IORT for recurrent rectal cancer 1994-2004

Harm Rutten, The Netherlands
Catharina Hospital Eindhoven

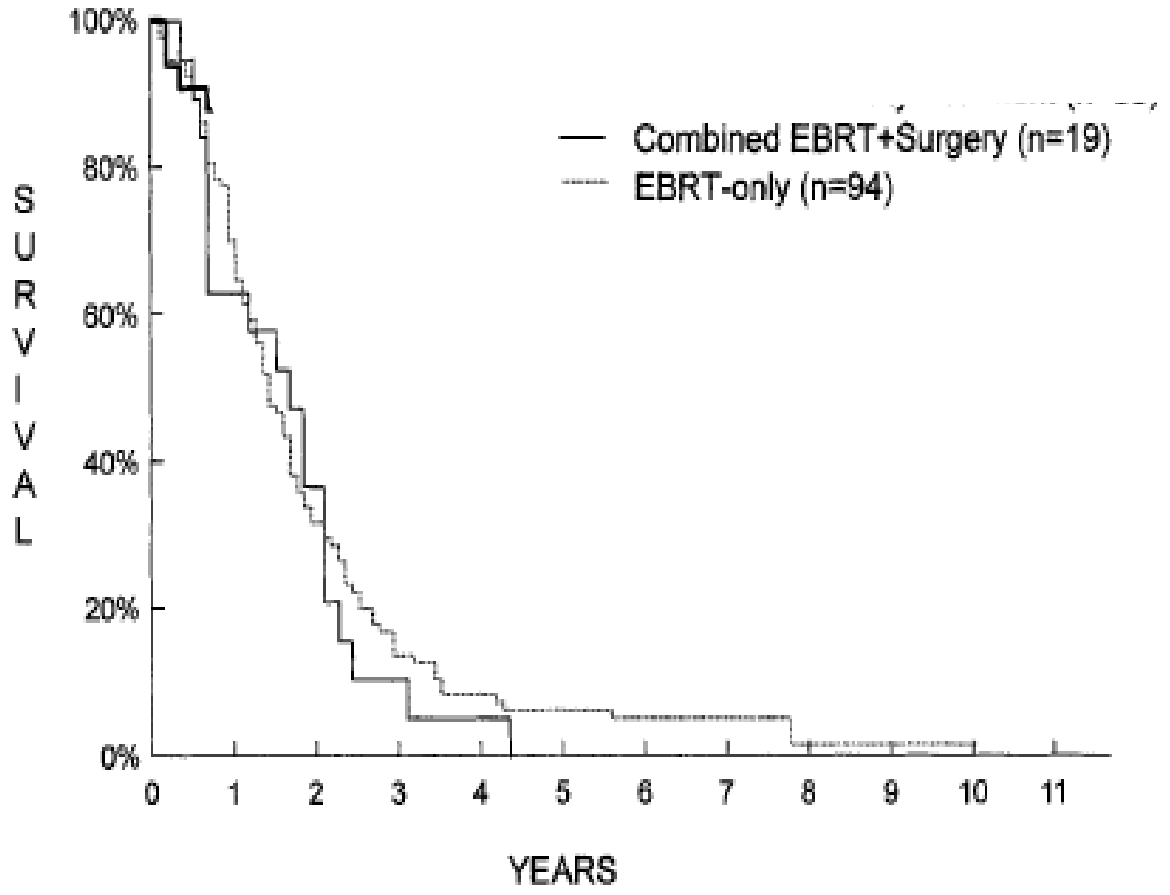
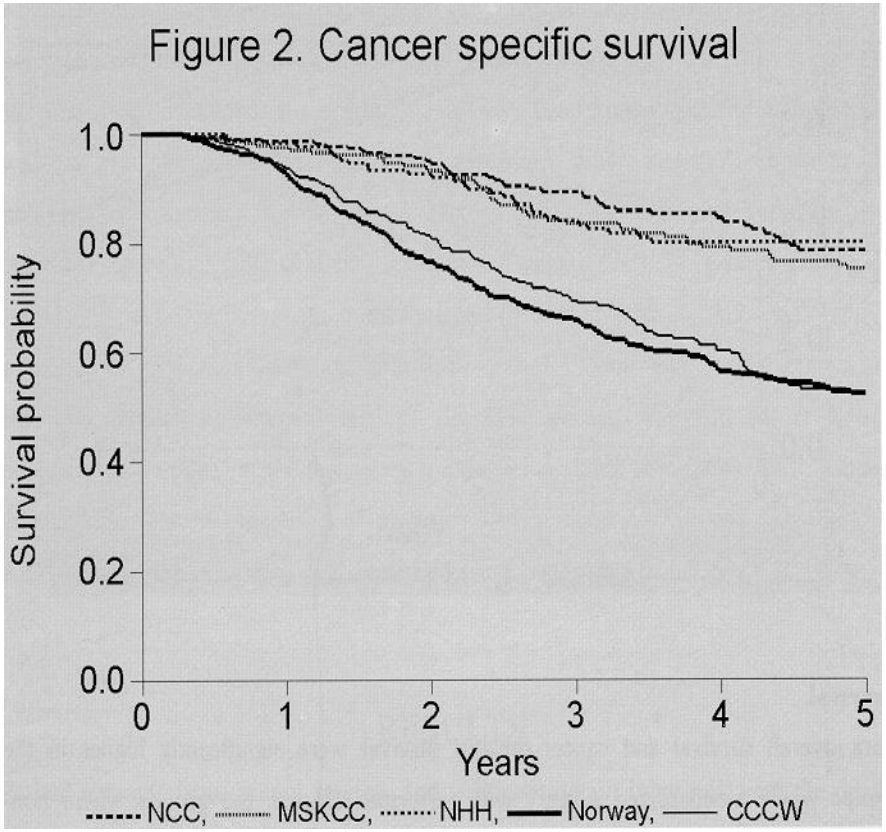
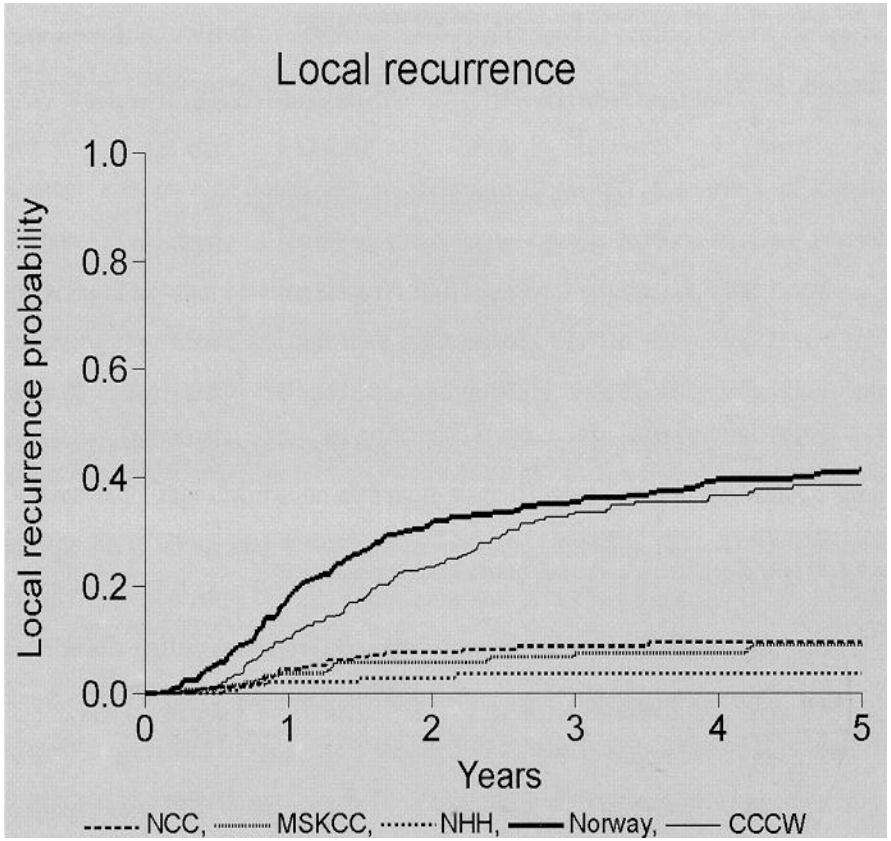
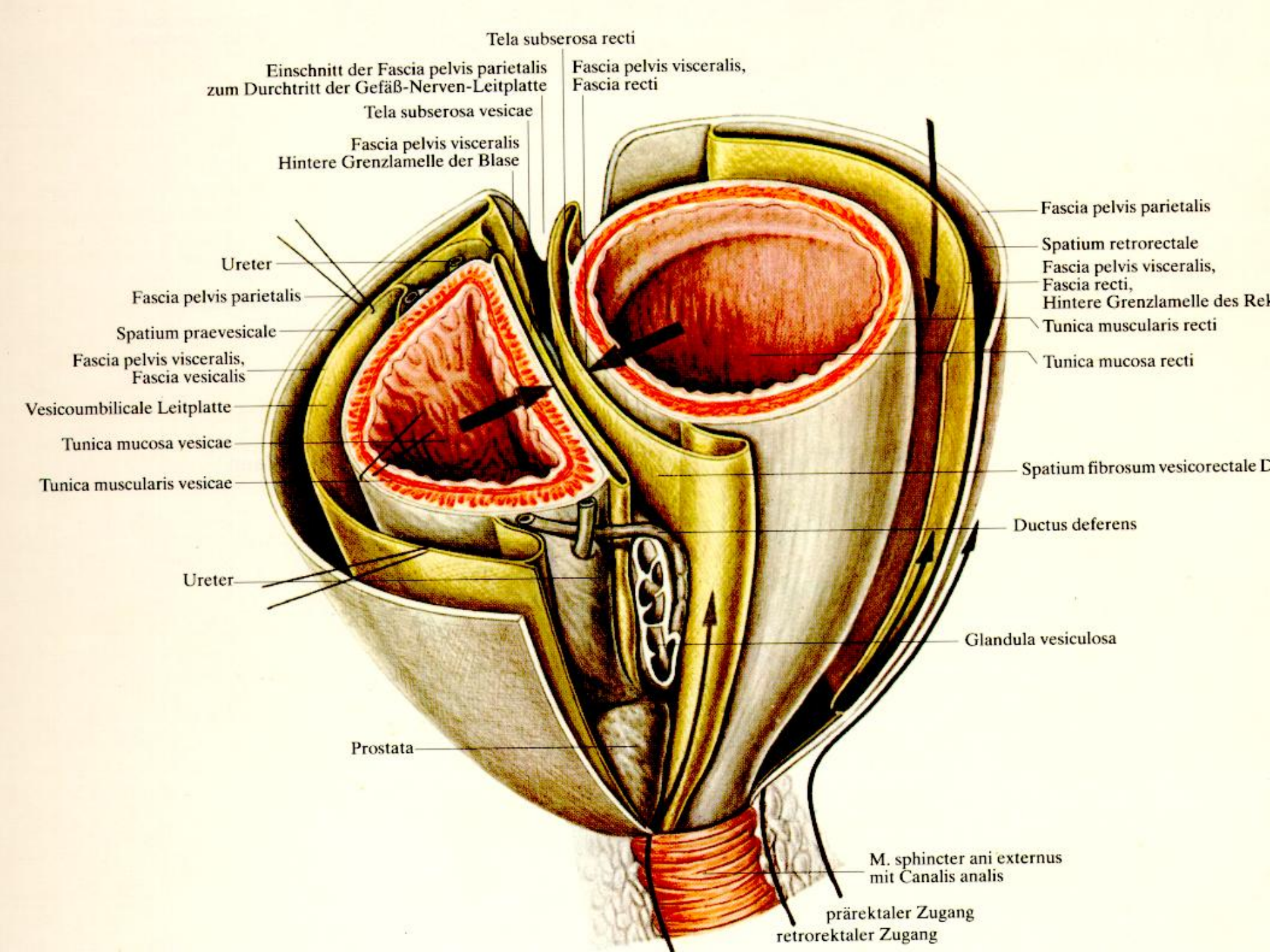


Figure 1. Survival comparing electron-beam radiation therapy (EBRT) only *vs.* combined EBRT and surgery *vs.* intraoperative radiation therapy (IORT)–multimodality treatment (EBRT-only *vs.* IORT-multimodality treatment, $P = 0.00001$; combined EBRT-surgery *vs.* IORT-multimodality treatment, $P = 0.0001$).



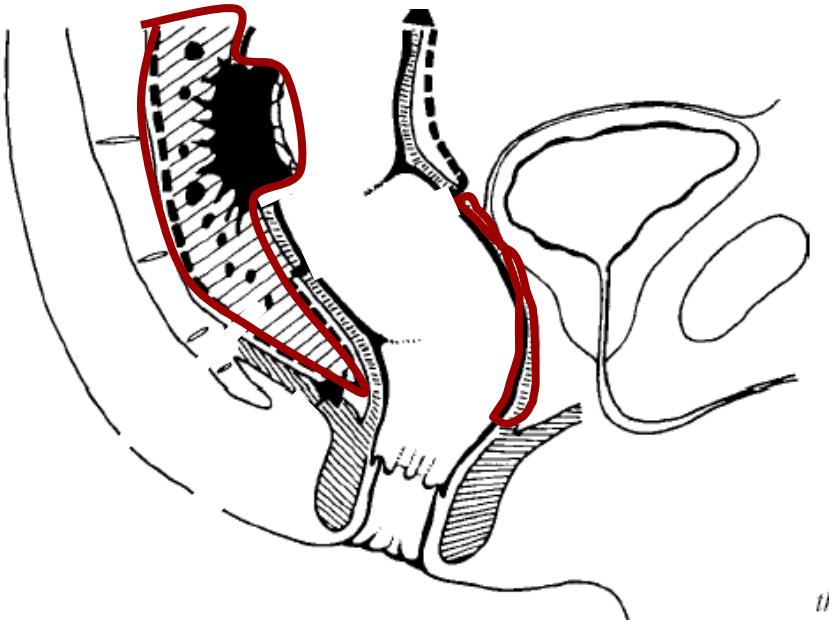


Havenga K. European Journal of Surgical Oncology 1999; 25: 368–374


Tela subserosa recti
Einschnitt der Fascia pelvis parietalis
zum Durchtritt der Gefäß-Nerven-Leitplatte
Fascia pelvis visceralis,
Fascia recti
Tela subserosa vesicae
Fascia pelvis visceralis
Hintere Grenzlamelle der Blase
Fascia pelvis parietalis
Spatium retrorectale
Fascia pelvis visceralis,
Fascia recti,
Hintere Grenzlamelle des Rek
Tunica muscularis recti
Tunica mucosa recti
Ureter
Fascia pelvis parietalis
Spatium praevesicale
Fascia pelvis visceralis,
Fascia vesicalis
Vesicoumbilicale Leitplatte
Tunica mucosa vesicae
Tunica muscularis vesicae
Spatium fibrosum vesicorectale D
Ductus deferens
Ureter
Glandula vesiculosa
Prostata
M. sphincter ani externus
mit Canalis analis
prärektaler Zugang
retrorektaler Zugang

Total mesorectal excision

Why ‘total mesorectal excision’?

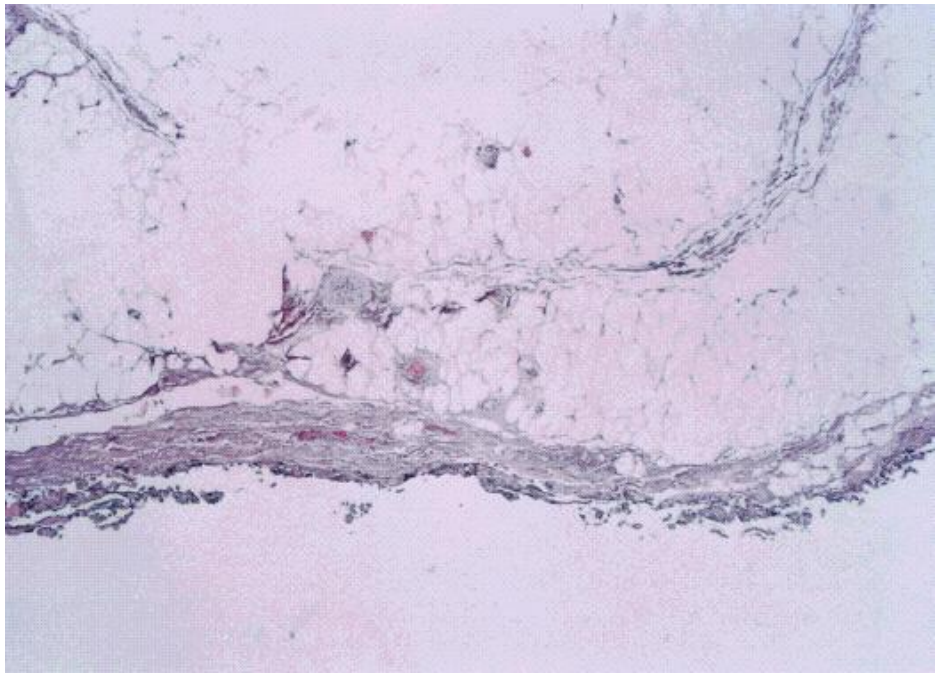


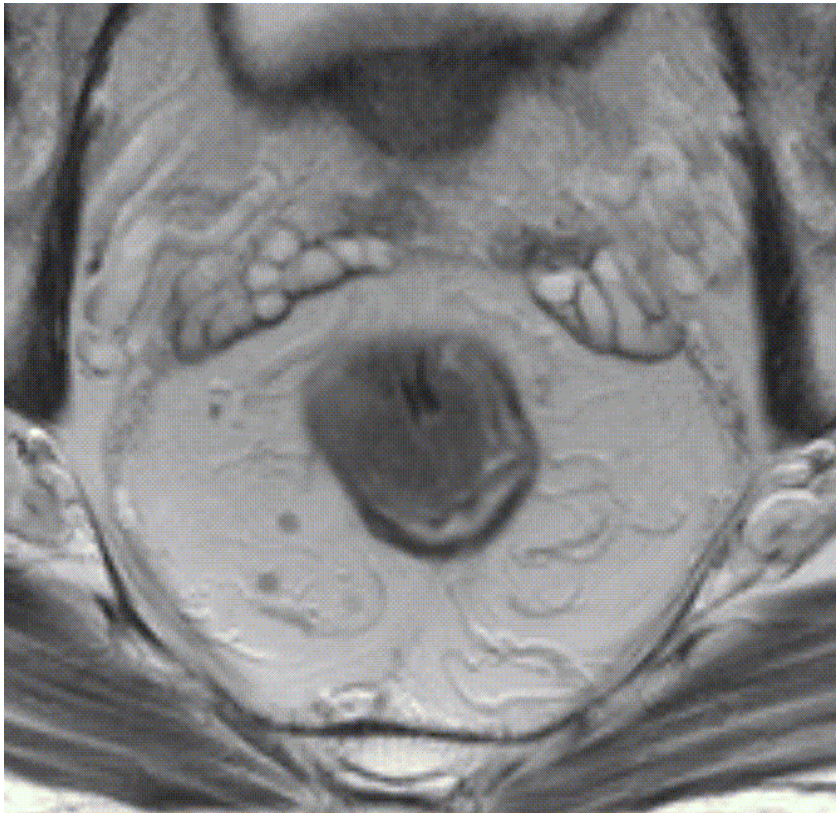
Lymph nodes in mesorectum

T3+ tumor

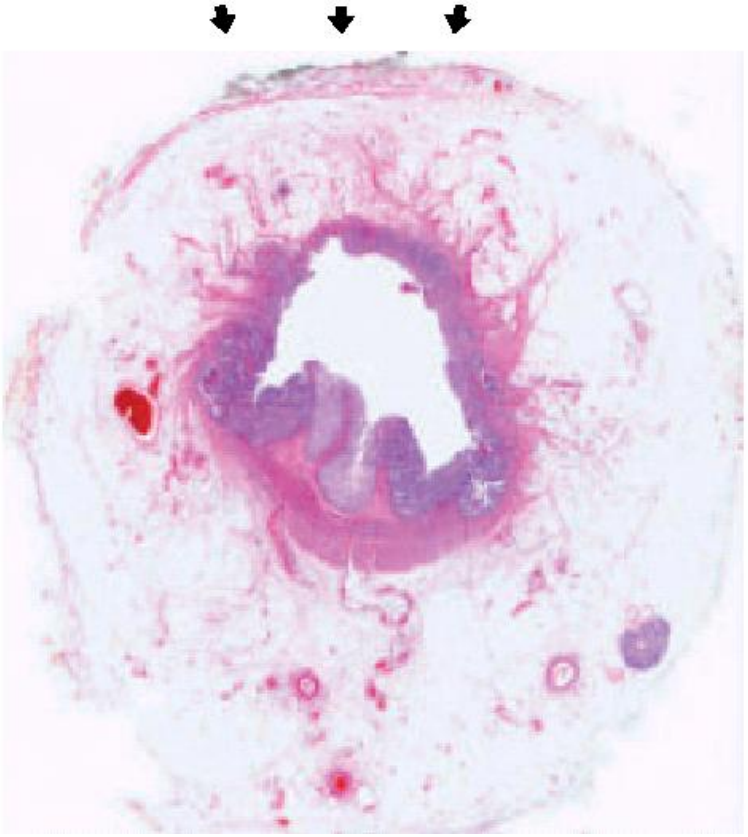
Ingrowth primary tumor

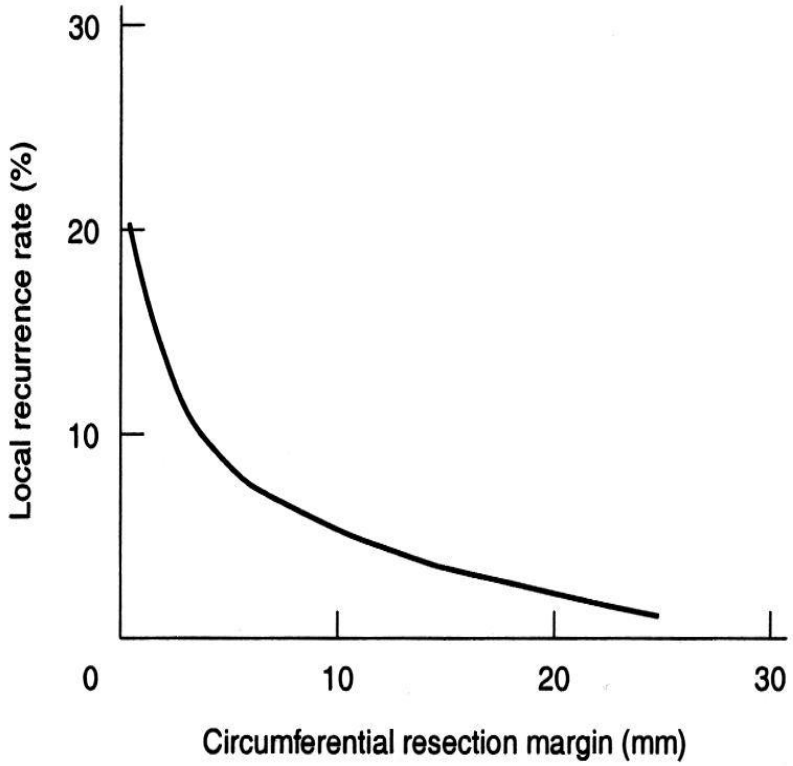
TME – mesorectal fascia



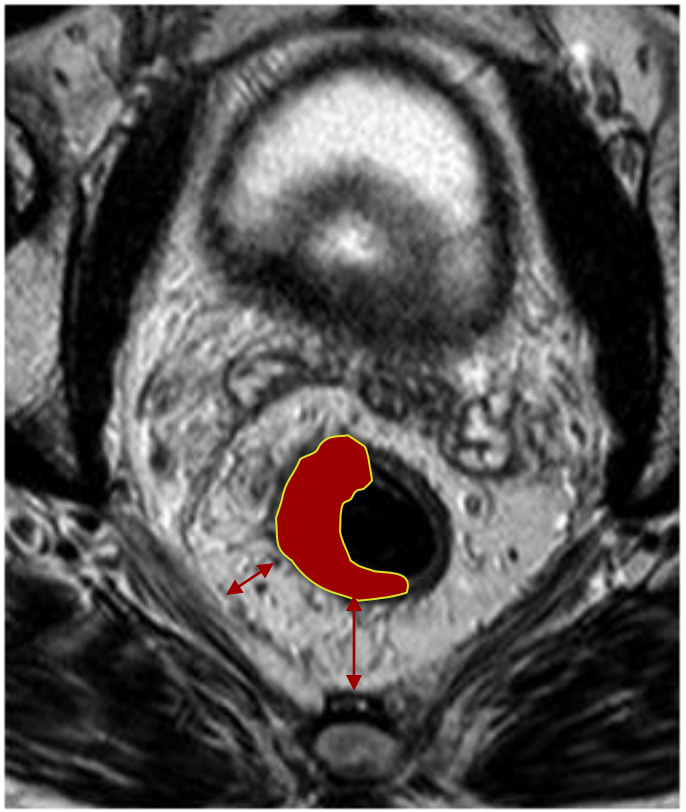


Enker et al. Sem Surg Oncol 2000; 18: 199-206

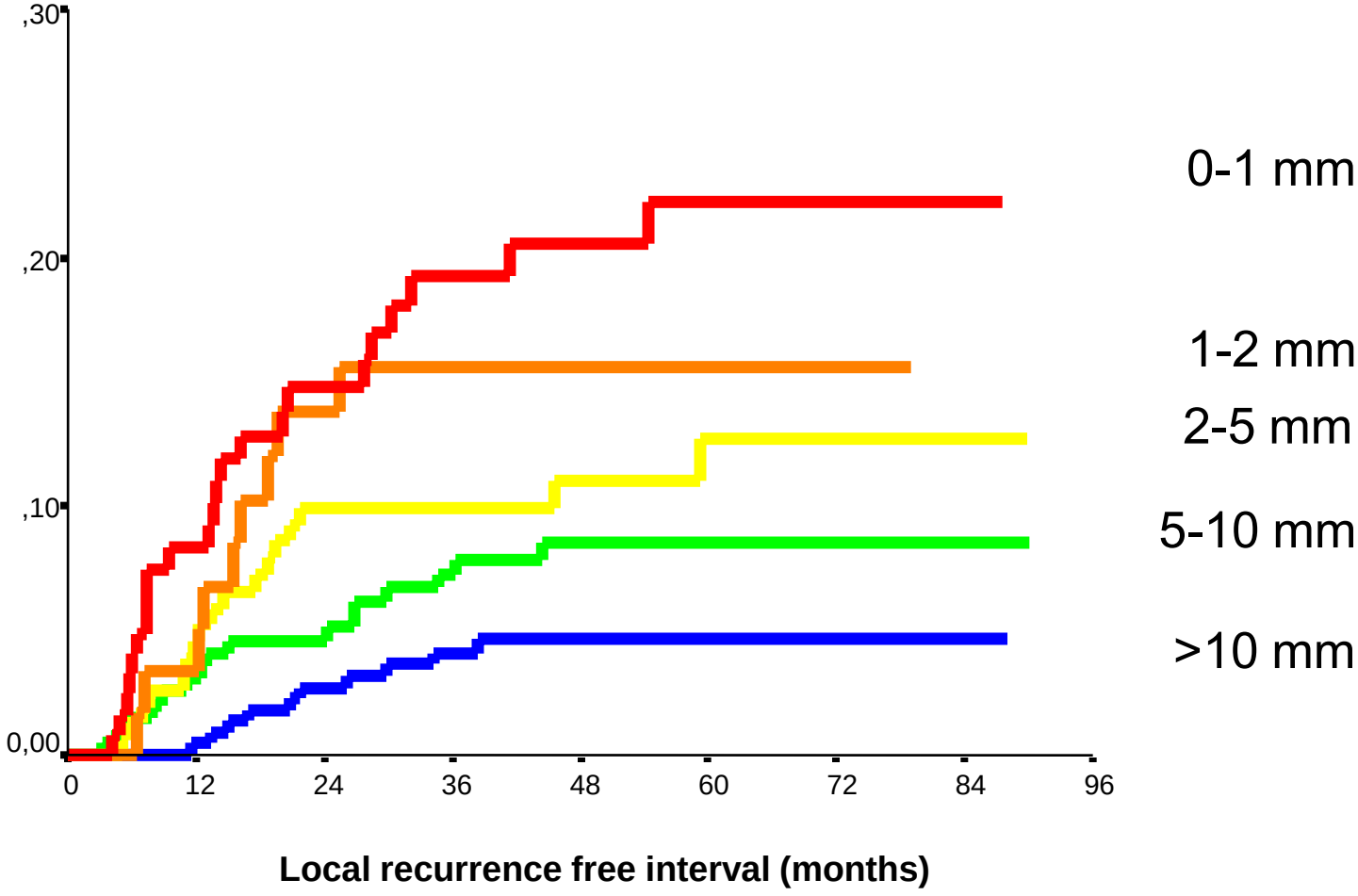




Relationship between circumferential resection margin and local recurrence rate

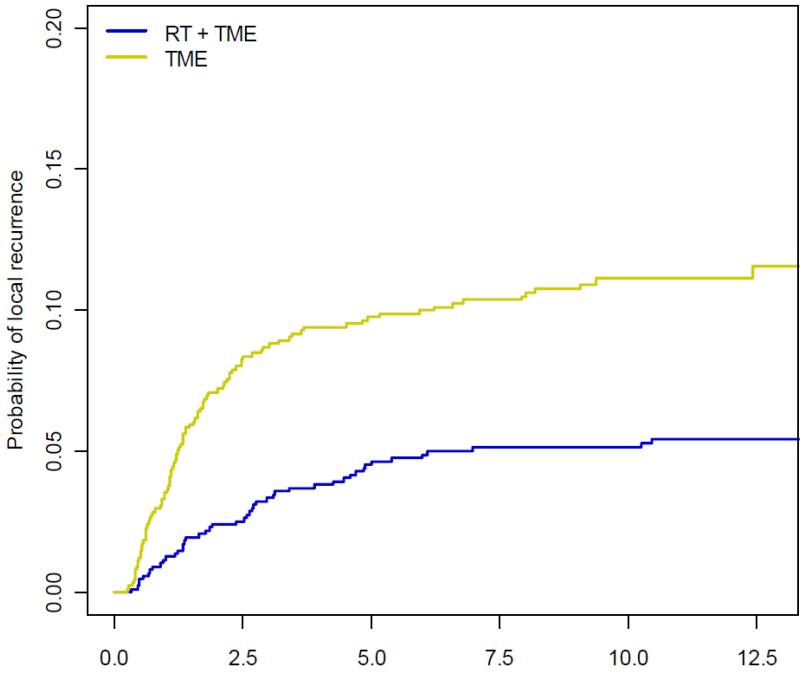


Wibe A, et al. Br J Surg 2002; 89:327-34.



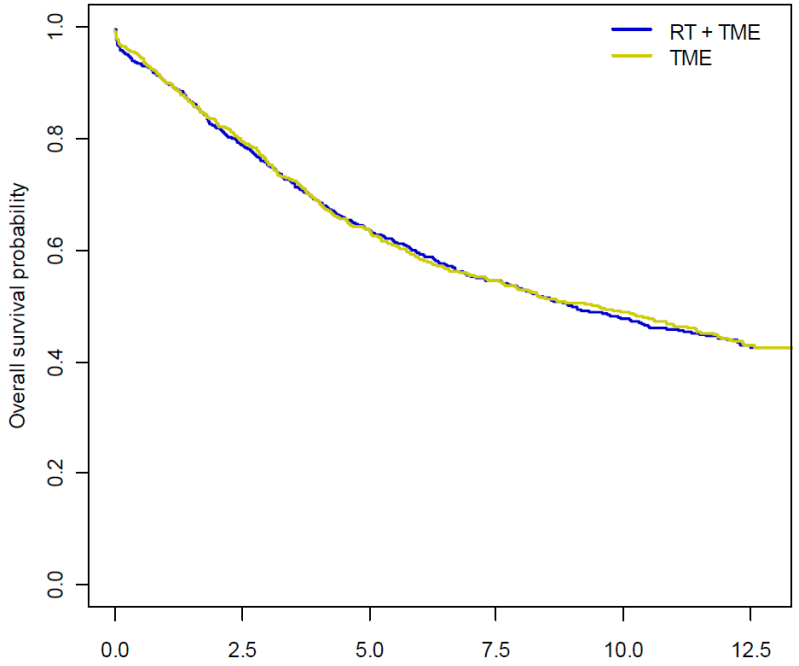
Nagtegaal ID, et al. Am J Surg Pathol 2002; 26:350-7.

A: Rates of local recurrence



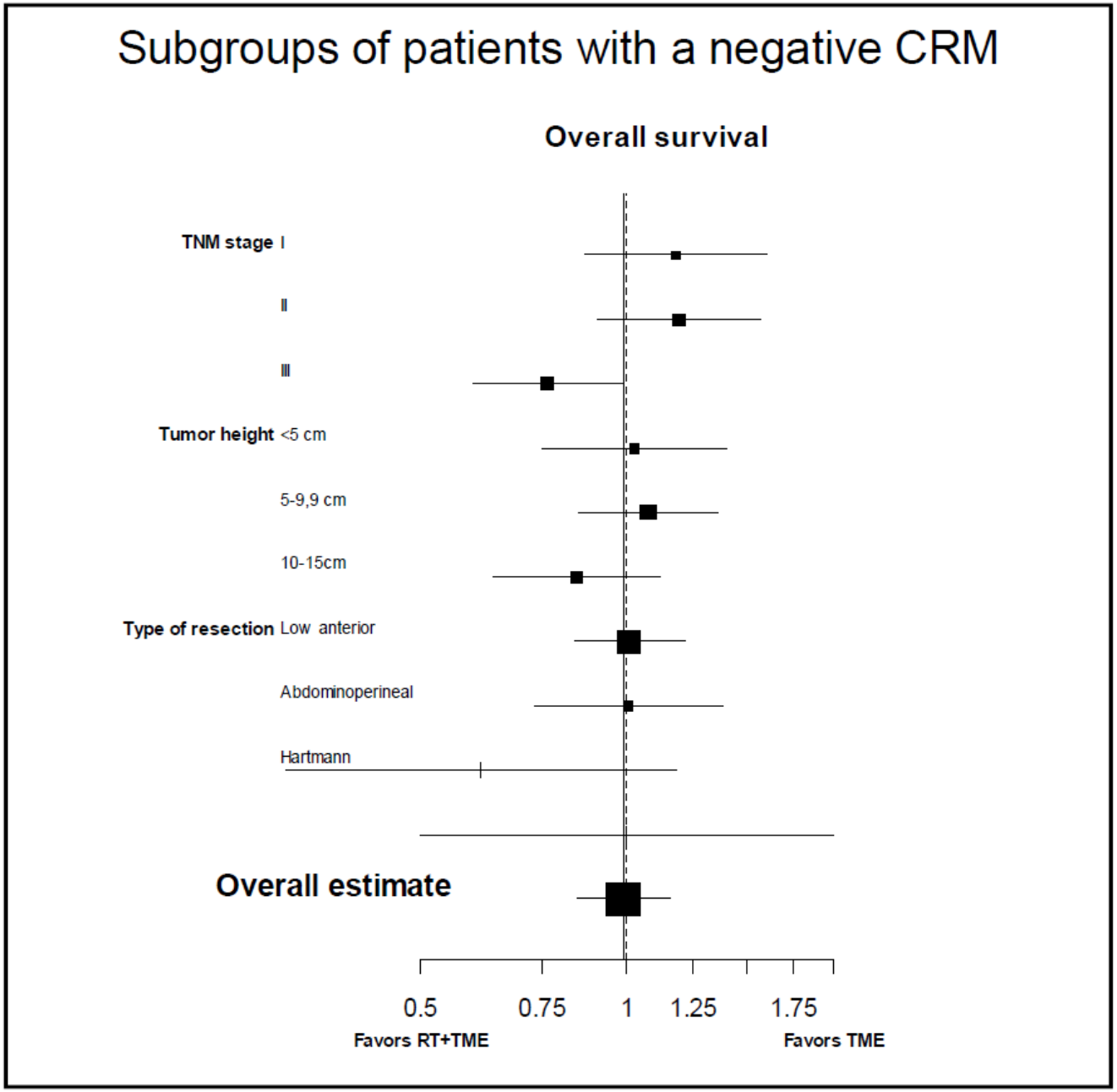
- Rates of local recurrence among 1748 eligible patients who underwent a macroscopically complete local resection, according to randomisation

B: Rates of overall survival



- Rates of overall survival among 1805 eligible patients according to randomisation

Lancet Oncology, 2011



A forest plot showing hazard ratios of RT+TME with respect to TME for survival among subgroups of patients with a negative CRM

Lancet Oncology, 2011

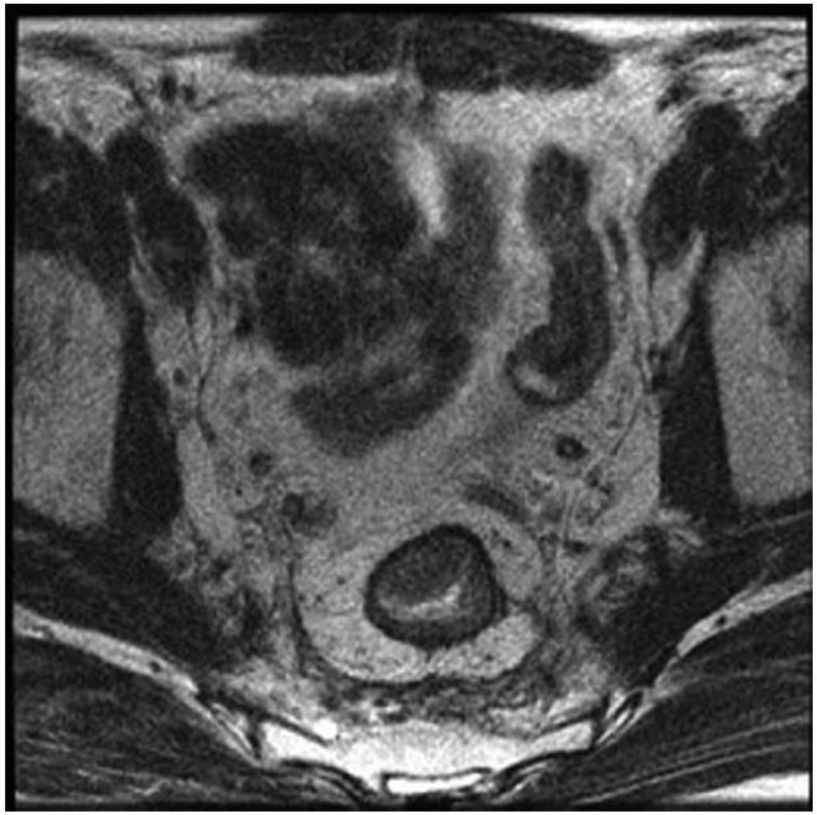


Fig. 1. Axial recurrence.

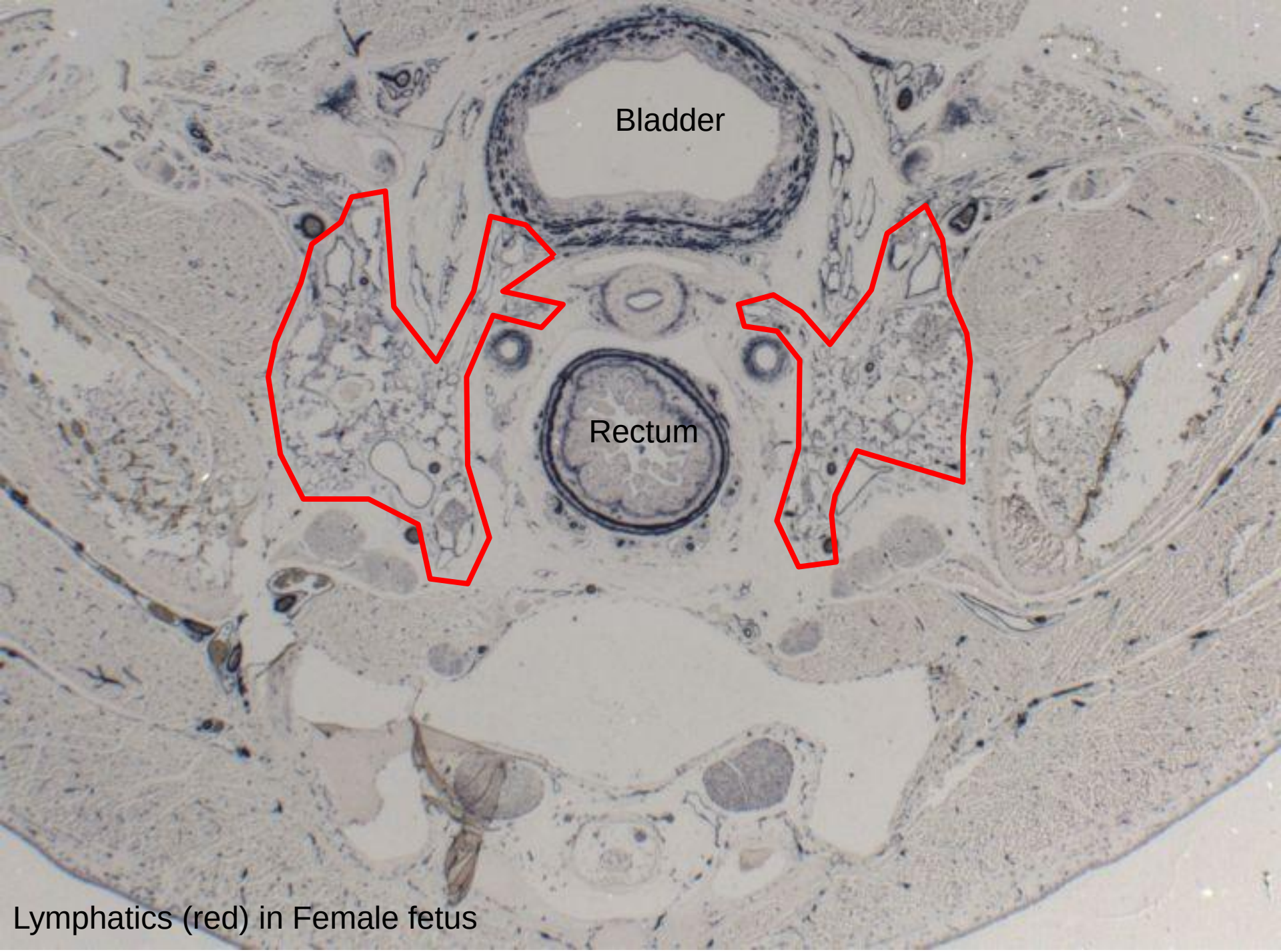
Fig. 2. Anterior recurrence.

Journal of Surgical Oncology 2014;109:47–52

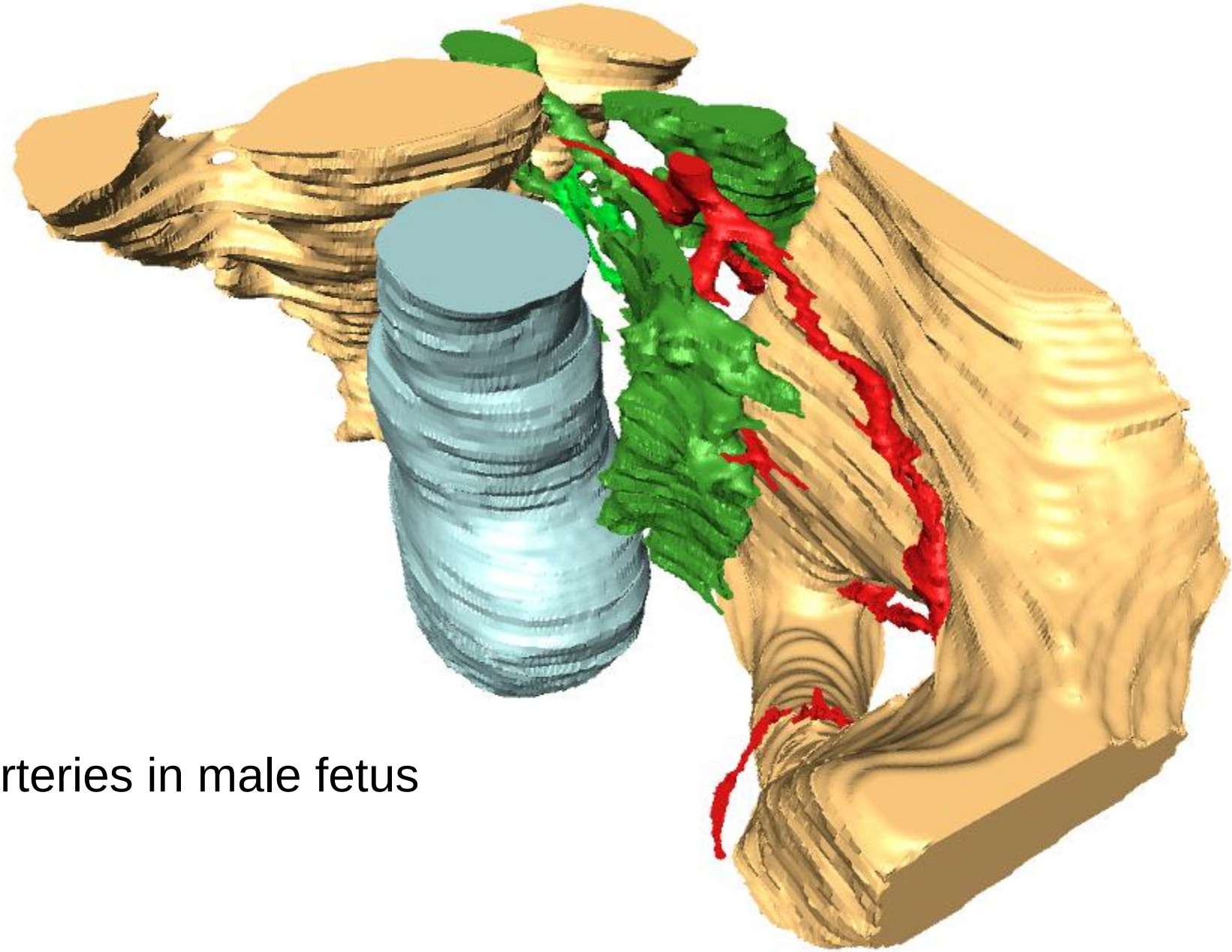
Management of Recurrent Rectal Cancer: Practical Insights in Planning and Surgical Intervention

HEATHER L. YEO, MD[1] AND PHILIP B. PATY, MD[1,2]*

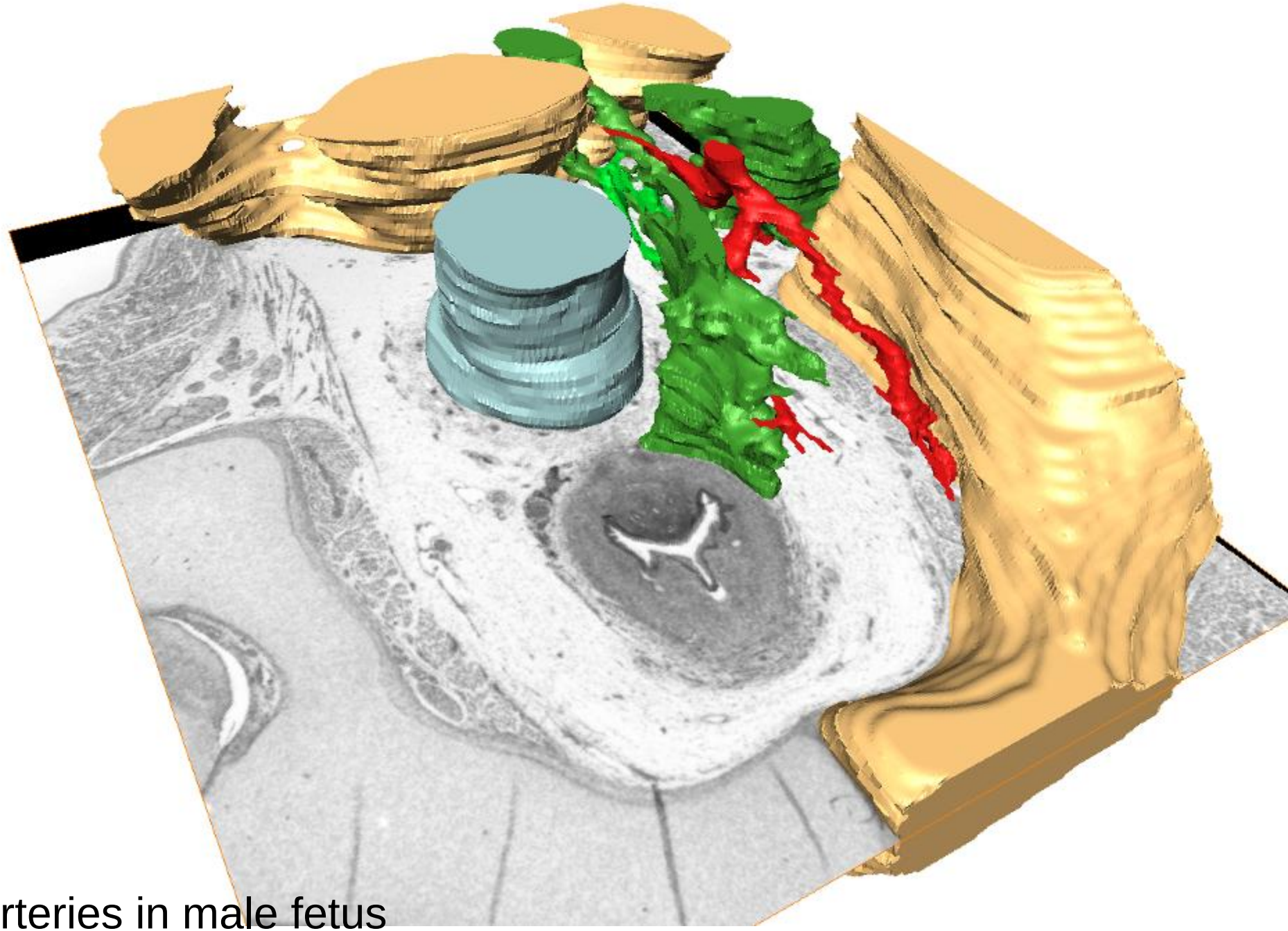
[1]Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York
[2]Department of Surgery, Cornell Weill Medical College, New York, New York



Lymphatics (red) in Female fetus



Arteries in male fetus



Arteries in male fetus

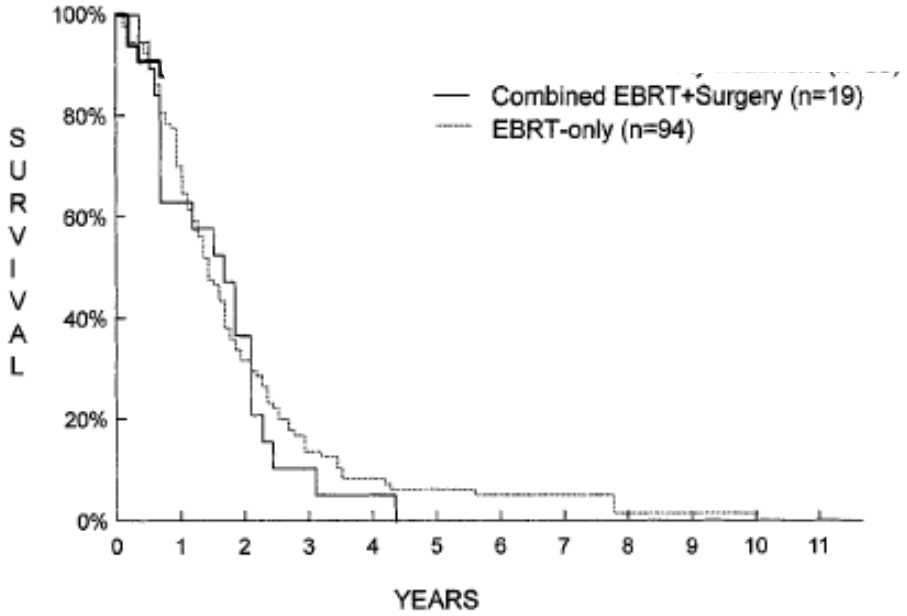
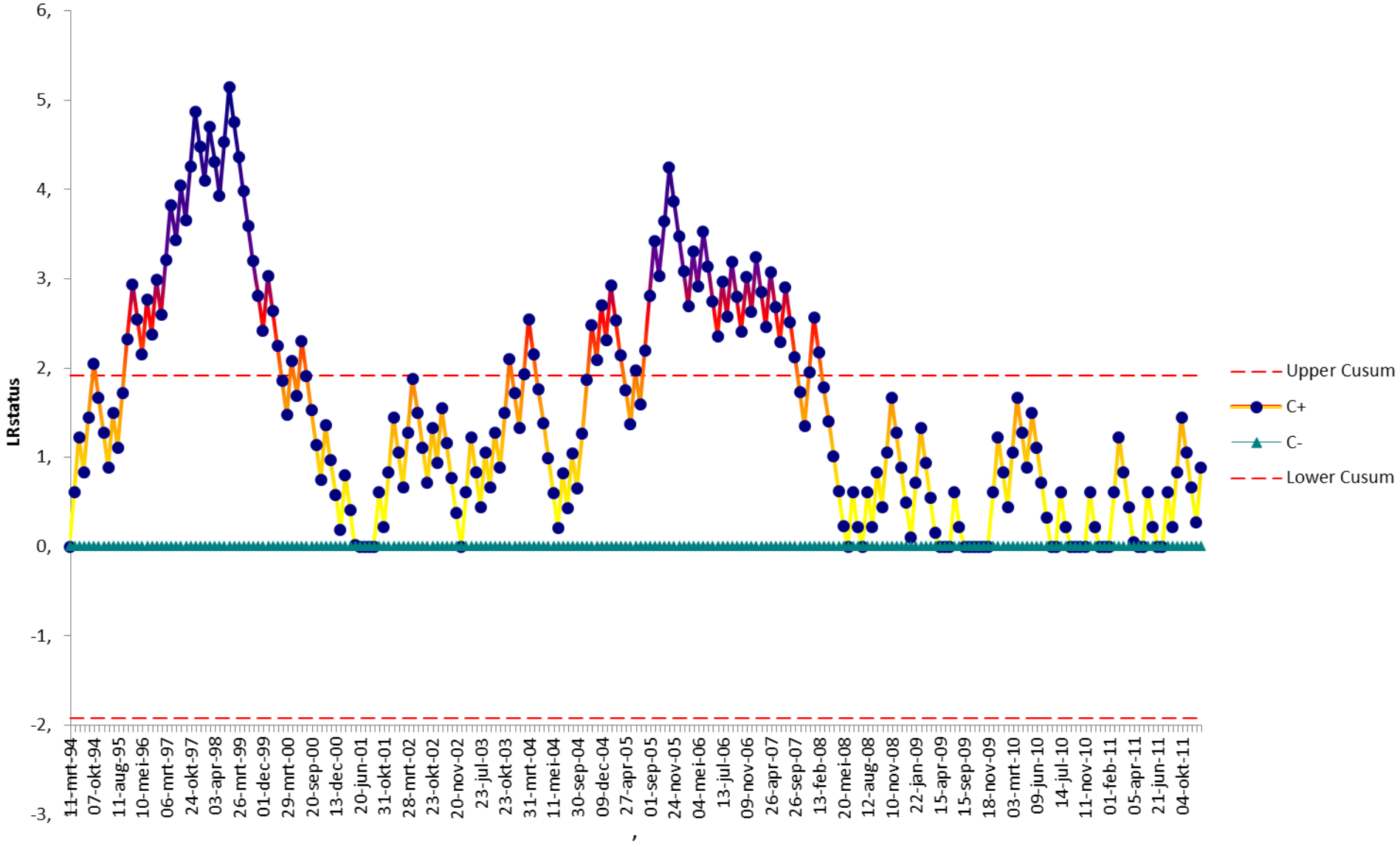


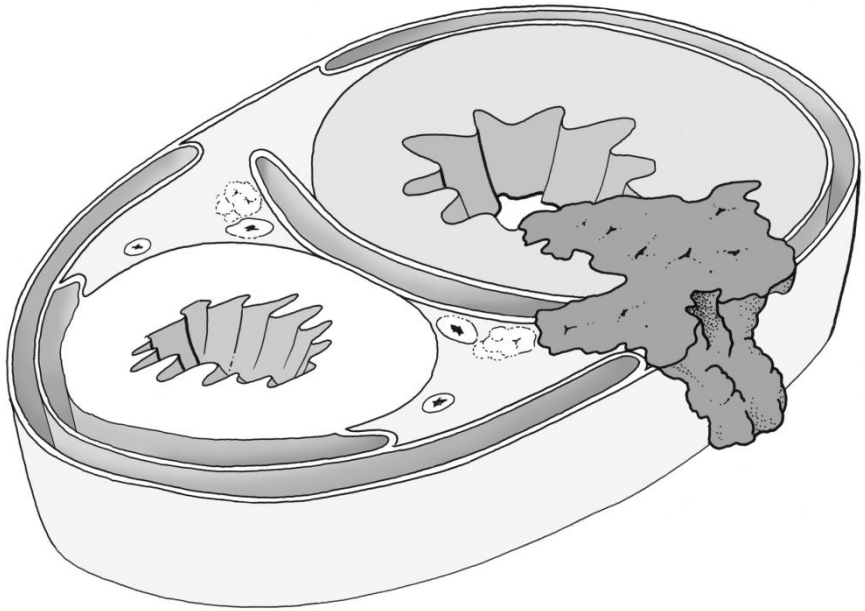
Figure 1. Survival comparing electron-beam radiation therapy (EBRT) only *vs.* combined EBRT and surgery *vs.* intraoperative radiation therapy (IORT)–multimodality treatment (EBRT-only *vs.* IORT-multimodality treatment, $P = 0.00001$; combined EBRT-surgery *vs.* IORT-multimodality treatment, $P = 0.0001$).

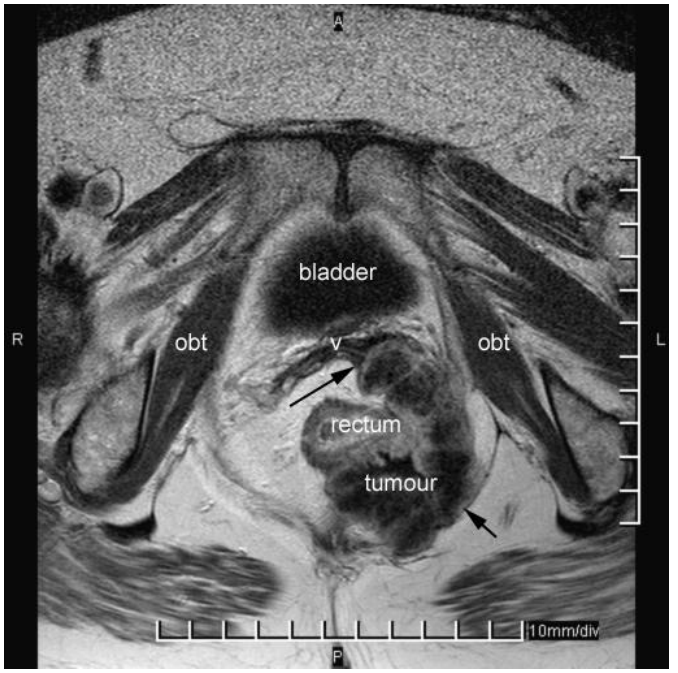
Comparison of Intraoperative Radiation Therapy-Containing Multimodality Treatment with Historical Treatment Modalities for Locally Recurrent Rectal Cancer

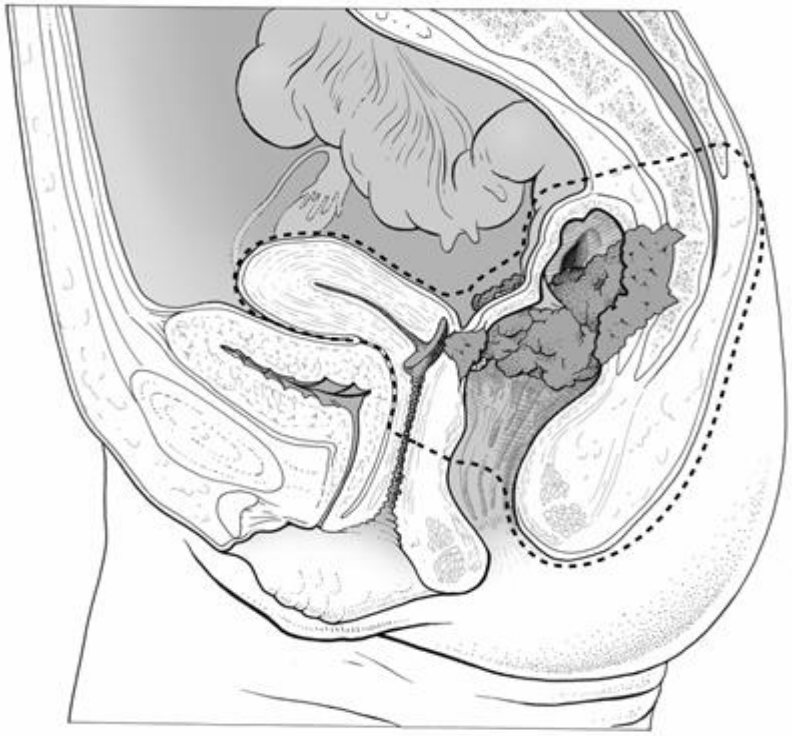
Guido H. H. Mannaerts, M.D., Ph.D.,* Harm J. T. Rutten, M.D., Ph.D., F.R.C.S.,*
Hendrik Martijn, M.D., Ph.D.,† Patrick E. J. Hanssens, M.D.,‡
Theo Wiggers, M.D., Ph.D., F.R.C.S.§

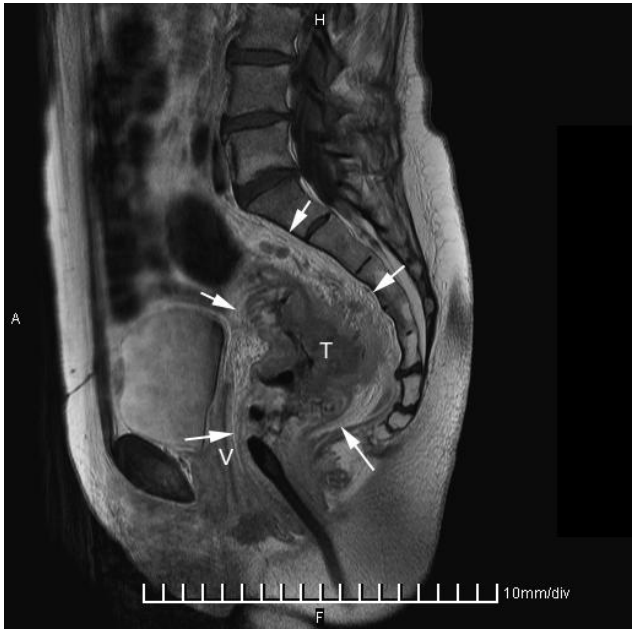
Re Local Recurrence 15% (normally 40%)






A
bladder
R
obt
v
obt
L
rectum
tumour
10mm/div
P




H
A
T
V
10mm/div
F

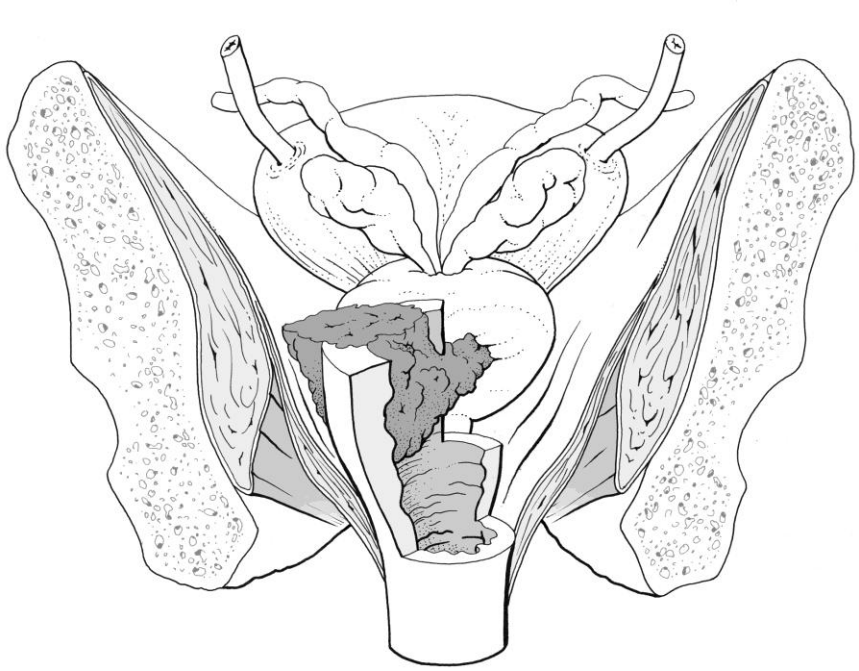
Third step

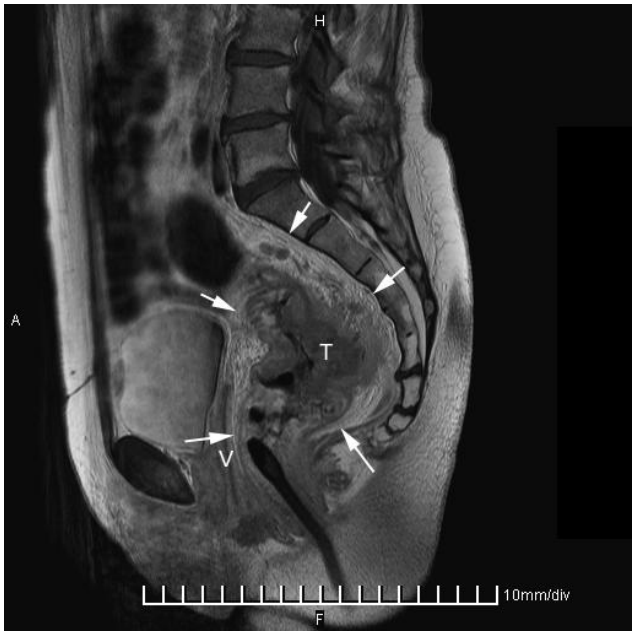
Waiting period 8-12 weeks

R0 resection

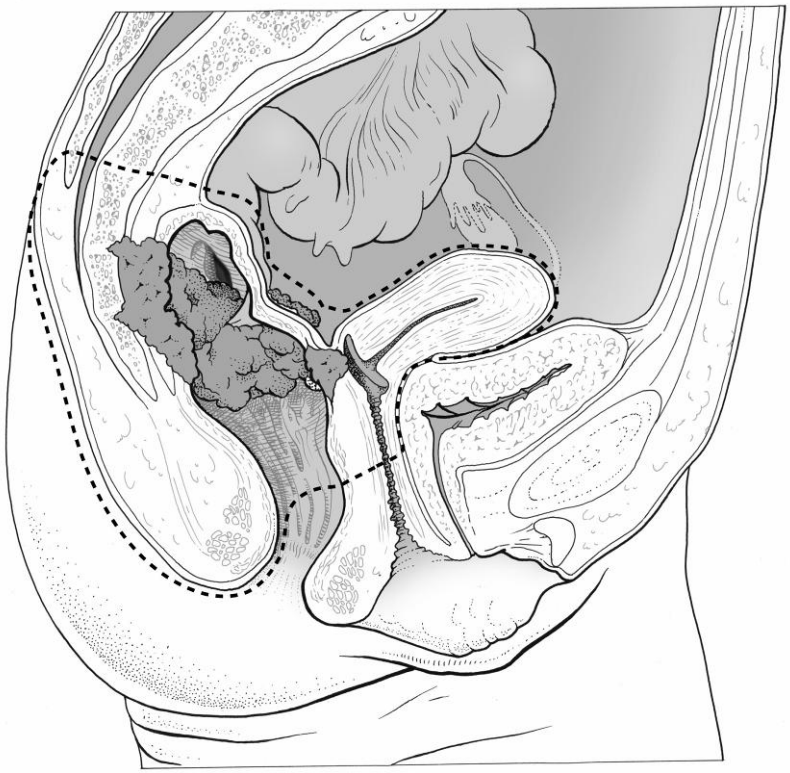
Extended as needed

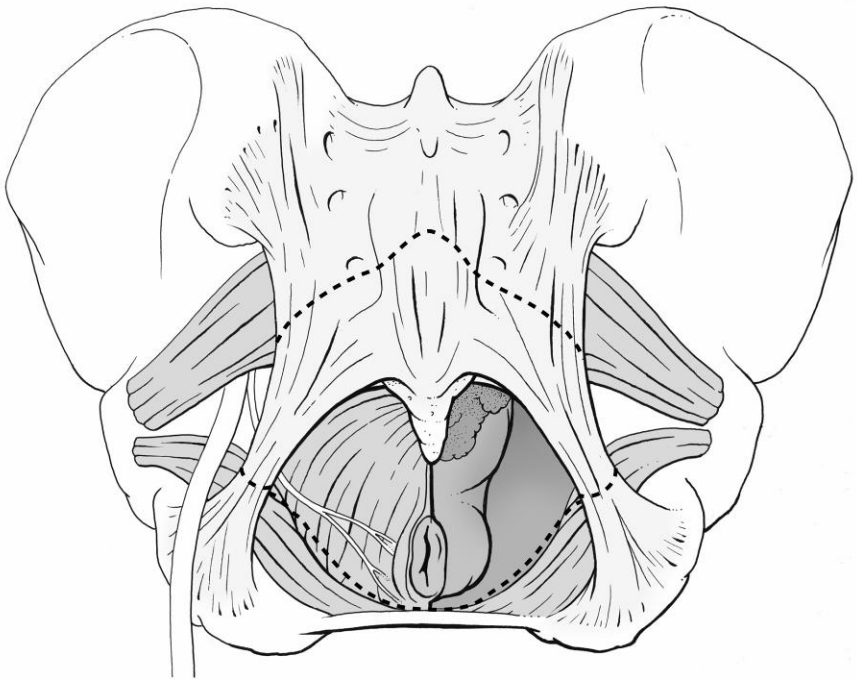
IORT

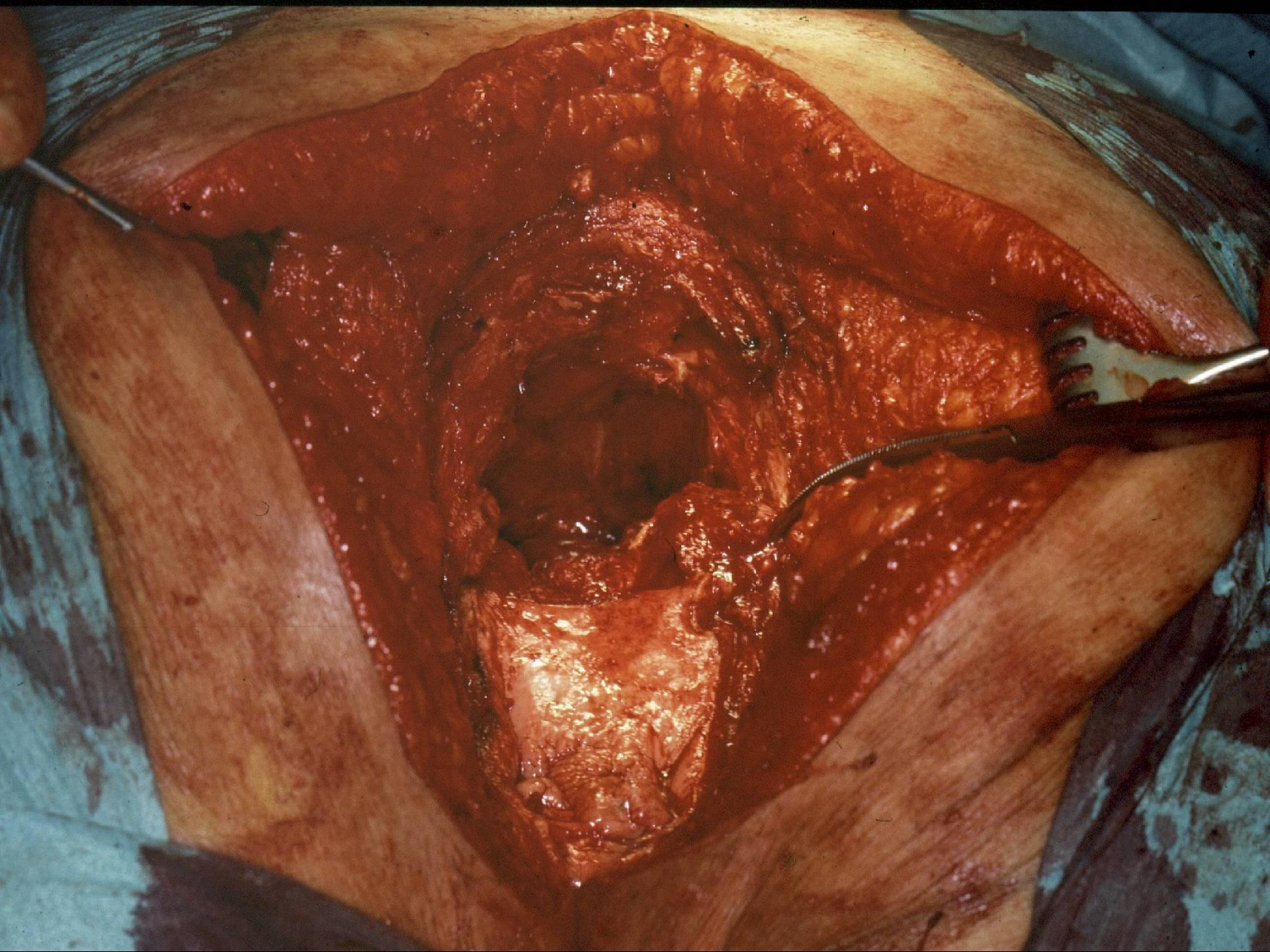


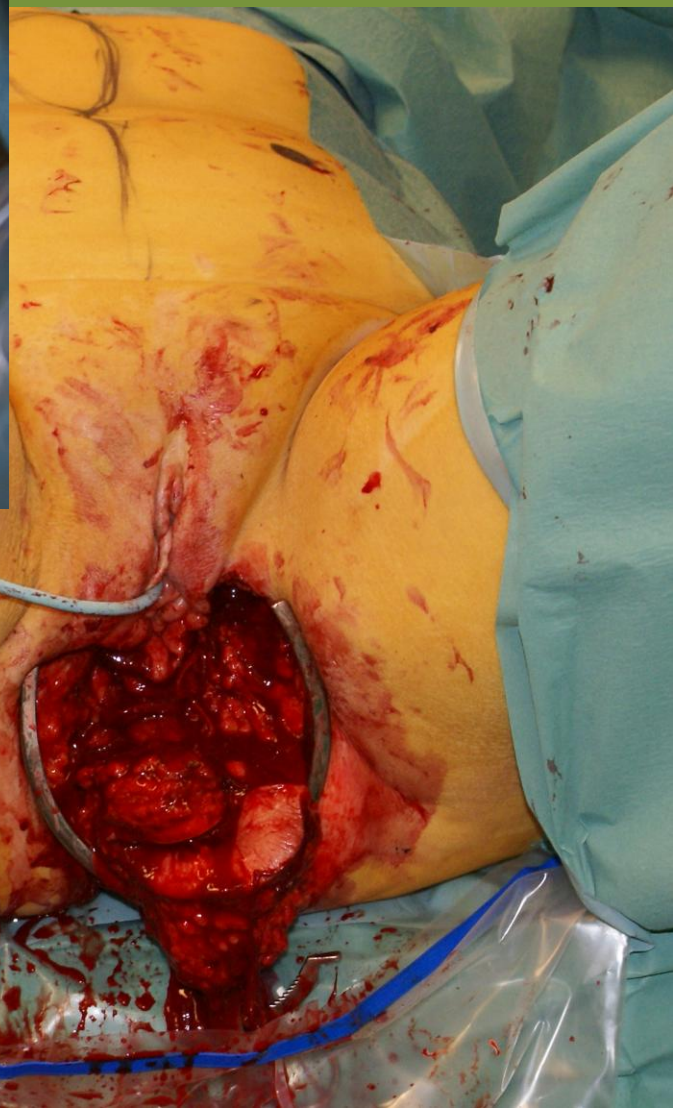


Extended resections

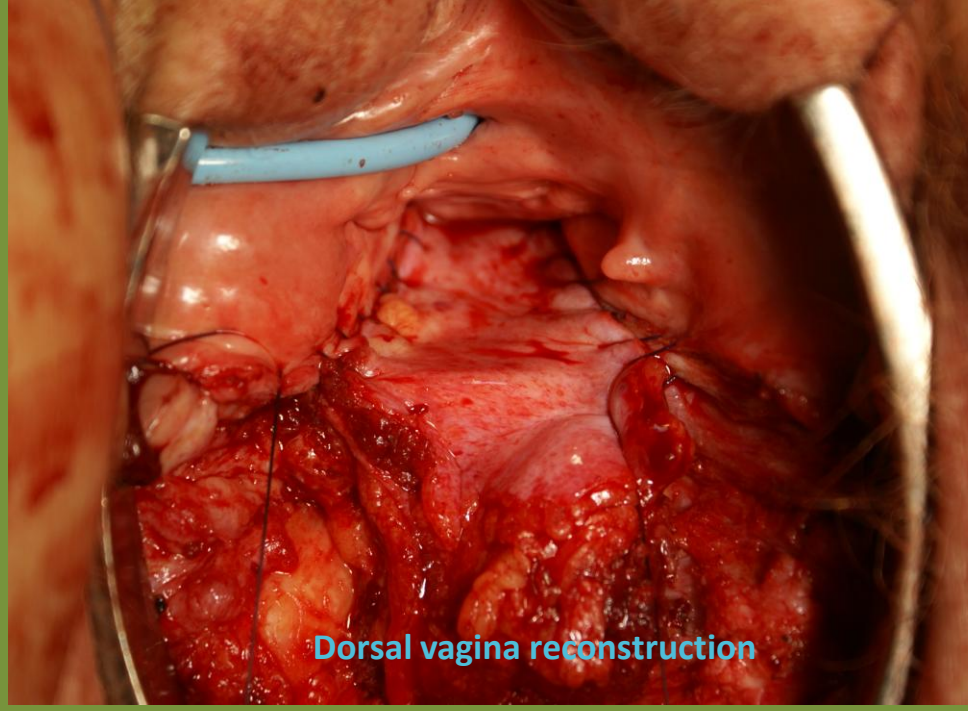








Perineal reconstruction



Dorsal vagina reconstruction

Perineal and vaginal reconstruction

Role of IORT

Table 16.5 Summarized European results with IORT±EBRT for locally recurrent colorectal cancer with regard to local control rates and actuarial 3-year survival

Institution	Reference	Number of patients	LC[a] (%)	Survival[b] (%)
Pamplona	[40]			
IOERT alone		12	0	12
IOERT + EBRT		25	30	38
France	[56]			
IORT alone		30	0	24[c]
IORT + EBRT		16	61	68[c]
Heidelberg				
IOERT + EBRT	[55a]	31	71	58[d]
R0		14	79	71
R1		9	61	33
R2		8	60	25
Eindhoven	[55b]			
IOERT alone[e]		24	38	25
IOERT + EBRT		66	69	49
R0		84[f]	75	59
R1		34[f]	29	27
R2		29[f]	29	24

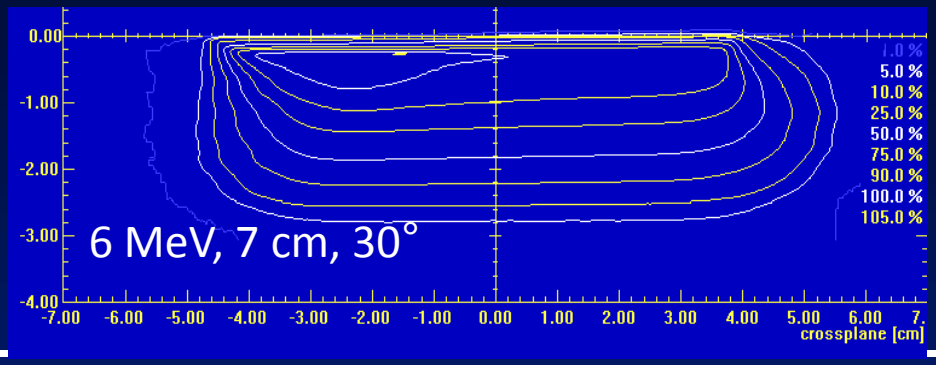
[a]LC: actuarial local control rates
[b]Survival: 3-year actuarial survival rates
[c]No long-term survivors beyond 42 months
[d]4-year actuarial survival and local control
[e]Previously irradiated patients

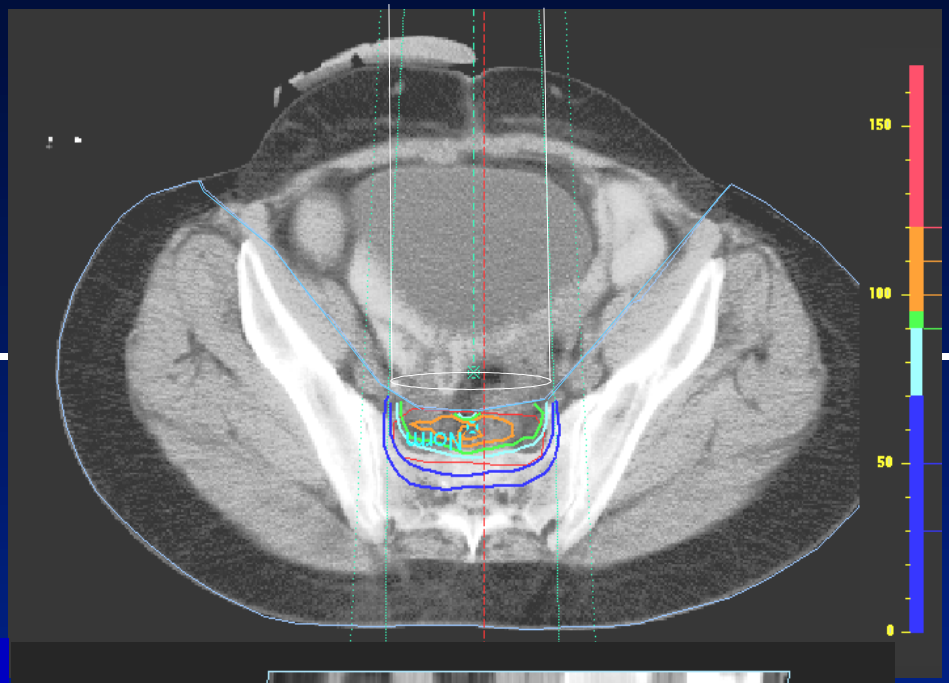
Leonard L. Gunderson, Christopher G. Willett, Felipe A. Calvo, Louis B. Harrison. Intraoperative Irradiation: Techniques and Results (Current Clinical Oncology). ISBN: 1617790141

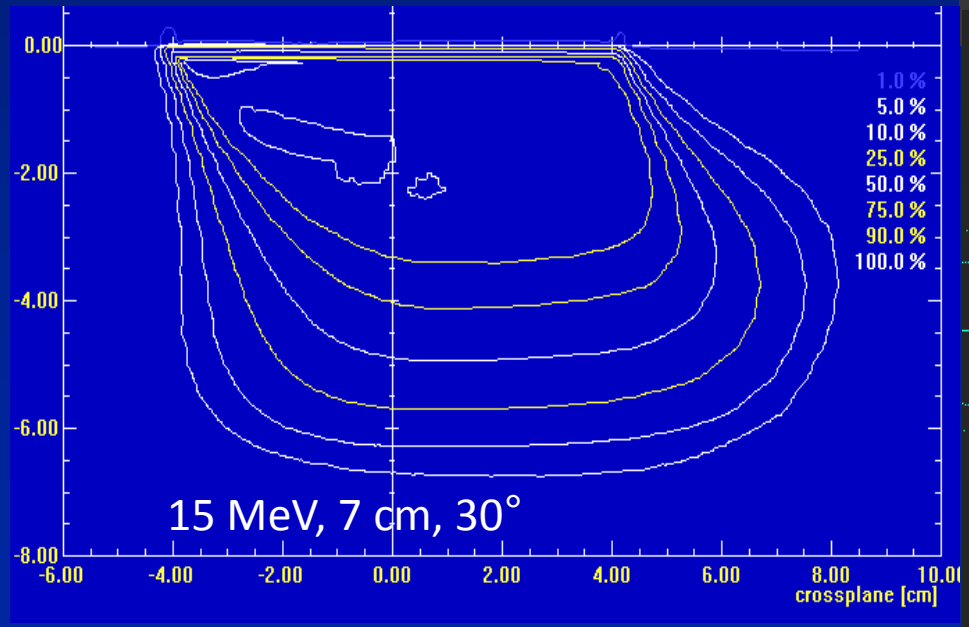
- 106 patients with locally recurrent rectal cancer
- 42 patients IORT
- IORT improves local control and survival

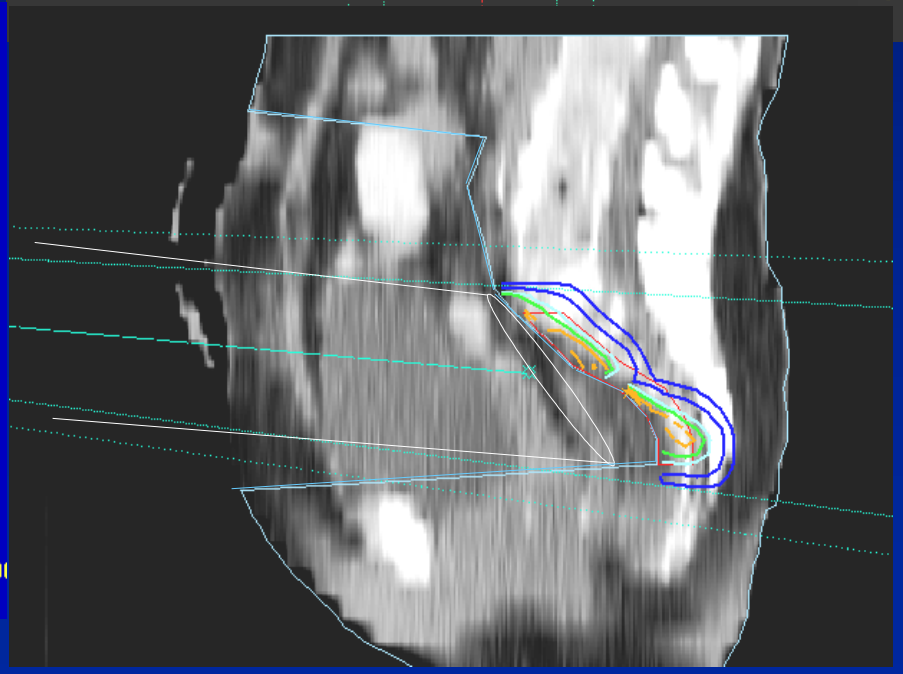
Mayo Suzuki	No patients	5 year Survival	Relapse
No IORT	64	7	93
IORT + EBRT	42	19	40

Suzuki K, Gunderson LL, Devine RM et al. Intraoperative irradiation after palliative surgery for locally recurrent rectal cancer. Cancer 1995; 75: 939-952


0.00
-1.00
-2.00
-3.00
-4.00
5.0 %
10.0 %
25.0 %
50.0 %
75.0 %
90.0 %
100.0 %
105.0 %
6 MeV, 7 cm, 30°
-7.00 -6.00 -5.00 -4.00 -3.00 -2.00 -1.00 0.00 1.00 2.00 3.00 4.00 5.00 6.00
crossplane [cm]


150
100
50
0


0.00
-2.00
-4.00
-6.00
-8.00
1.0 %
5.0 %
10.0 %
25.0 %
50.0 %
75.0 %
90.0 %
100.0 %
15 MeV, 7 cm, 30°
-6.00 -4.00 -2.00 0.00 2.00 4.00 6.00 8.00
crossplane [cm]



- **Pooled analysis**

- Mayo Clinic, Rochester, Mn, USA
- 1981
- Catharina Hospital, Eindhoven, The Netherlands
- 1994

- **Radicality of the resection**

- R0: 237/449 patients (53%)
- The main predictive factor for radicality: preoperative treatment ($p = 0.017$).
    - No preoperative treatment: radicality rate 34%
    - Preoperative treatment: radicality rate 46-62%
- The highest radicality rate (62%): preoperative chemoradiotherapy with a full course of radiotherapy.

	Radical (R0)	Irradical (R1/R2)	P-value
Age			**0.390**
Up to 69 years	165 (51)	156 (49)	
70 years or older	71 (56)	56 (44)	
Gender			**0.456**
Female	101 (55)	83 (45)	
Male	136 (51)	129 (49)	
Preoperative treatment			**0.017**
No therapy	**15 (34)**	**29 (66)**	
Chemo + re-irradiation	**95 (52)**	**89 (48)**	
Chemo + full-course RT	**94 (62)**	**58 (38)**	
Only re-irradiation	**17 (46)**	**20 (54)**	
Only full-course RT	**16 (50)**	**16 (50)**	

- **Local recurrence**

- 42.3% 5-year LR rate.
- Risk factors associated with local re-recurrence:
  - radicality of the resection ($p < 0.001$)
    - 5 year local recurrence:
      - R0: 25.9%
      - R1/2: 61.3%
  - preoperative treatment.
-

- **Distant metastases**

- 5-Year distant metastases rate: 55.0%.
- Risk factors (P<0.001)
    - Irradical resection
        - R0: 45.9%
        - R1/2: 65.6%

-

- **Overall Survival**

- Overall 5 year survival: 34%.
- Overall 10 year survival: 18%.

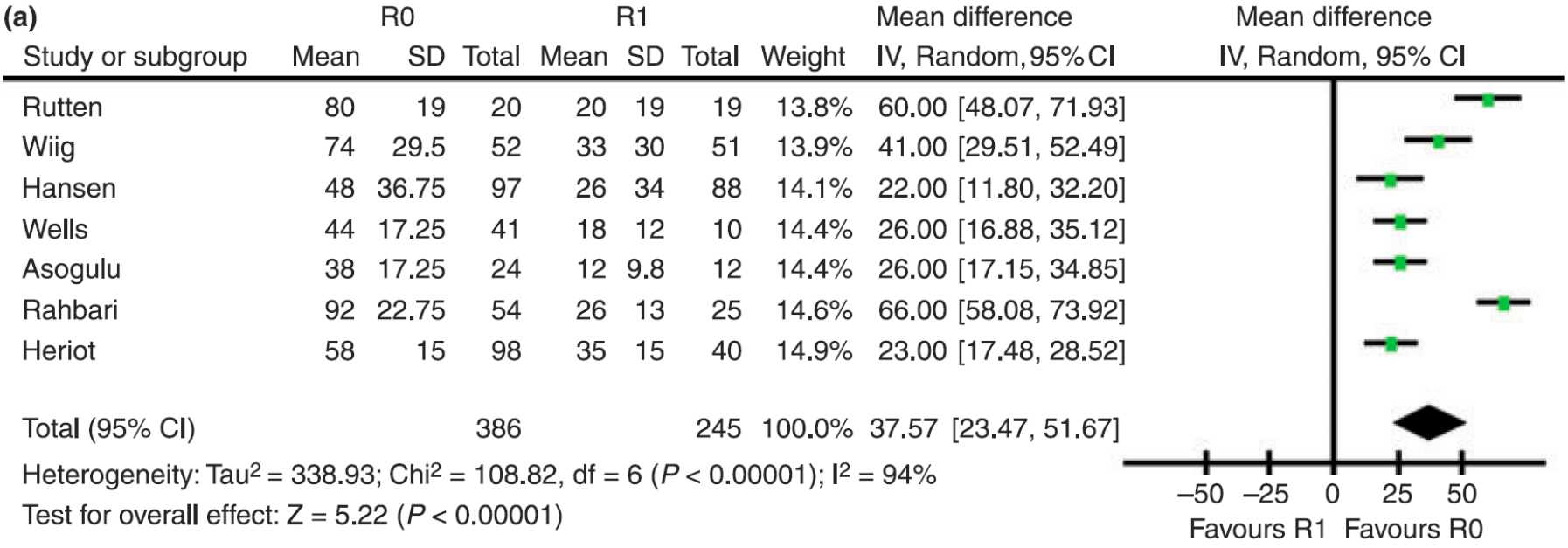
- **R0 resection**
- Overall 5 year survival: 47%.
- Overall 10 year survival: 25%.

- Irradical surgery resulted in 5 year overall survival of 21%.

Time Effect

- Radical Resection

- 1994-2000: 52%
- 2000-2004: 56%
- 2004-2007: 58%
- 2007-2010: 61%



Systematic review

doi:10.1111/j.1463-1318.2012.03005.x

Meta-analysis of survival based on resection margin status following surgery for recurrent rectal cancer

A. Bhangu*†, S. M. Ali*†, A. Darzi‡, G. Brown§ and P. Tekkis*†

*Department of Colorectal Surgery, the Royal Marsden Hospital, Fulham Road, London, UK, †Division of Surgery, Imperial College, Chelsea and Westminster Campus, London, UK, ‡Academic Surgical Unit, Department of Biosurgery and Surgical Technology, Imperial College, St Mary's Hospital, London, UK and §Department of Radiology, The Royal Marsden Hospital, Fulham Road, London, UK

Received 12 October 2011; accepted 1 December 2011; Accepted Article online 22 February 2012

IORT


MOBETRON
MOBETRON


XENION

Original article

Feasibility of reirradiation in the treatment of locally recurrent rectal cancer

S. J. Bosman[1], F. A. Holman[1], G. A. P. Nieuwenhuijzen[1], H. Martijn[2], G.-J. Creemers[3] and H. J. T. Rutten[1,4]

BJS 2014; 101: 1280–1289

Reirradiation

- 59 patients
- Median dose of 50,4 Gy
- Reirradiation 30 Gy, 51 completed radiation therapy
- R0: 21, R1: 3, R2: 35
- 5 year survival: 39,3% (R0: 66,8%, R1/2: 22,3%)
- Grade 3 toxicity or lower: 5.1%
- Neoadjuvant chemoradiation can be applied with a low grade of acute toxicity and acceptable incidence of late complications

Valentini V, Morganti AG, Gambacorta MA et al. Preoperative hyperfractionated chemoradiation for locally recurrent rectal cancer in patients previously irradiated to the pelvis: A multicentric phase II study. Int J Radiat Oncol Biol Phys 2006; 64: 1129-1139

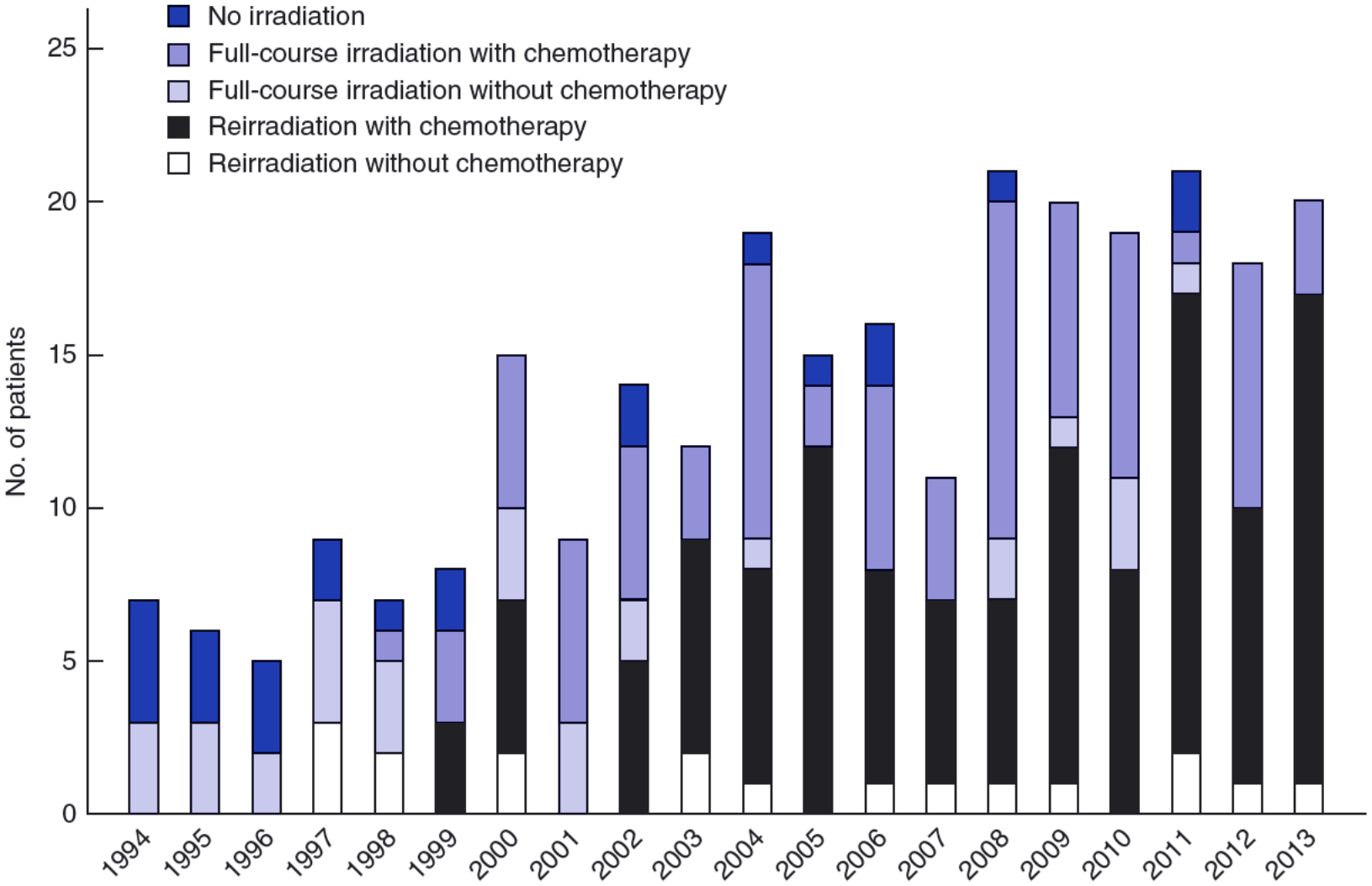
Reirradiation

- 103 patients
- Previous median dose of 50,4 Gy
- Median Reirradiation dose: 34,8 Gy
- Grade 3 toxicity or higher: 15 patients (15%)
- Late complications: 22 patients
- In patients with recurrent rectal carcinoma, high doses of reirradiation can be delivered with acceptable risks without prohibitive long-term side effects.

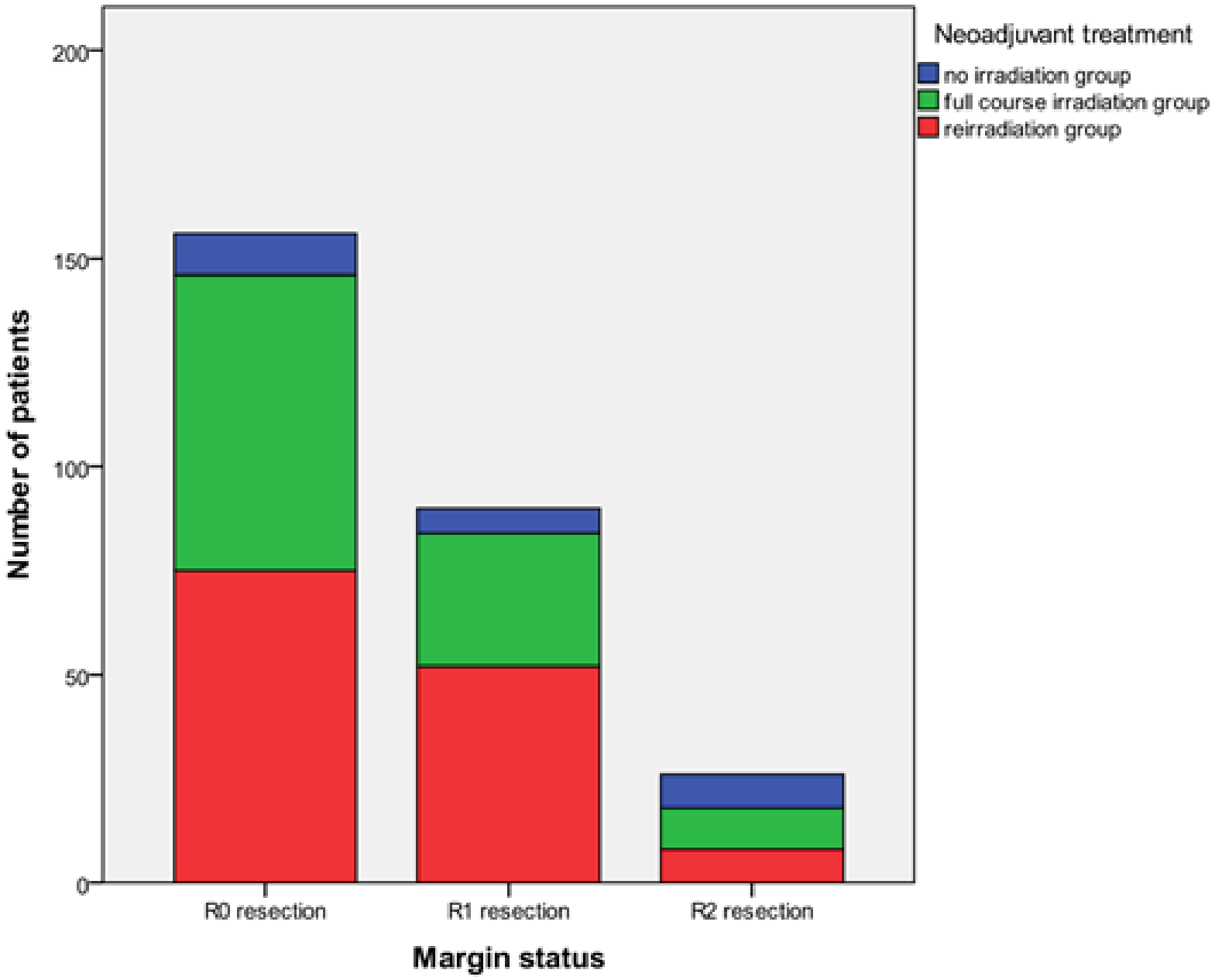
Mohiuddin M, Marks G, Marks J. Long-term results of reirradiation for patients with recurrent rectal carcinoma. Cancer 2002; 95: 1144-1150

	No irradiation ($n = 24$)	Full-course irradiation ($n = 113$)	Reirradiation ($n = 135$)	P†
Surgical procedure for recurrence				< 0·001
LAR	3 (13)	34 (30·1)	3 (2·2)	
APE	2 (8)	28 (24·8)	25 (18·5)	
ASR	11 (46)	21 (18·6)	41 (30·4)	
Exenteration	2 (8)	13 (11·5)	27 (20·0)	
Debulking	2 (8)	7 (6·2)	30 (22·2)	
Hartmann's procedure	4 (17)	10 (8·8)	5 (3·7)	
Other	0 (0)	0 (0)	4 (3·0)	
Multivisceral resection				0·252
None	10 (42)	50 (44·2)	46 (34·1)	
Uterus/adnexa				0·833
None	5 (56)	22 (52)	35 (60)	
Without adnexa	0 (0)	3 (7)	4 (7)	
With adnexa	4 (44)	17 (40)	19 (33)	
Vagina				0·011
None	4 (44)	24 (57)	25 (43)	
Partial	5 (56)	18 (43)	33 (57)	
Prostate/seminal vesicles				
None	11 (73)	46 (65)	45 (58)	0·484
Partial/complete prostate resection	3 (20)	11 (15)	19 (25)	0·320
Resection of seminal vesicles	3 (20)	21 (30)	28 (36)	0·773
Exenteration				0·001
None	15 (63)	87 (77·0)	90 (66·7)	
Partial bladder/urether resection	5 (21)	15 (13·3)	22 (16·3)	
Cystectomy	4 (17)	11 (9·7)	23 (17·0)	
Sacrum				< 0·001
None	13 (54)	90 (79·6)	72 (53·3)	
S2 partial	0 (0)	2 (1·8)	10 (7·4)	
S3	6 (25)	13 (11·5)	25 (18·5)	
S4	4 (17)	8 (7·1)	14 (10·4)	
More distal	1 (4)	0 (0)	14 (10·4)	
VRAM flap				0·006
No	23 (96)	111 (98·2)	115 (85·2)	
Yes, without skin island	0 (0)	1 (0·9)	8 (5·9)	
Yes, with skin island	1 (4)	1 (0·9)	12 (8·9)	
Blood loss (ml)*	4000 (400–34 000)	5500 (450–30 200)	4300 (50–33 028)	0·378‡

	No irradiation ($n = 24$)	Full-course irradiation ($n = 113$)	Reirradiation ($n = 135$)	P‡
Age (years)*	63 (39–80)	65 (41–87)	63 (30–84)	0·036§
Sex ratio (M : F)	15 : 9	71 : 42	77 : 58	0·627
Interval from primary surgery to local recurrence (months)*	29 (10–100)	28 (3–207)	34 (7–198)	0·476¶
Neoadjuvant treatment for recurrent rectal cancer				< 0·001
No concomitant chemotherapy	24 (100)	31 (27·4)	18 (13·3)	
Concomitant chemotherapy	0 (0)	82 (72·6)	117 (86·7)	
Initial surgery				< 0·001
Sigmoid resection	5 (21)	29 (25·7)	4 (3·0)	
LAR	11 (46)	58 (51·3)	67 (49·6)	
APE	7 (29)	12 (10·6)	53 (39·3)	
ASR	0 (0)	2 (1·8)	0 (0)	
Exenteration	0 (0)	1 (0·9)	1 (0·7)	
TEM	0 (0)	4 (3·5)	7 (5·2)	
Hartmann's procedure	1 (4)	7 (6·2)	3 (2·2)	
Stage of primary rectal cancer				0·465
I	2 (8)	22 (20·1)	20 (15·2)	
II	9 (38)	44 (40·4)	49 (37·1)	
III	13 (54)	43 (39·4)	63 (47·7)	
Unknown	0	4	3	
ASA grade†				0·212
I	11 (55)	27 (28)	36 (29·0)	
II	9 (45)	59 (62)	76 (61·3)	
III	0 (0)	8 (8)	12 (9·7)	
IV	0 (0)	1 (1)	0 (0)	
Unknown	4	18	11	


No irradiation
Full-course irradiation with chemotherapy
Full-course irradiation without chemotherapy
Reirradiation with chemotherapy
Reirradiation without chemotherapy
No. of patients
0
5
10
15
20
25
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013

	No irradiation	Full-course irradiation	Reirradiation	*P**
Total complications	*n* = 23	*n* = 111	*n* = 131	0·887
None	5 (22)	25 (22·5)	29 (22·1)	
Grade I	4 (17)	19 (17·1)	29 (22·1)	
Grade II	6 (26)	16 (14·4)	21 (16·0)	
Grade III	7 (31)	42 (37·8)	39 (29·8)	
Grade IV	0 (0)	5 (4·5)	7 (5·3)	
Grade V	1 (4)	4 (3·6)	6 (4·6)	
Wound problems	*n* = 23	*n* = 111	*n* = 131	
Abdominal wound infection	2 (9)	9 (8·1)	14 (10·7)	0·794
Perineal wound infection	8 (35)	25 (22·5)	31 (23·7)	0·512
Abdominal wound dehiscence	0 (0)	3 (2·7)	5 (3·8)	0·572
Perineal wound dehiscence	2 (9)	3 (2·7)	8 (6·1)	0·323
Abscess	*n* = 23	*n* = 111	*n* = 131	0·936
Presacral	2 (9)	13 (11·7)	18 (13·7)	
Intra-abdominal	3 (13)	13 (11·7)	16 (12·2)	
Abscess treatment	*n* = 23	*n* = 111	*n* = 131	0·537
Conservative management	0 (0)	4 (3·6)	8 (6·1)	
Drainage	3 (13)	15 (13·5)	16 (12·2)	
Surgical intervention	2 (9)	7 (6·3)	10 (7·6)	
Death	1 (4)	0 (0)	1 (0·8)	
Surgical	*n* = 23	*n* = 111	*n* = 131	
Urethra damage	0 (0)	4 (3·6)	1 (0·8)	0·192
Ureter damage	1 (4)	13 (11·7)	12 (9·2)	0·530
Enterocutaneous fistula	*n* = 23	*n* = 111	*n* = 131	0·586
Conservative management	4 (17)	18 (16·2)	7 (5·3)	
Surgical intervention	1 (4)	4 (3·6)	6 (4·6)	
Medical	*n* = 22	*n* = 107	*n* = 128	
Urinary tract infection	3 (14)	17 (15·9)	30 (23·4)	0·269
Pneumonia	1 (5)	16 (15·0)	17 (13·3)	0·429
Bowel ischaemia	0 (0)	0 (0)	0 (0)	–
Shock/multiple organ failure	1 (5)	6 (5·6)	4 (3·1)	0·652
ARDS	0 (0)	2 (1·9)	1 (0·8)	0·806
Acalculous cholecystitis/ileus	3 (14)	10 (9·3)	18 (14·1)	0·513
Myocardial infarction/stroke	0 (0)	4 (3·7)	1 (0·8)	0·203
Thrombosis				0·494
Deep venous thrombosis	1 (5)	3 (2·8)	1 (0·8)	
Pulmonary embolism	0 (0)	1 (0·9)	0 (0)	
Incisional hernia	*n* = 21	*n* = 104	*n* = 125	0·862
Conservative management	0 (0)	2 (1·9)	2 (1·6)	
Surgical intervention	0 (0)	4 (3·8)	5 (4·0)	


Neoadjuvant treatment
no irradiation group
full course irradiation group
reirradiation group
Number of patients
200
150
100
50
0
R0 resection
R1 resection
R2 resection
Margin status

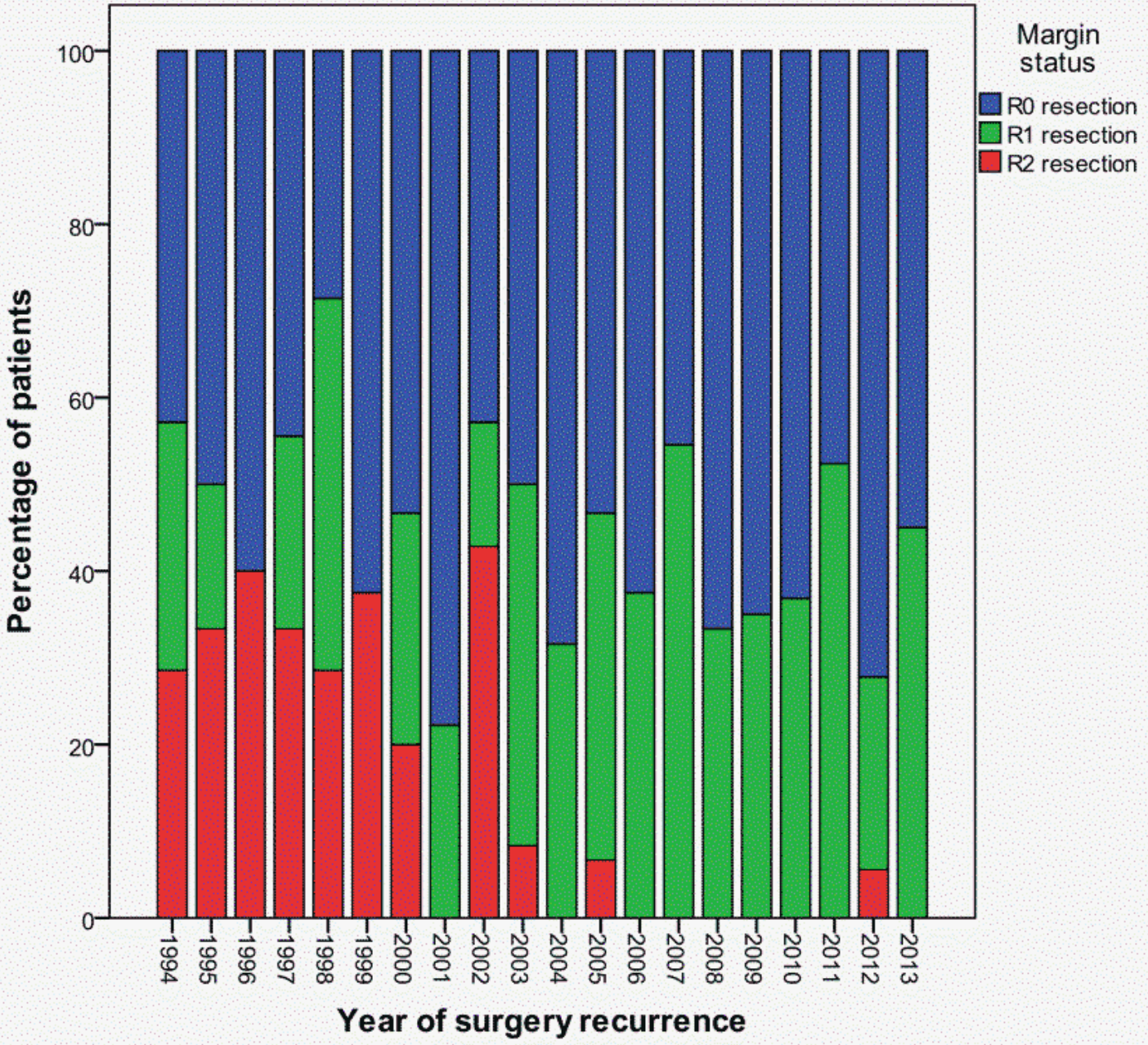
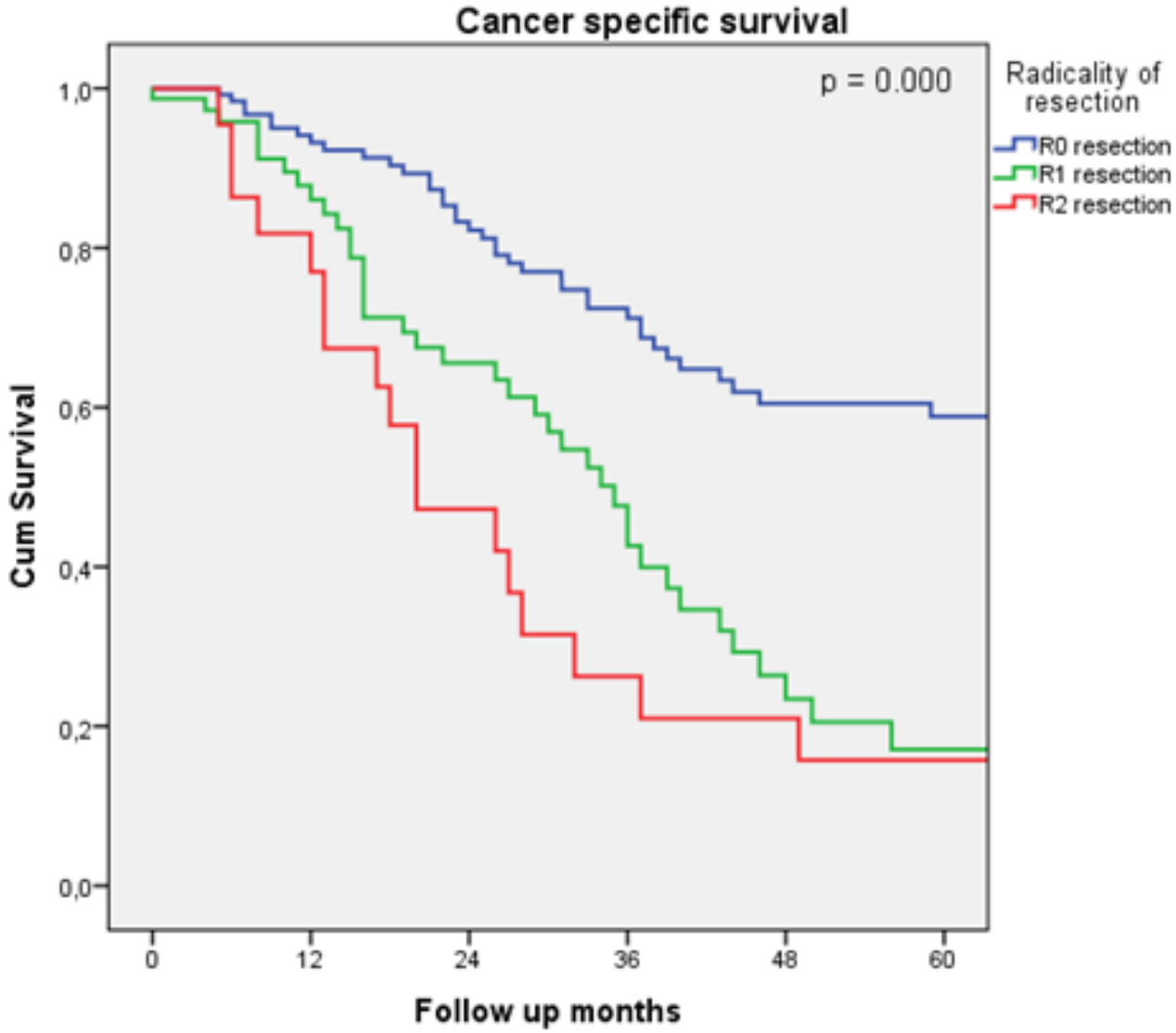

Margin status
R0 resection
R1 resection
R2 resection
Percentage of patients
100
80
60
40
20
0
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Year of surgery recurrence

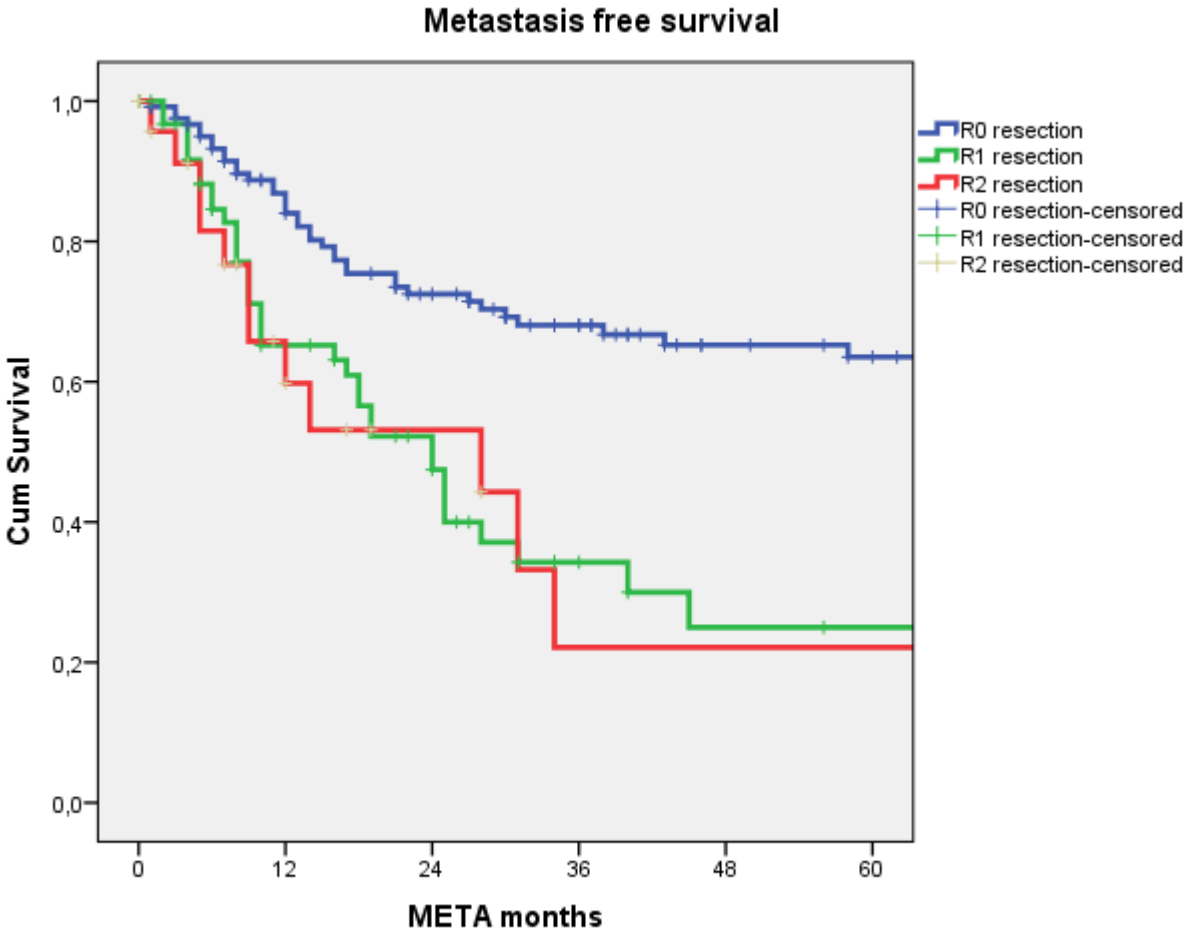
Table Univariate analysis of predictive values for survival after rectal resection for locally recurrent rectal cancer

	Cancer specific survival			Relapse free survival			Distant Metastasis			Local Recurrence			Overall survival		
	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	**p-value**
Median time to local recurrence			0.016			0.069			0.144			0.328			**0.030**
< 3 year	1.00	1.10-2.53		1.00			1.00	0.90-2.11		1.00	0.80-1.94		1.00		
> 3 year	1.67			1.40	0.97-2.00		1.38			1.25			1.47	1.04-2.09	
Neoadjuvant treatment															
No irradiation	1.92	1.01-3.65	0.046	1.99	1.12-3.53	0.018	3.22	1.71-6.07	0.000	1.68	0.85-3.32	0.137	1.62	0.92-2.85	0.094
Reirradiation with CT	1.00			1.00			1.00			1.00			1.00		
Full course RCT	0.86	0.52-1.42	0.554	0.86	0.56-1.33	0.496	1.16	0.69-1.96	0.576	0.62	0.36-1.08	0.091	0.81	0.53-1.26	0.351
Reirradiation without CT	1.52	0.75-3.08	0.246	1.88	0.99-3.55	0.053	1.94	0.88-4.28	0.100	1.76	0.84-3.68	0.134	1.82	1.03-3.22	0.039
Full course irradiation	1.14	0.63-2.06	0.673	1.04	0.60-1.80	0.882	1.18	0.60-2.33	0.636	0.73	0.36-1.49	0.387	1.19	0.73-1.96	0.485
Initial surgery															
APR	1.49	0.97-2.29	0.070	1.46	0.99-2.14	0.056	1.81	1.16-2.82	0.009	1.44	0.89-2.32	0.134	1.33	0.91-1.95	**0.142**
LAR	1.00			1.00			1.00			1.00			1.00		
Other	0.72	0.40-1.30	0.273	0.70	0.42-1.17	0.172	0.64	0.33-1.23	0.181	0.69	0.37-1.31	0.261	0.88	0.56-1.40	**0.601**
Stage of primary rectal cancer								.							
Stage 1	0.51	0.28-0.95	0.034	0.57	0.34-0.97	0.038	0.39	0.20-0.77	0.007	0.79	0.43-1.45	0.443	0.47	0.27-0.82	0.007
Stage 2	0.75	0.49-1.14	0.174	0.68	0.46-0.99	0.043	0.61	0.39-0.95	0.028	0.73	0.45-1.17	0.189	0.80	0.56-1.14	0.220
Stage 3	1.00			1.00			1.00			1.00			1.00		
N stage			0.018			0.007			0.002						0.013
N0	1.00			1.00			1.00			1.00			1.00		
N1/2	0.62	0.42-0.92		1.63	1.14-2.31		0.51	0.33-0.77		0.72	0.47-1.12	0.724	0.65	0.47-0.91	
Multivisceral resection			0.979			0.974			0.891			0.256			**0.661**
No	1.01	0.68-1.49		0.99	0.70-1.41		1.03	0.68-1.56		1.30	0.83-2.03		1.08	0.77-1.51	
Yes	1.00			1.00			1.00			1.00			1.00		
Margins															
Negative (R0)	1.00			1.00			1.00			1.00			1.00		
Positive (R1)	2.51	1.62-3.89	0.000	2.94	2.00-4.30	0.000	2.61	1.65-4.11	0.000	3.17	1.96-5.11	0.000	2.10	1.44-3.04	0.000
Positive (R2)	3.82	2.22-6.85	0.000	3.15	1.86-5.33	0.000	2.96	1.61-5.47	0.001	4.15	2.21-7.81	0.000	2.79	1.73-4.49	0.000

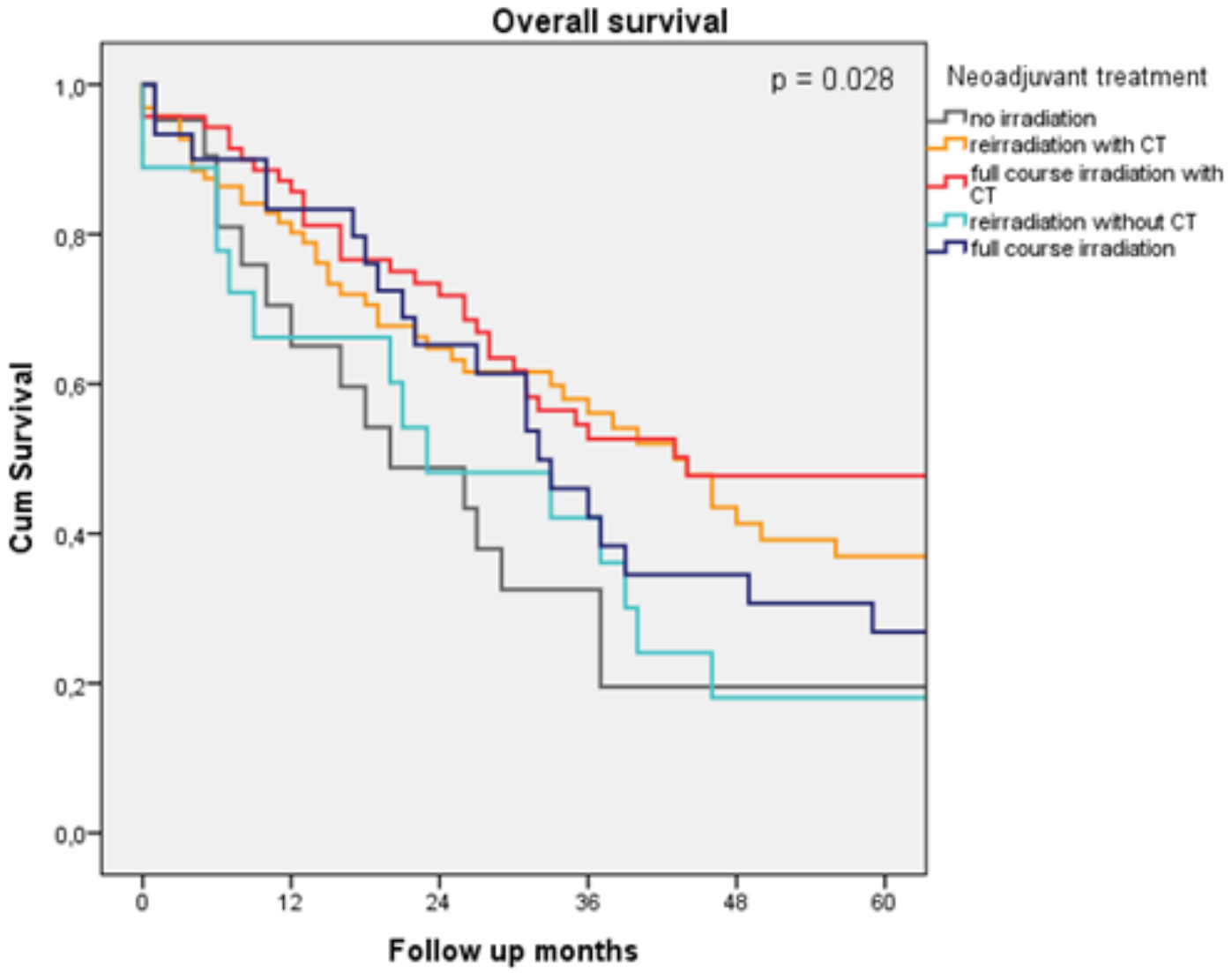
Table : Univariate analysis of predictive values for survival after rectal resection for locally recurrent rectal cancer in reirradiated patients.

	Cancer specific survival			Relapse free survival			Distant Metastasis			Local Recurrence			Overall survival		
	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value
Gender			0.796			0.990			0.274			0.962			0.423
Male	1.00			1.00			1.00			1.00			1.00		
Female	0.92	0.51-1.68		1.00	0.59-1.70		1.45	0.75-2.81		1.02	0.55-1.87		1.23	0.75-2.02	
Median time to local recurrence			0.287			0.289			0.737			0.532			0.287
< 3 year	1.00			1.00			1.00			1.00			1.00		
> 3 year	1.39	0.76-2.53		1.33	0.79-2.25		0.89	0.46-1.74		0.82	0.45-1.52		0.76	0.46-1.26	
Initial surgery			0.481			0.292			**0.005**			0.671			0.061
APR	1.46	0.79-2.72	0.229	1.46	0.84-2.52	0.176	**2.96**	**1.42-6.14**	**0.004**	1.17	0.62-2.19	0.634	1.54	0.90-2.63	0.117
LAR	1.00			1.00			**1.00**			1.00			1.00		
Other	1.20	0.36- 4.08	0.765	0.77	0.23-2.55	0.667	**0.65**	**0.08-5.05**	**0.683**	0.63	0.15-2.67	0.526	2.42	1.09-5.40	0.031
Stage of primary rectal cancer															
Stage 1	0.55	0.19-1.60	0.355	0.76	0.32-1.84	0.525	0.34	0.08-1.44	0.215	1.13	0.46-2.81	0.567	0.56	0.22-1.43	0.415
Stage 2	0.69	0.36-1.30	0.275	0.73	0.42-1.29	0.545	0.67	0.33-1.35	0.143	0.74	0.38-1.44	0.792	0.82	0.48-1.38	0.222
Stage 3	1.00		0.250	1.00		0.280	1.00		0.259	1.00		0.368	1.00		0.447
N stage			0.135			0.342			0.167			0.591			0.245
N0	1.00			1.00			1.00			1.00			1.00		
N1/2	0.64	0.35-1.15		0.77	0.45-1.32		1.63	0.82-3.23		0.84	0.45-1.57		1.35	0.82-2.22	
Multivisceral resection			0.423			0.379			0.125			0.482			0.347
No	1.29	0.69-2.39		1.28	0.74-2.24		1.78	0.85-3.73		1.26	0.66-2.41		1.29	0.76-2.17	
Yes	1.00			1.00			1.00			1.00			1.00		
IOERT			0.804			0.698			0.388			0.883			0.141
No	0.84	0.20-3.47		1.32	0.32-5.43		21.8	0.02-23691		0.90	0.22-3.73		0.65	0.24-1.81	
Yes	1.00			1.00			1.00			1.00			1.00		
Margins			**0.000**			**0.000**			**0.000**			**0.011**			**0.002**
Negative (R0)	**1.00**			**1.00**			**1.00**			**1.00**			**1.00**		
Positive (R1)	**2.78**	**1.46-5.27**	**0.002**	**3.24**	**1.84-5.71**	**0.000**	**4.31**	**2.06-9.05**	**0.000**	**2.00**	**1.05-3.80**	**0.035**	**2.10**	**1.24-3.56**	**0.006**
Positive (R2)	**5.59**	**2.03-15.3**	**0.001**	**5.38**	**2.02-14.4**	**0.001**	**7.37**	**2.02-26.9**	**0.002**	**4.65**	**1.36-15.9**	**0.015**	**3.47**	**1.42-8.47**	**0.006**


Cancer specific survival
p = 0.000
Radicality of resection
R0 resection
R1 resection
R2 resection
Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
12
24
36
48
60
Follow up months

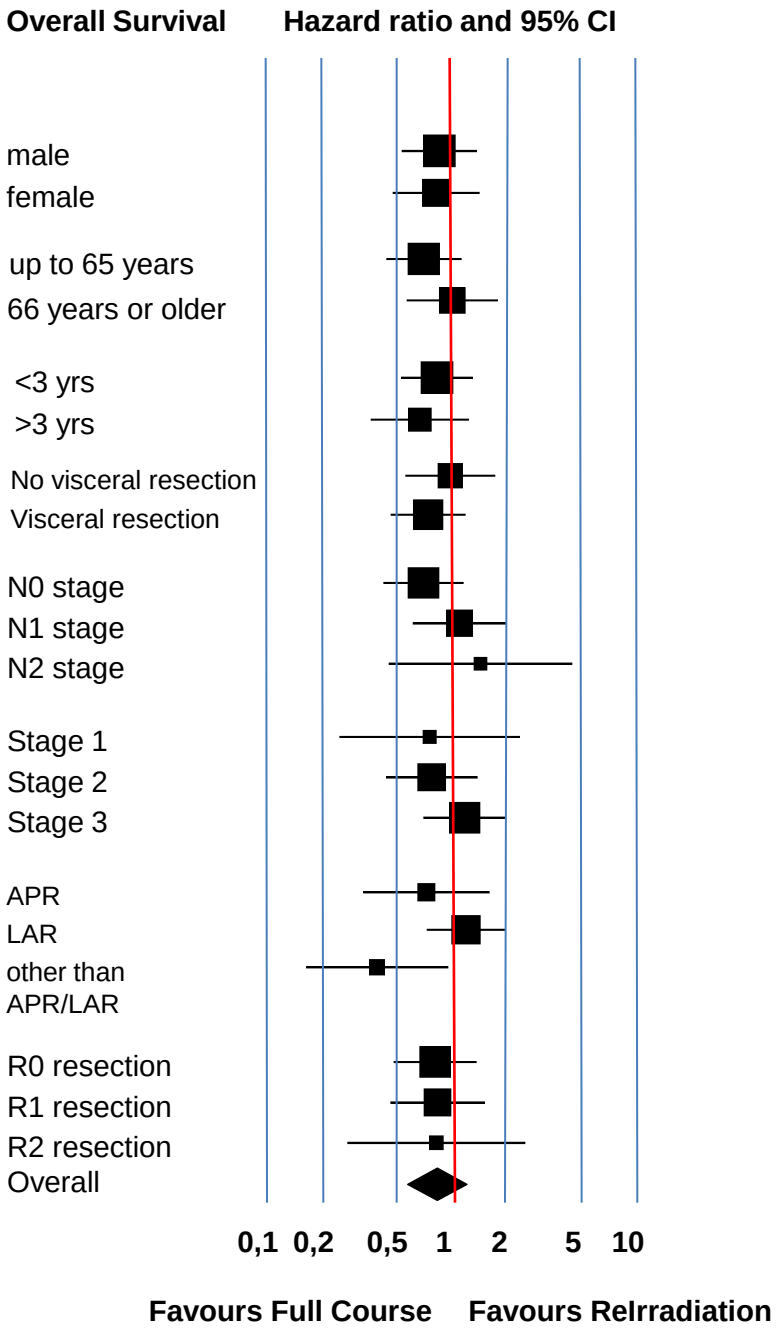

Metastasis free survival
Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
12
24
36
48
60
META months
R0 resection
R1 resection
R2 resection
R0 resection-censored
R1 resection-censored
R2 resection-censored

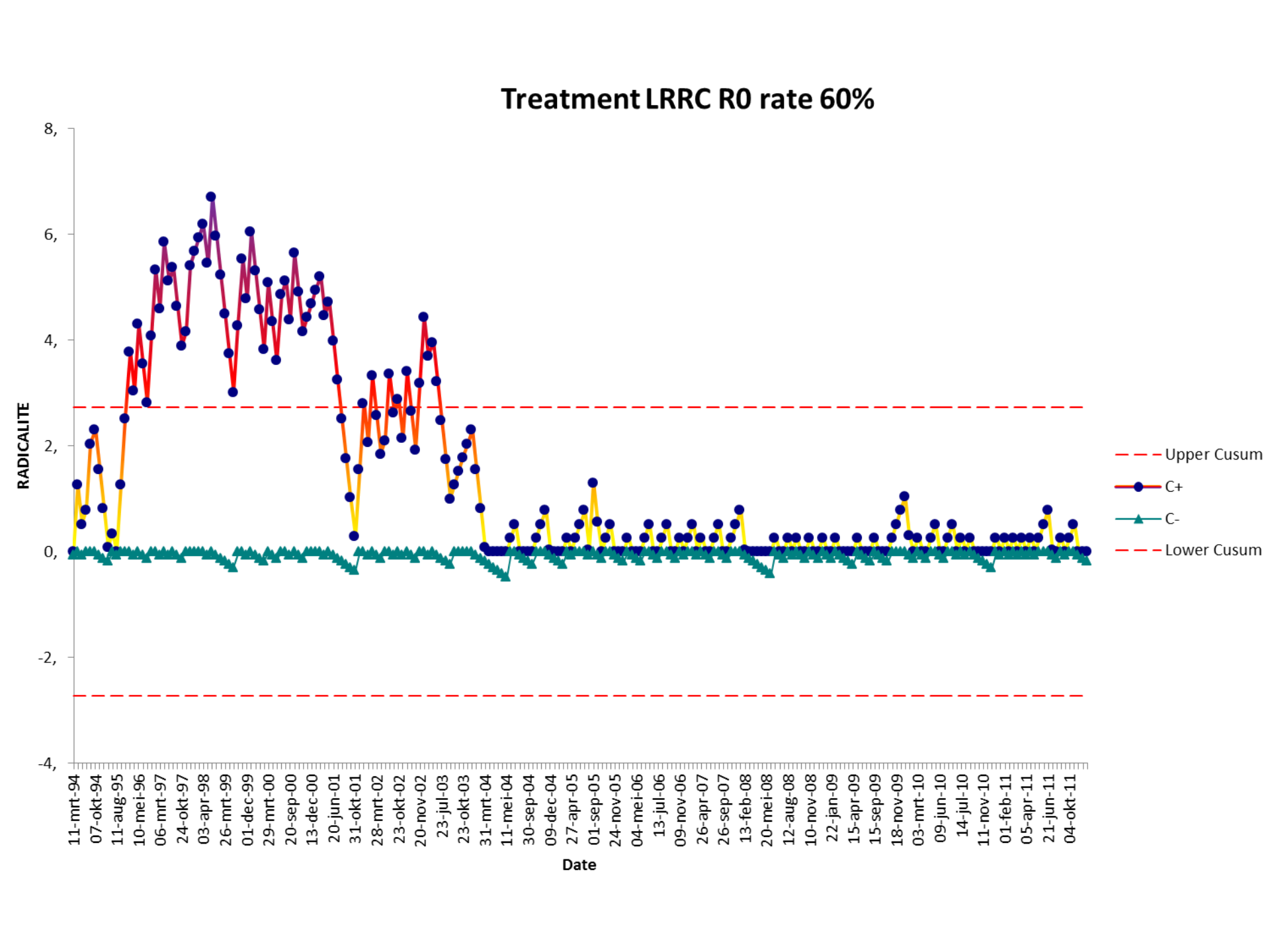
p=0.000


Overall survival
p = 0.028
Neoadjuvant treatment
no irradiation
reirradiation with CT
full course irradiation with CT
reirradiation without CT
full course irradiation
Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
12
24
36
48
60
Follow up months

5 yr overall survival

- No treatment: 19.1%
- reirradiatie with CT 39.7%
- full course irradiatie with CT 44.5%
- reirradiatie without CT 20.5%
- full course irradiation 27.2%


Overall Survival
Hazard ratio and 95% CI
male
female
up to 65 years
66 years or older
<3 yrs
>3 yrs
No visceral resection
Visceral resection
N0 stage
N1 stage
N2 stage
Stage 1
Stage 2
Stage 3
APR
LAR
other than APR/LAR
R0 resection
R1 resection
R2 resection
Overall
0,1
0,2
0,5
1
2
5
10
Favours Full Course
Favours ReIrradiation


Treatment LRRC R0 rate 60%
RADICALITE
8,
6,
4,
2,
0,
-2,
-4,
Date
11-mrt-94
07-okt-94
11-aug-95
10-mei-96
06-mrt-97
24-okt-97
03-apr-98
26-mrt-99
01-dec-99
29-mrt-00
20-sep-00
13-dec-00
20-jun-01
31-okt-01
28-mrt-02
23-okt-02
20-nov-02
23-jul-03
23-okt-03
31-mrt-04
11-mei-04
30-sep-04
09-dec-04
27-apr-05
01-sep-05
24-nov-05
04-mei-06
13-jul-06
09-nov-06
26-apr-07
26-sep-07
13-feb-08
20-mei-08
12-aug-08
10-nov-08
22-jan-09
15-apr-09
15-sep-09
18-nov-09
03-mrt-10
09-jun-10
14-jul-10
11-nov-10
01-feb-11
05-apr-11
21-jun-11
04-okt-11
Upper Cusum
C+
C-
Lower Cusum


Thank You
CATHARINA-HOSPITAL