382 R0 (pCRM-)

12 years Update of Dutch Trial

	RT + TME (691)	TME (691)
Rectal cancer	38%	48%
Other	2%	52%



Van Gijn W et Al , Lancet Oncol 2011

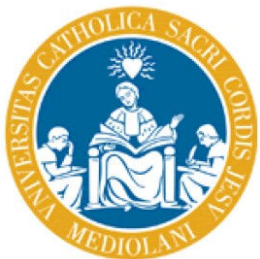
Cause di morte



12 years Update of Dutch Trial

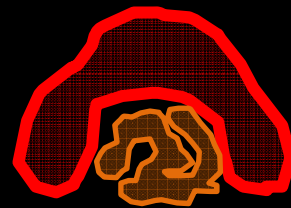
	RT+TME (n=315)	TME alone (n=319)
Rectal cancer	119 (38%)	152 (48%)
Radiotherapy complications	2 (<1%)	0 (0%)
Surgery complications	20 (6%)	16 (5%)
Secondary malignancy	43 (14%)	30 (9%)
Cardiovascular cause	46 (15%)	45 (14%)
Pulmonary cause	16 (5%)	15 (5%)
Infectious cause	3 (1%)	2 (<1%)
Neurological cause	4 (1%)	4 (1%)
Ileus	3 (1%)	2 (<1%)
Other	39 (12%)	32 (10%)
Unknown	20 (6%)	21 (7%)

Data are number (%). Pearson χ^2 test between all causes of death p=0.448.
RT=radiotherapy. TME=total mesorectal excision.

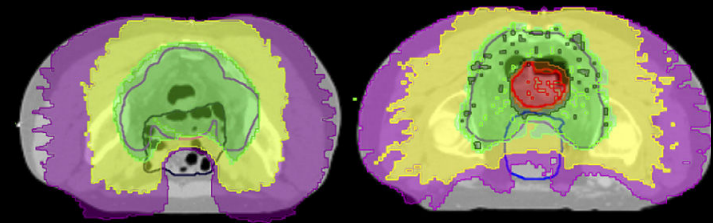


Impatto delle nuove tecnologie

- IMRT: target ideale a “ferro di cavallo” con OAR all’interno



- Esperienze IMRT:
 - pochi lavori in letteratura
 - Risparmio tenue SIB



TARGET nel tumore del retto

Tumore

Mesoretto

Fascia mesorettale

Regione presacrale

N extra mesorettali

N ed organi extra-pelvici



TARGET nel tumore del retto

Tumore
Mesoretto



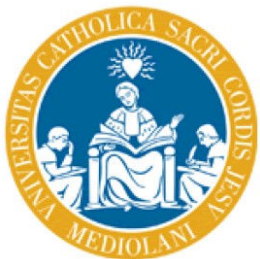
Fascia mesorettale

Regione presacrale

N extra mesorettali

N ed organi extra-pelvici

chirurgia



TARGET nel tumore del retto

Tumore
Mesoretto



Fascia mesorettale
Regione presacrale
N extra mesorettali



N ed organi extra-pelvici

chirurgia



radioterapia



I TARGET(s) nel tumore del retto

Tumore
Mesoretto

Fascia mesorettale
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N extra mesorettali

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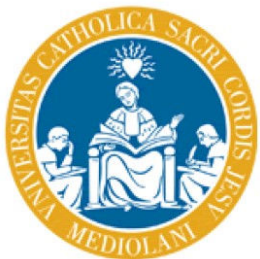
chirurgia



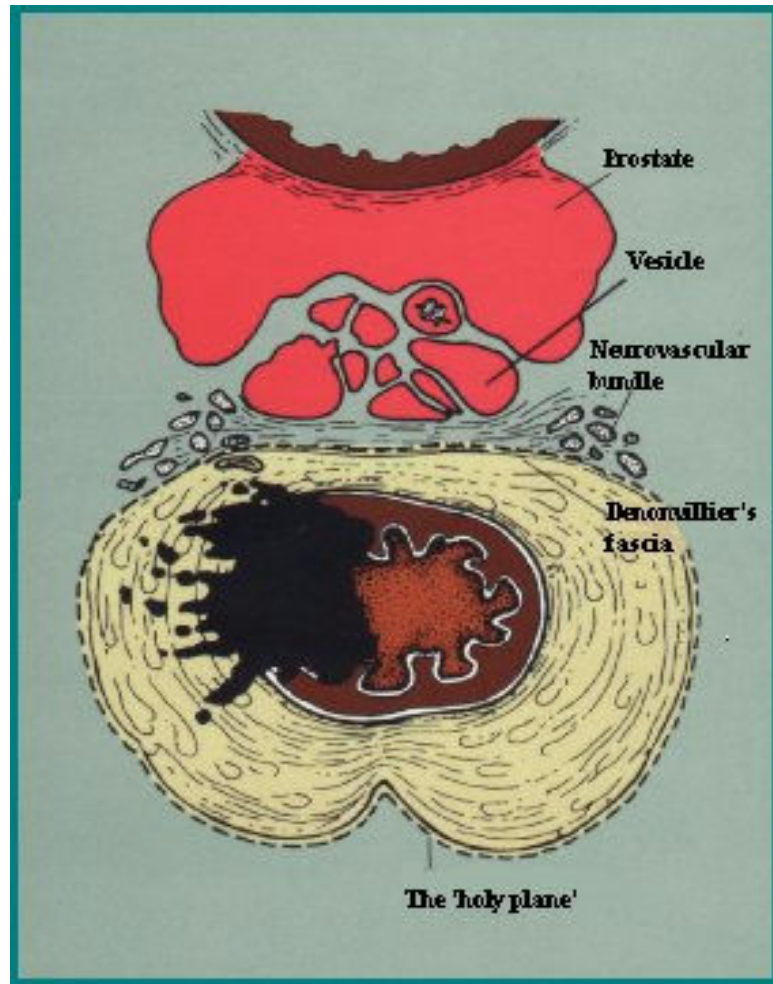
radioterapia



chemioterapia



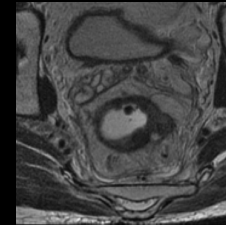
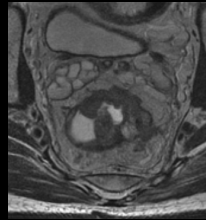
Tumore e mesoretto



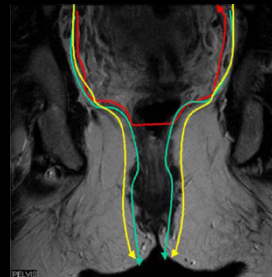
TME
Recidiva **L**ocale
5-15%

Tumore

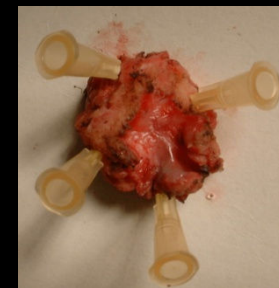
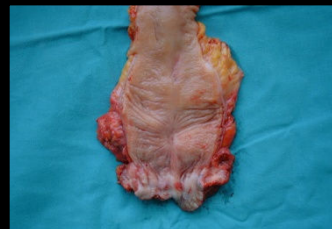
Resecabilità



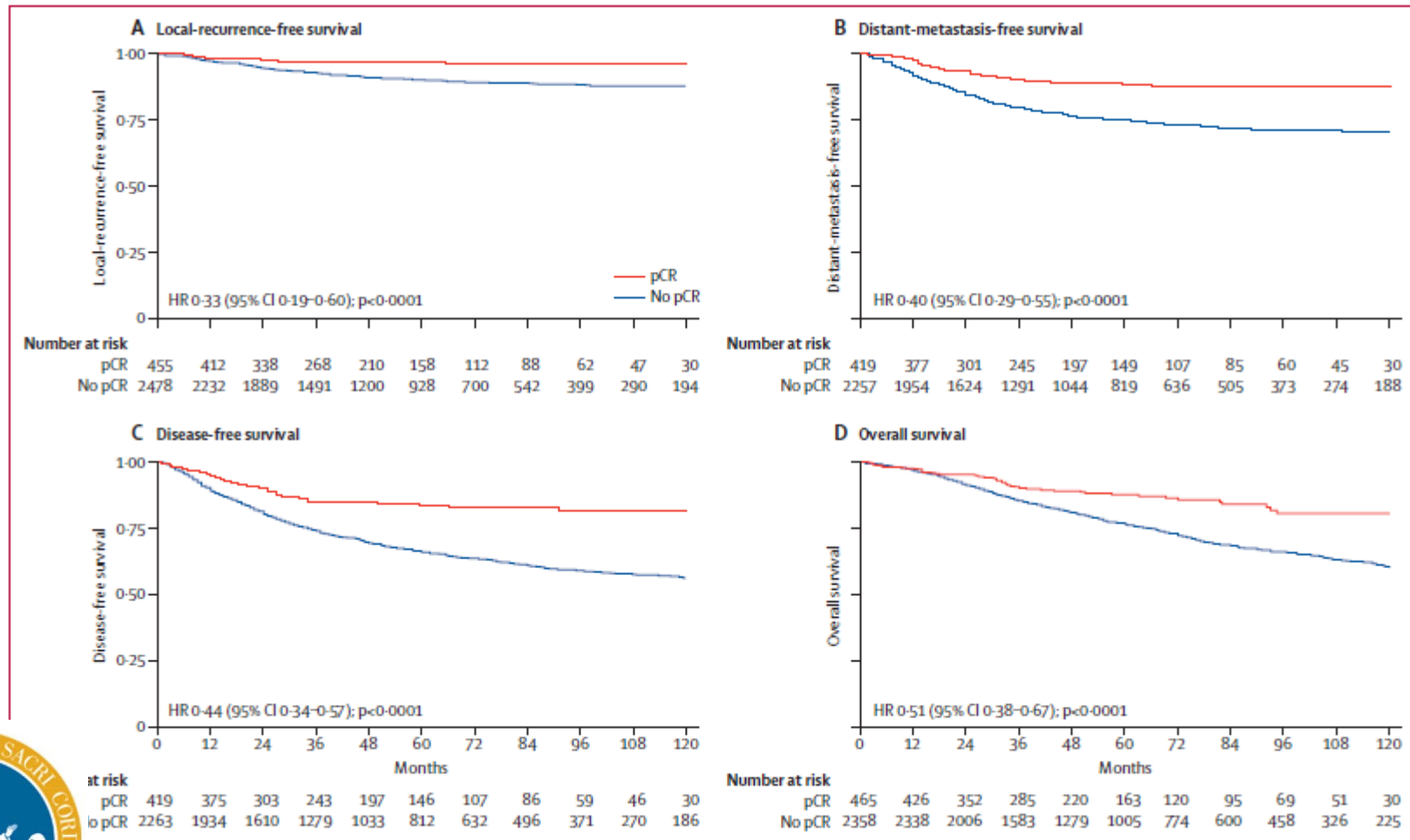
Salvataggio sfintere



Salvataggio organo



pCR & outcomes



Mesoretto

- Resezione completa del mesoretto: ~ 50%

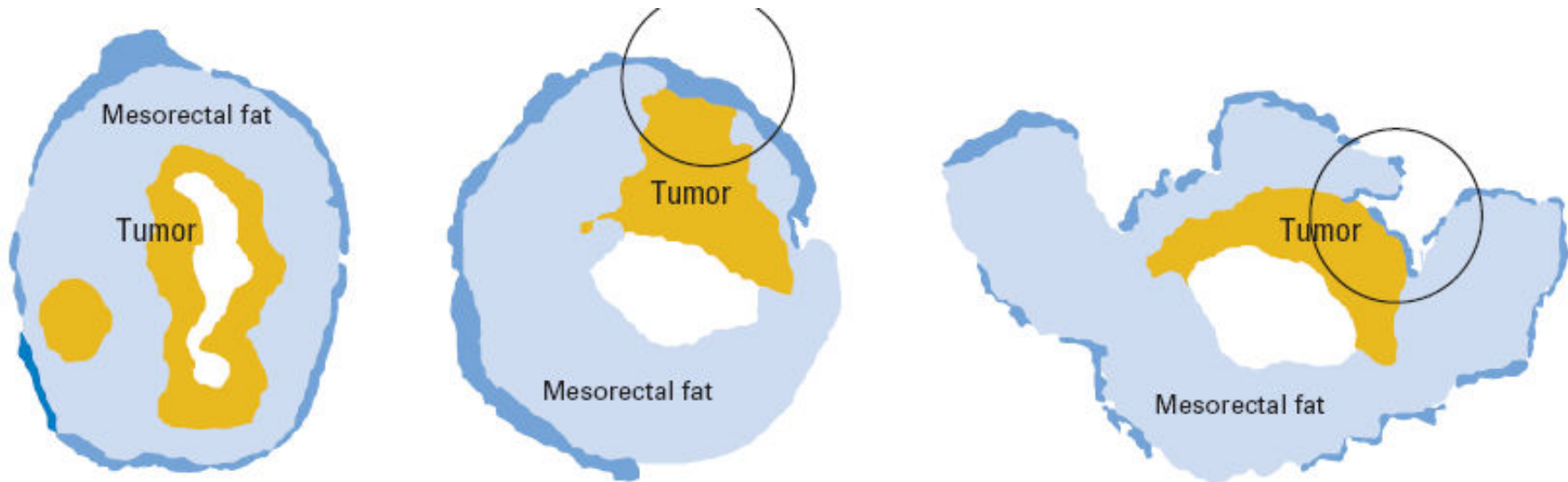
Local recurrence rate according to distal margin and lymph node status.

Distal margin	RT-		RT+			
	N0	N+	N0	N+		
0-5 mm	5.6	30.0	11.8	28.6		
6-10 mm	8.8	34.6	0	0		
11-20 mm	4.6	29.7	0	7.2		
>21 mm	5.5	8.6	1.7	5.8		
TOTAL	5.6	19.4	1.7	9.3	<0.001	<0.001

In LAR and Hartmann procedures. Values are 5-year local recurrence percentages.

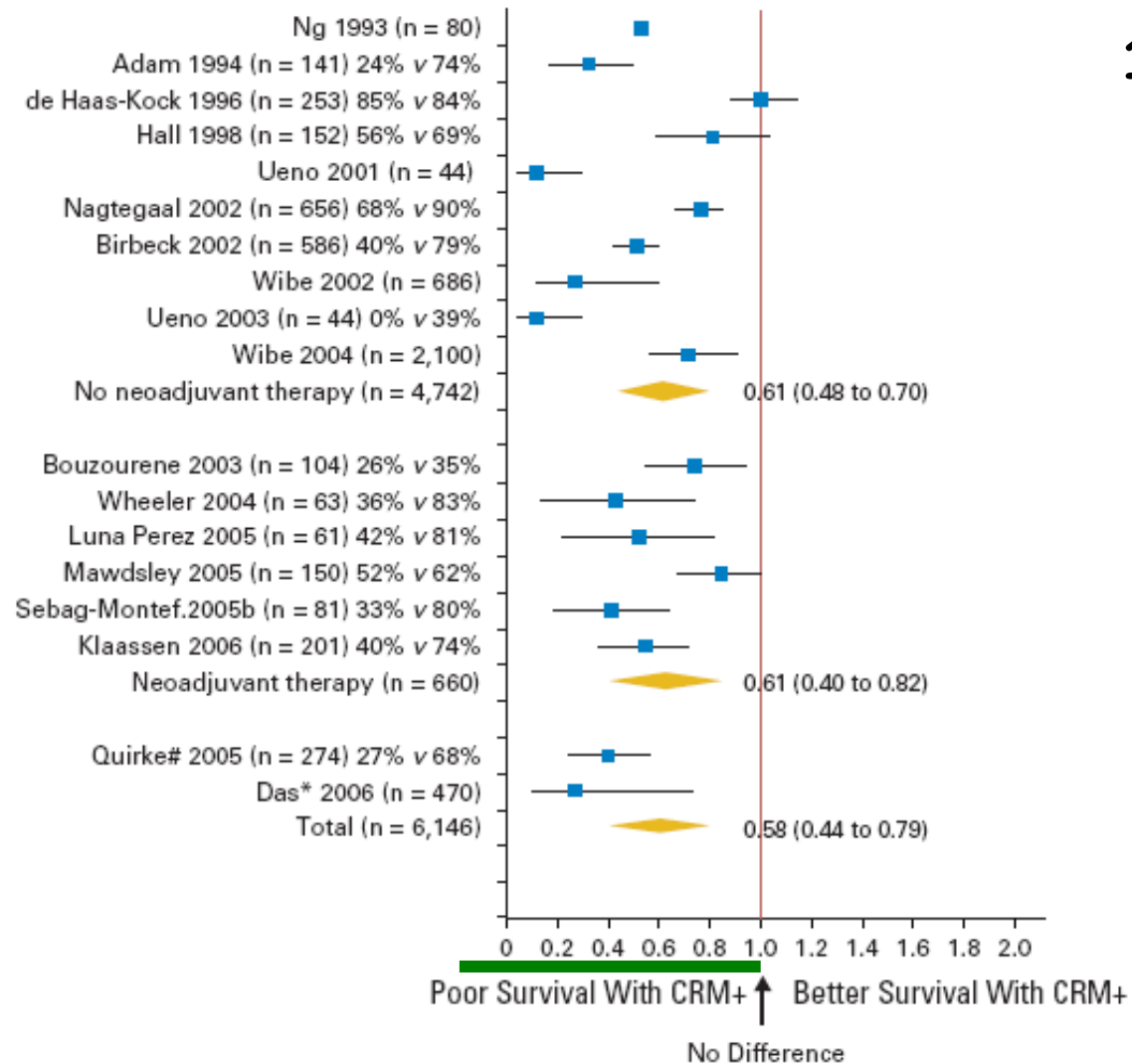
- Distal mesorectal deposits: 10-15% *Syc E et al IJROBP 2008*
Kusters M et al EJCO 2010
Chen W et al Eur Surg Res 2007

Fascia mesorettale

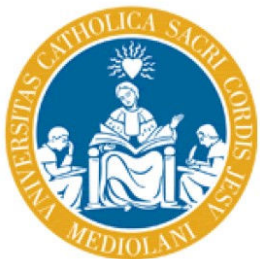


Circurferential **R**esection **M**argin

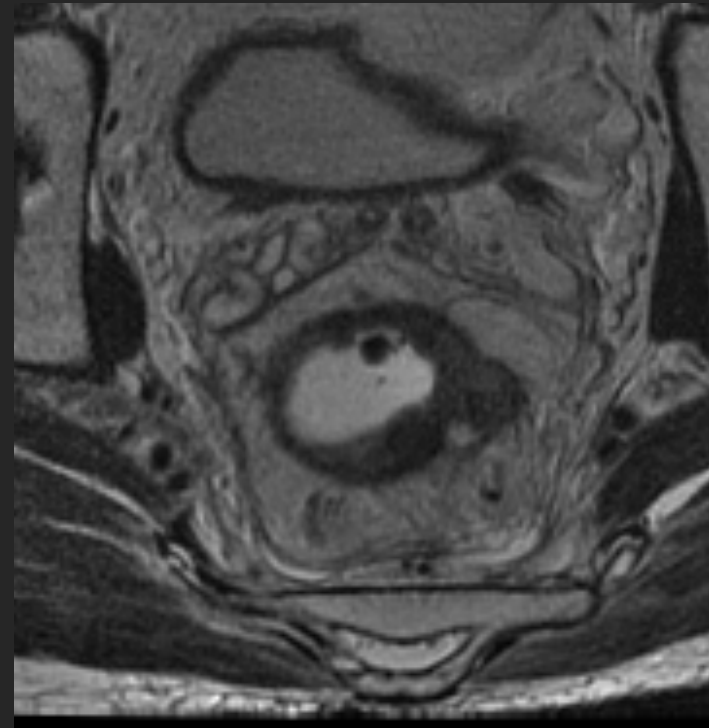
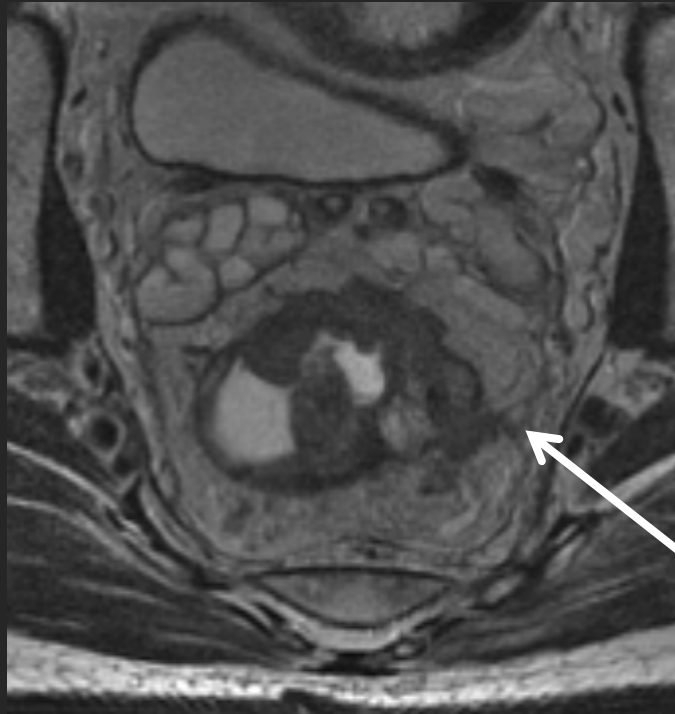
La fascia mesorettale: CRM e Sopravvivenza



17.500
pts



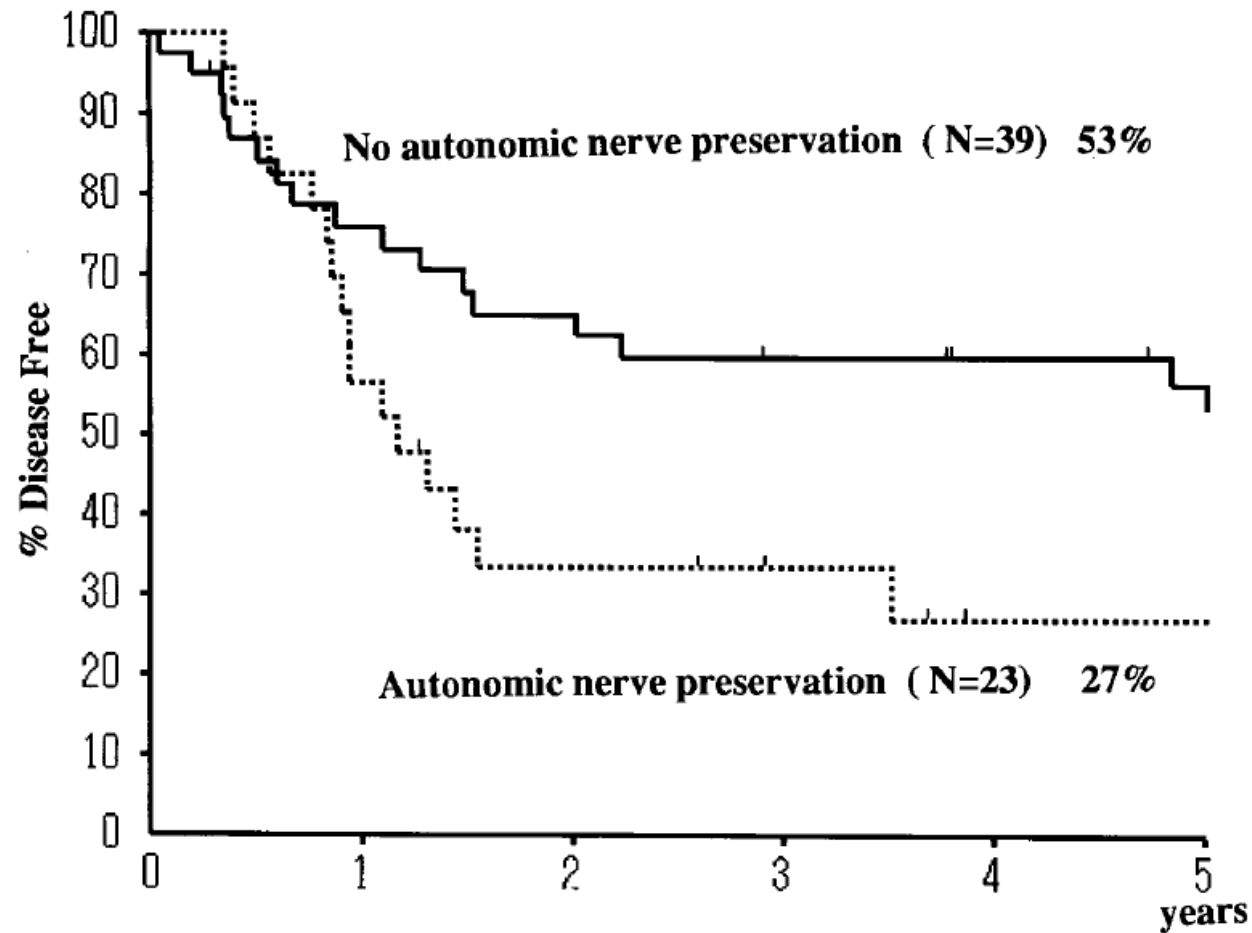
Fascia mesorettale



Fascia mesorettale

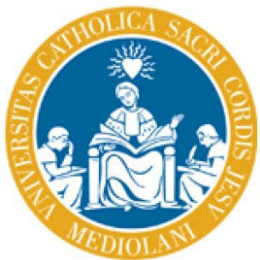
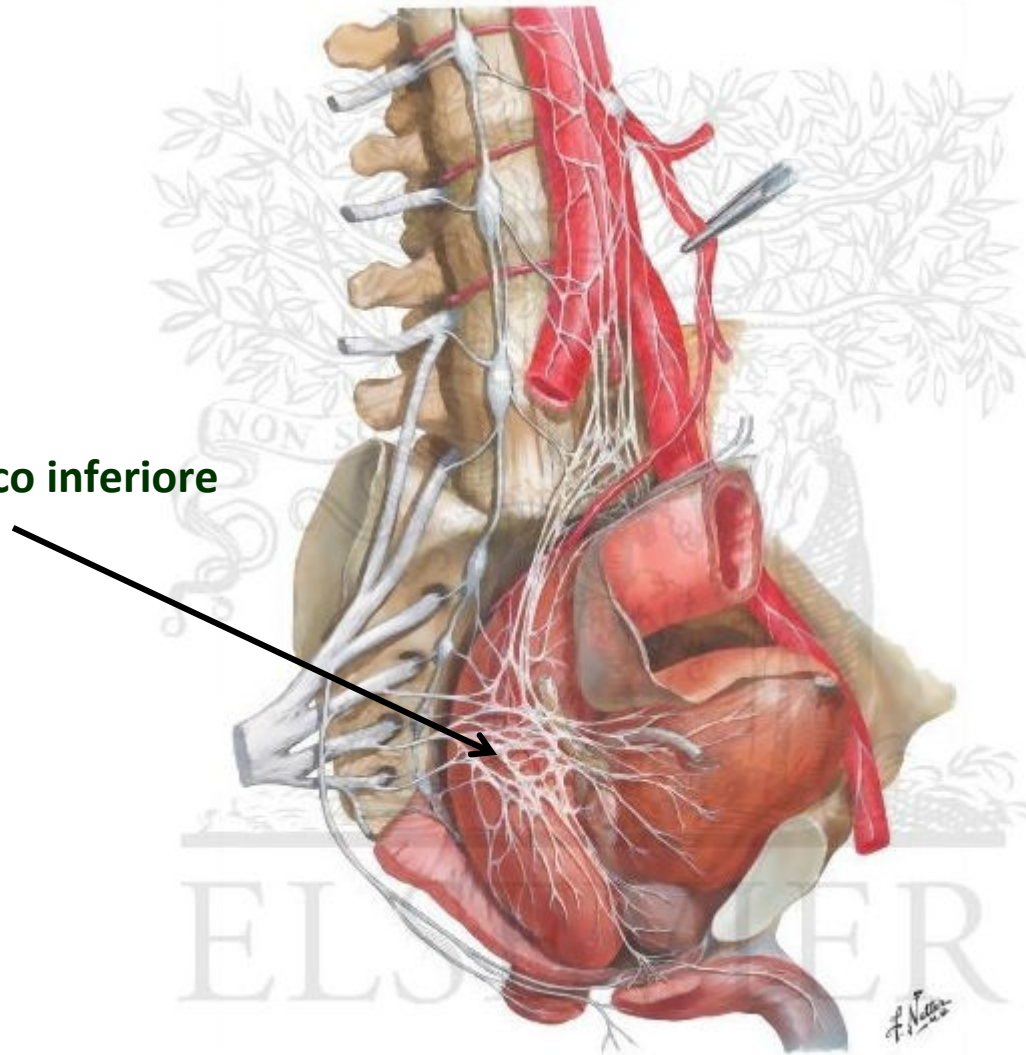
“[...] **margin involvement is not always present in the macroscopically most suspected area, but might be present in other areas [...]. The examination of additional microscopic slides had led to an increase in CRM-positive patients from 6% to 27% of patients and from 6 to 16 patients”**

Fascia mesorettale

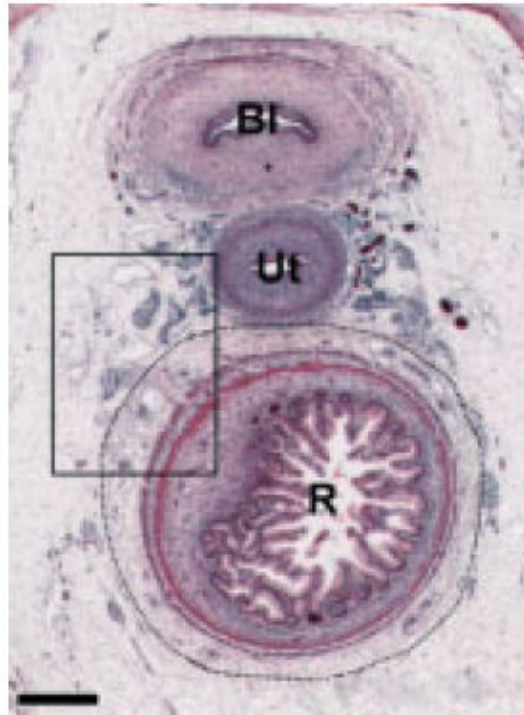


Fascia mesorettales

Plesso ipogastrico inferiore



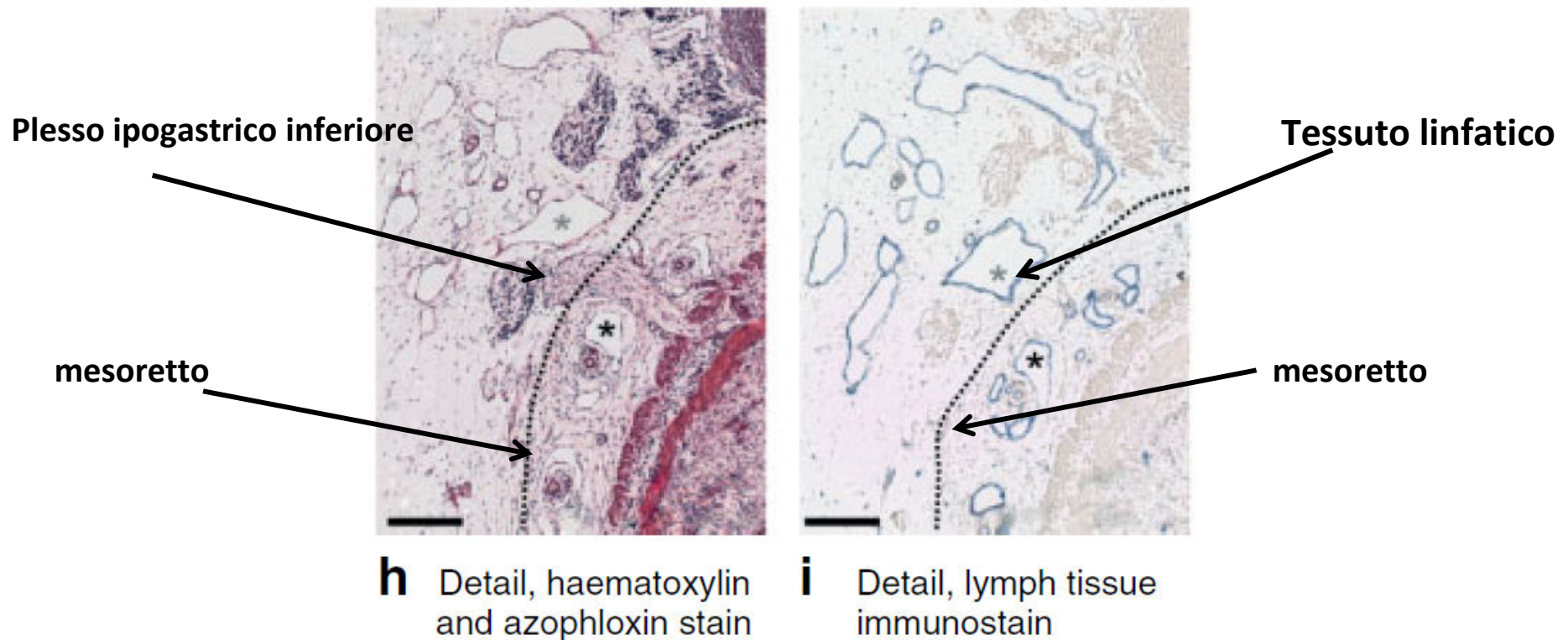
Fascia mesorettale



Ten serially sectioned human fetal pelvises were studied at high magnification and a three dimensional reconstruction of the fetal pelvis was made.

Kusters et al BJS 2010

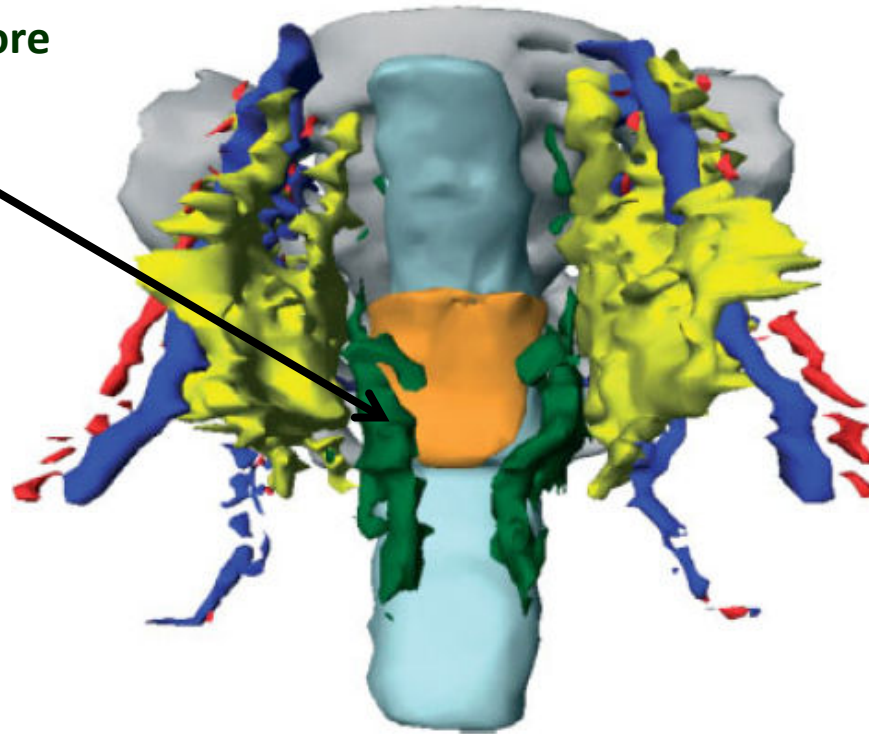
Fascia mesorettale



In the proximity of the mesorectum, the autonomic nervous system and the lymph vessels had a very close relationship.

Fascia mesorettale

Plesso ipogastrico inferiore



Regione presacrale

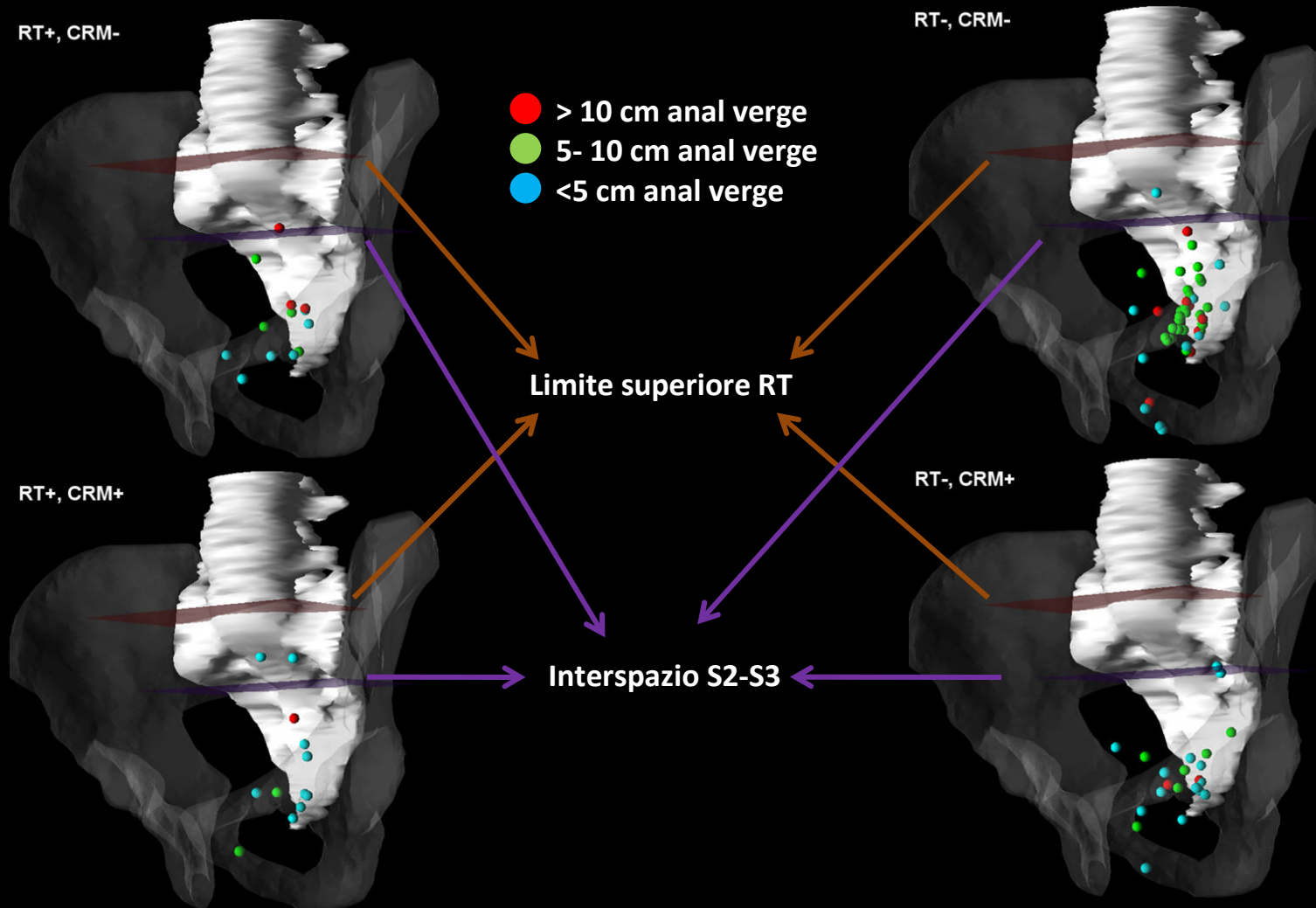
Subsites of local recurrence.

	RT + (<i>n</i> = 713)	RT - (<i>n</i> = 704)
Presacral	15 (2.0)	25 (3.6)
Lateral	9 (1.1)	14 (1.9)
Anterior	6 (0.7)	14 (1.9)
Anastomosis	5 (0.7)	19 (2.7)
Perineum	0 (0)	4 (0.6)
Unknown	1 (0.1)	2 (0.3)
TOTAL	36 (4.6)	78 (11.0)

Values in parenthesis are 5-year LR-rates, by competing risks analysis.

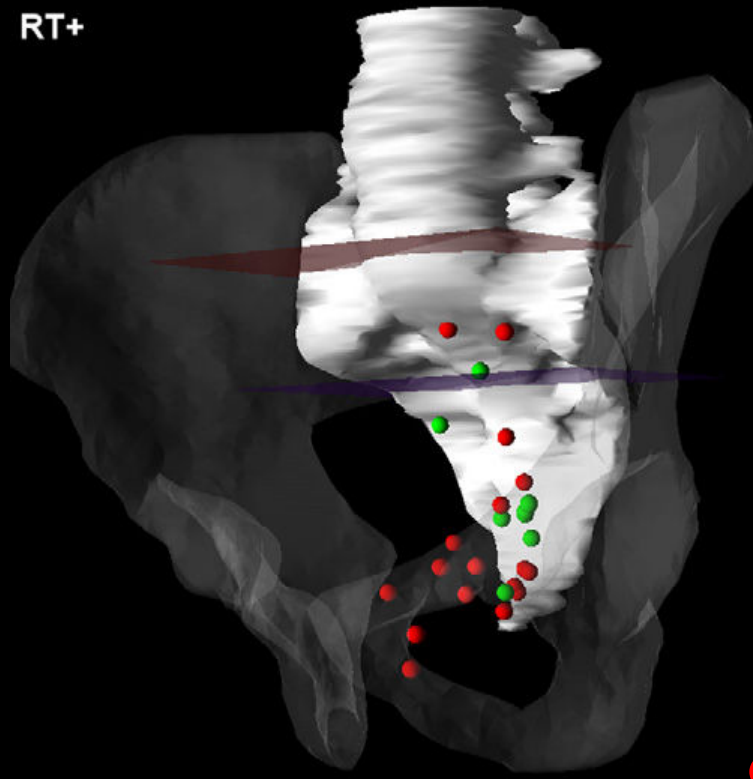
RT = preoperative radiotherapy.

Regione presacrale: Recidiva Locale & RT, CRM

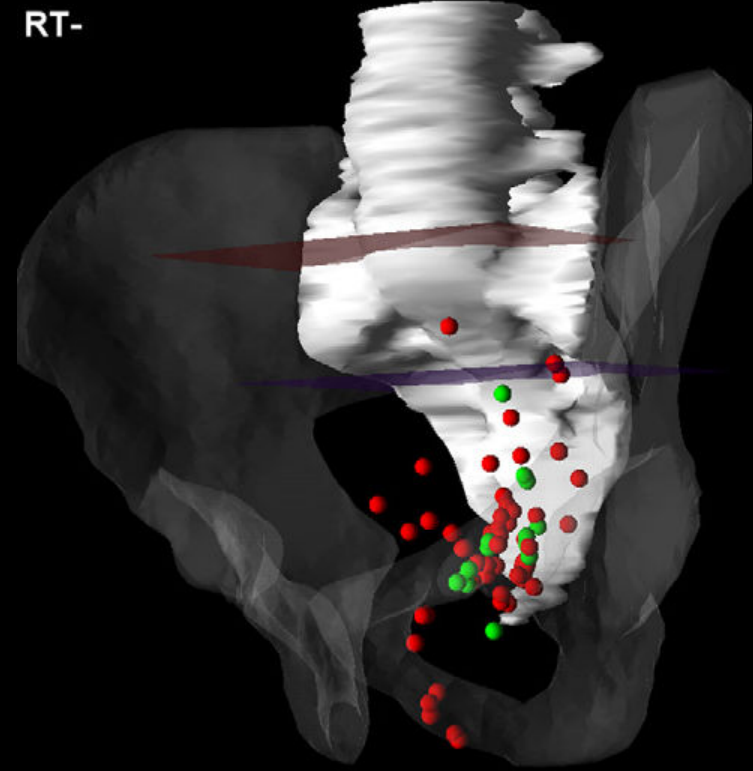


Regione presacrale: Recidiva Locale & N

RT+



RT-



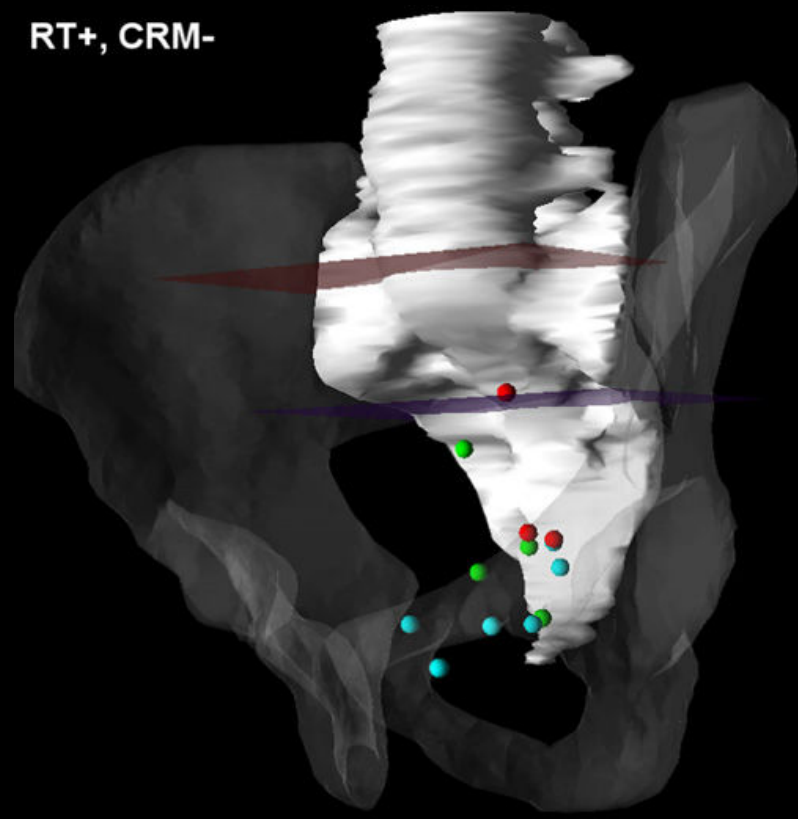
Limite superiore RT

Interspazio S2-S3

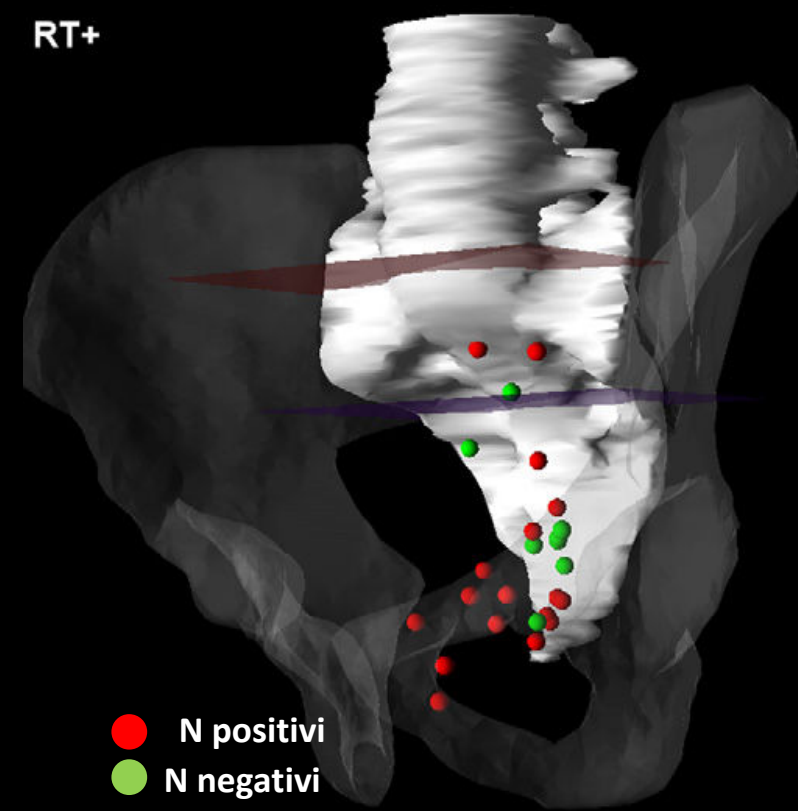
- N positivi
- N negativi

Regione presacrale: Recidiva Locale & N

RT+, CRM-



RT+



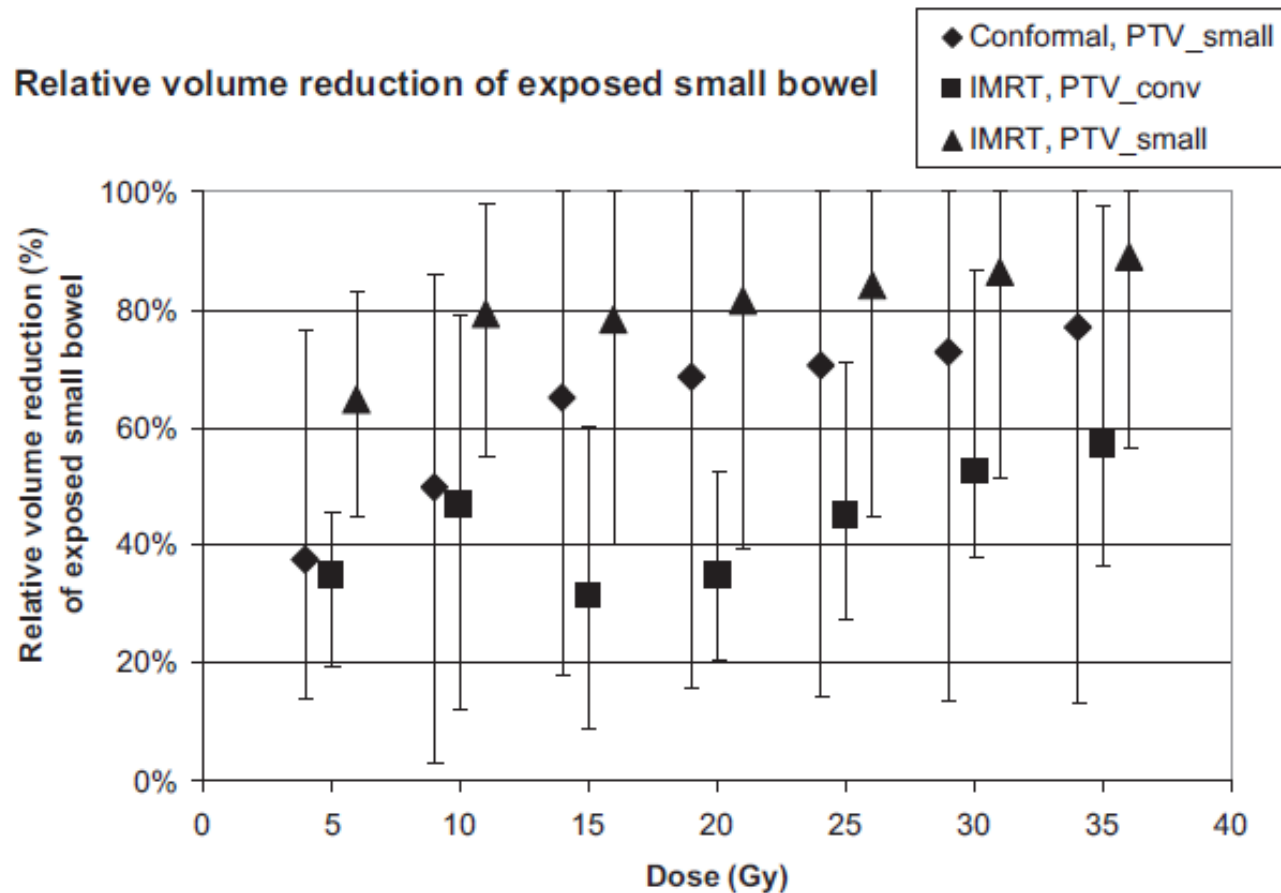
● N positivi
● N negativi

Regione presacrale: Recidiva Locale & N



Nijkamp et al IJROBP 2011

CTV reduction & small bowel



PTV small: CRM-; cN0, retto medio/basso

Nijkamp et al IJROBP 2011

N extra-mesorettali

OS 5 aa N+ extra-mesorettali: ~40%

Recidive casistiche radiologiche: 5%

Recidive casistiche chirurgiche: > 15 %

T sede e stadio,
N+mesorettali
grading

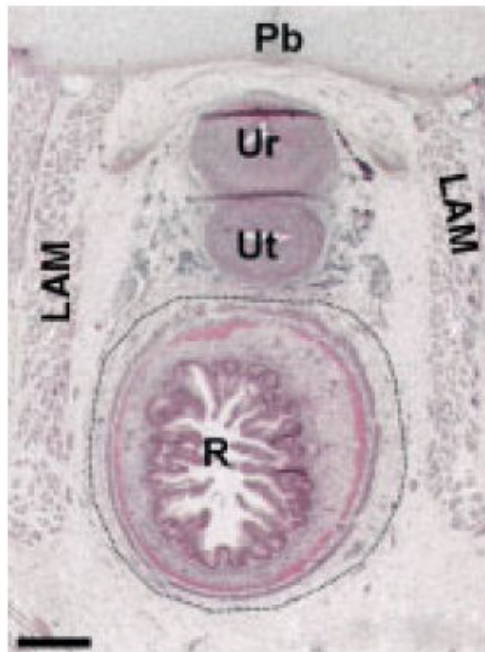
Radioterapia vs LLND*:

risultati sovrapponibili con minori effetti collaterali
(incontinenza impotenza)

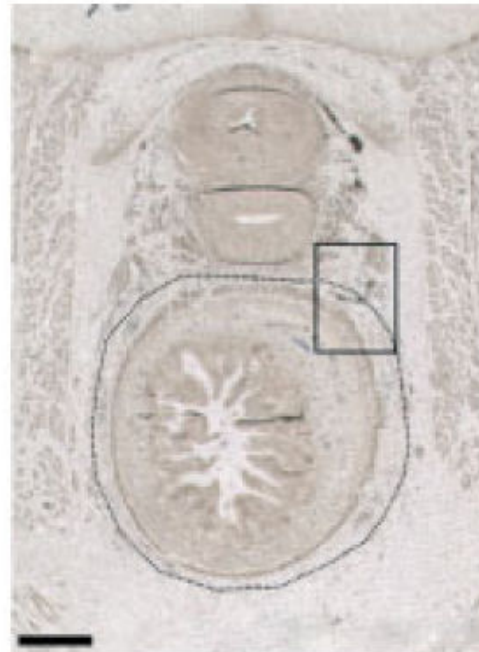
*Lateral Lymph Node Dissection

Sato et al Dis Colon Rectum 2006
Syc et al IJROBP 2008
Ueno et al Br J Surg 2005
Ueno et al Ann Surg 2007
Nagawa et al Dis Colon Rectum 2001
Kusters et al Ann Surg 2009

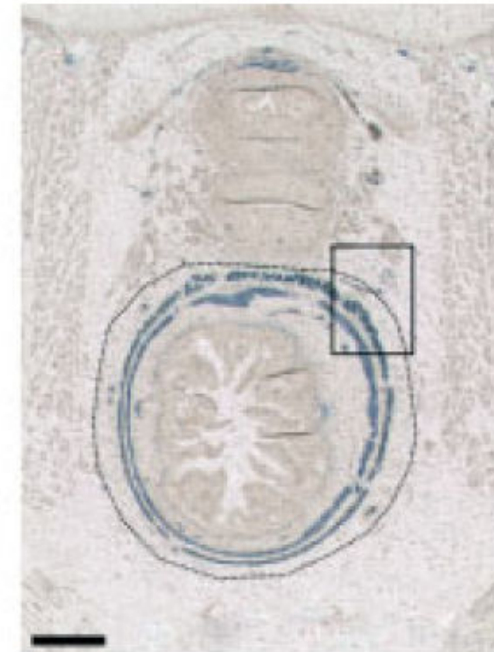
N extra-mesorectali



a Overview, haematoxylin and azophloxin stain



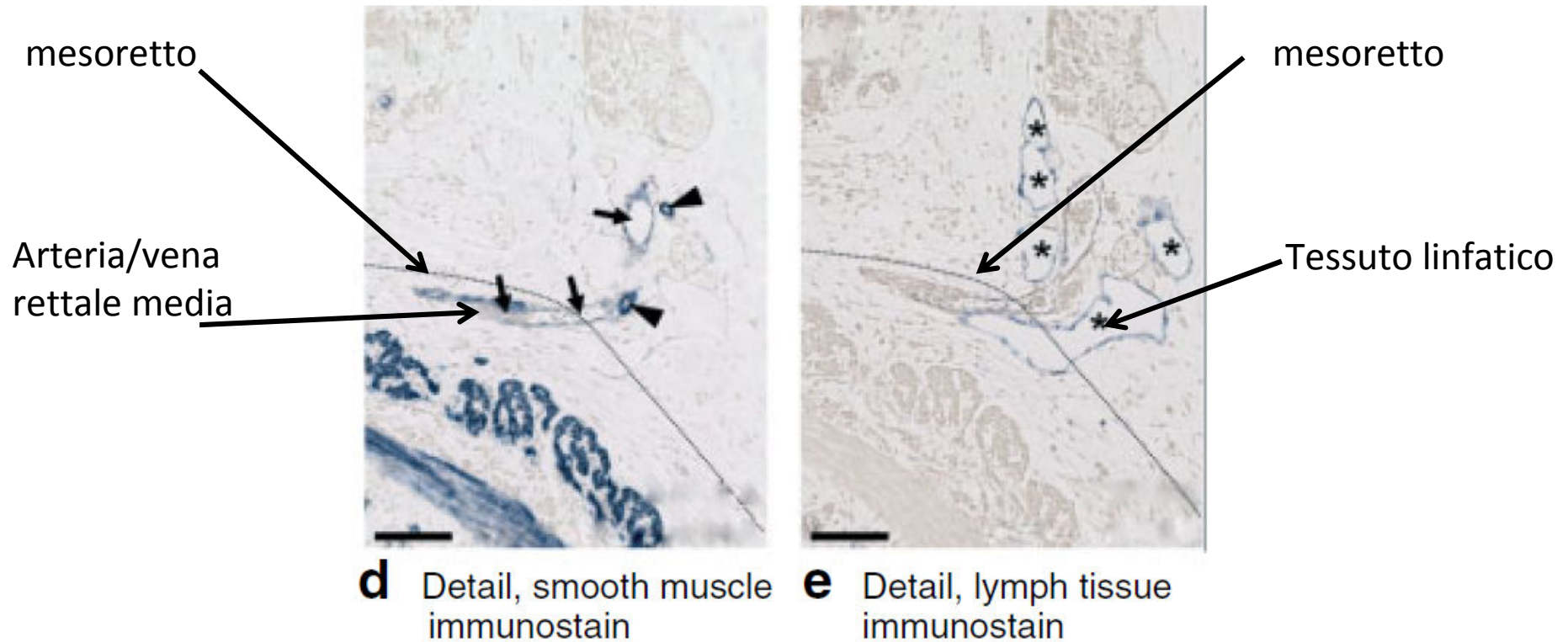
b Overview, lymph tissue immunostain



c Overview, smooth muscle immunostain

Ten serially sectioned human fetal pelvises were studied at high magnification and a three dimensional reconstruction of the fetal pelvis was made.

N extra-mesorettali

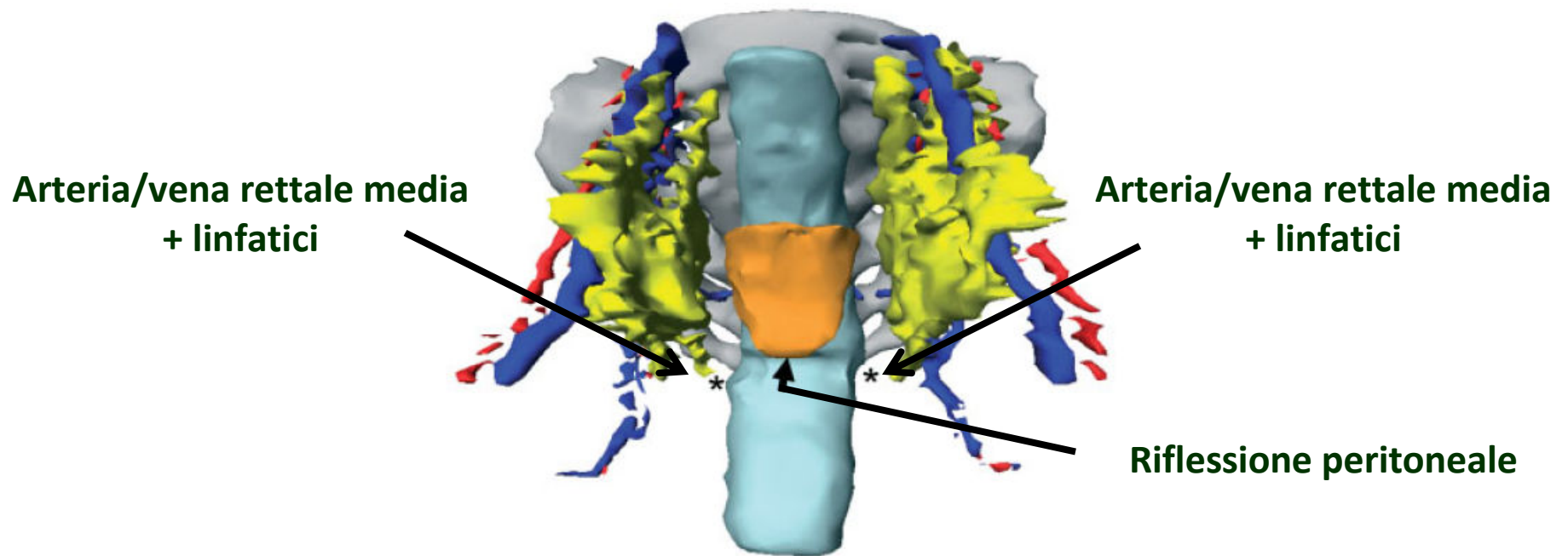


“[...] **No lymph node** tissue in the **presacral area** [...]”

The **middle rectal artery/veins** entered the **mesorectum** below the **peritoneal reflection** [...]

Vessels were accompanied by **lymph tissue** [...]”

N extra-mesorettali



“[...]No lymph node tissue in the presacral area [...]”

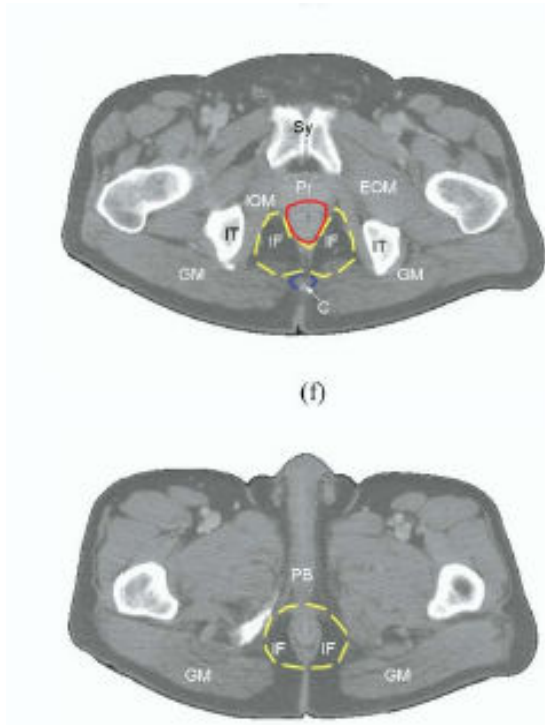
The middle rectal artery/veins entered the mesorectum below the peritoneal reflection[...]

Vessels were accompanied by lymph tissue [...]”

N extra-mesorectali

The authors hypothesized that, when mobilizing the rectum during surgical excision, lymph fluid and tumour cells flow into the lateral lymph node system. As this lateral lymph tissue is left behind in a standard TME and partly damaged during sharp dissection of the lateral ligament, one would expect the basins to start leaking after the procedure. This lymph fluid, collected presacrally in a seroma, might give rise to local tumour recurrence.

Sfintere e fosse ischio-rettali



- 4% di tutte le RL
- 8% $T \leq 6$ cm OAE
- 11% APR

ma...

- No N in fosse ischio-rettali
- M elevatore
- Intramural spread raro $> 1-1.5$ cm

T > 1.5 dall'OAI: mesoretto

T ≤ 1.5 OAI: 1 cm canale anale

T con invasione canale anale: sphincter complex

T con invasione fossa IR: entrambe le fosse

Roels S et Al IGROBP 2006

Myerson RJ IJROBP 2009

Ippolito E et Al Acta Oncol 2008

Gambacorta MA et Al. submitted

Conclusioni

Table 13.2 Target volume delineation according to tumor stage and location

	Presacral space	Mesorectum	Internal iliac nodes	Obturator nodes	External iliac nodes	Sphincter complex	Ischio-rectal fossae
cT3 high (above the peritoneal reflection)	+	+	+				
cT3 mid-low (at the peritoneal reflection)	+	+	+	+		+ (when anal canal invasion)	+ (when direct tumor infiltration)
Any cT with massive positive internal iliac nodes	+	+	+	+		+ (when anal canal invasion)	+ (when direct tumor infiltration)
Any cT with massive positive obturator nodes	+	+	+	+	+	+ (when anal canal invasion)	+ (when direct tumor infiltration)
cT4 with for anterior pelvic organ	+	+	+	+	+	+ (when anal canal invasion)	+ (when direct tumor infiltration)