IORT for primary Locally Advanced Rectal Cancer

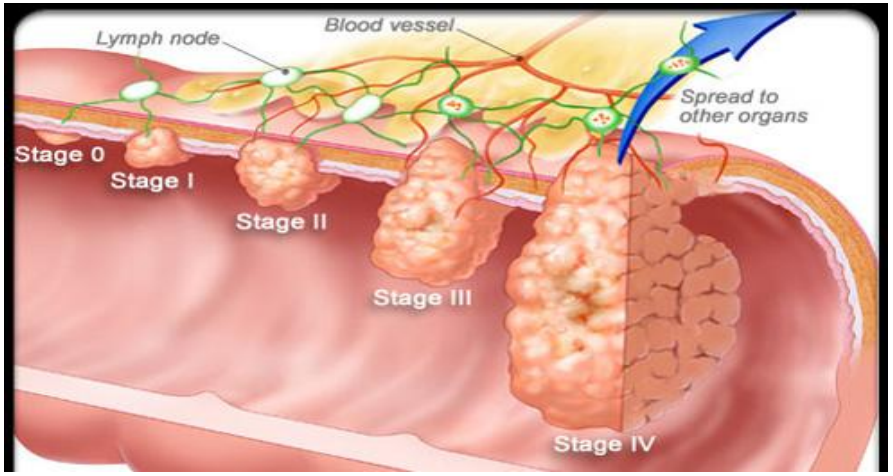
Fabian Holman

LUMC

catharina ziekenhuis

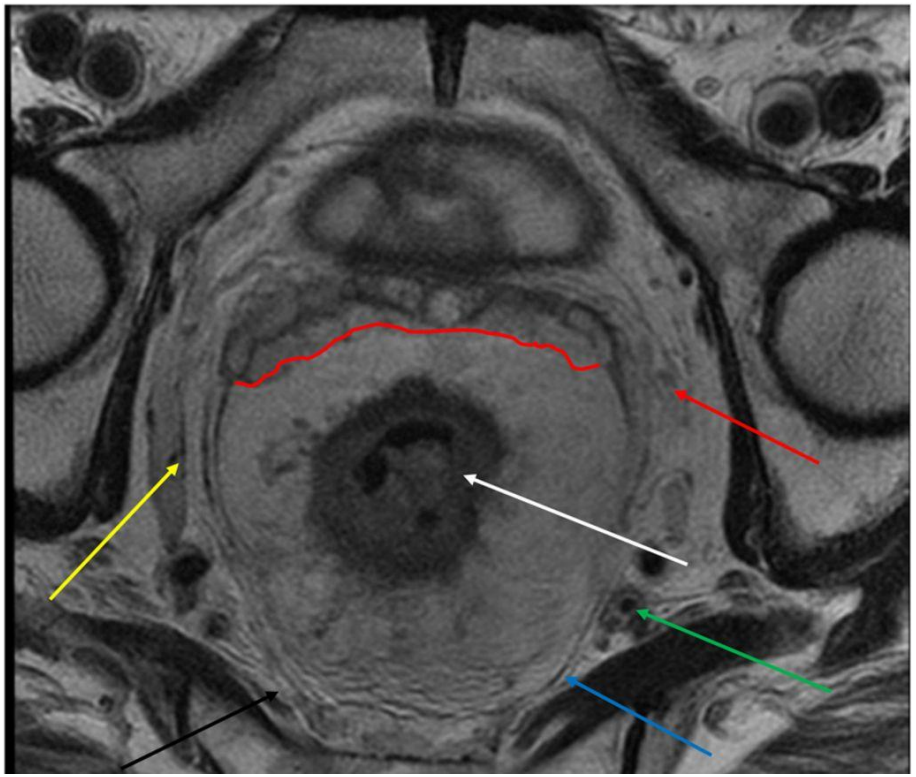
Introduction

- Incidence colorectal malignancies: 1.000.000
- 30% rectal cancer
- 25% locally advanced

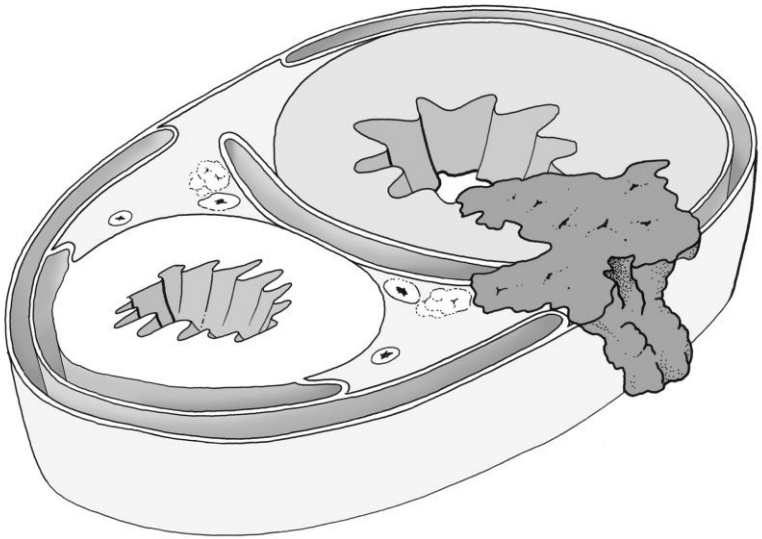


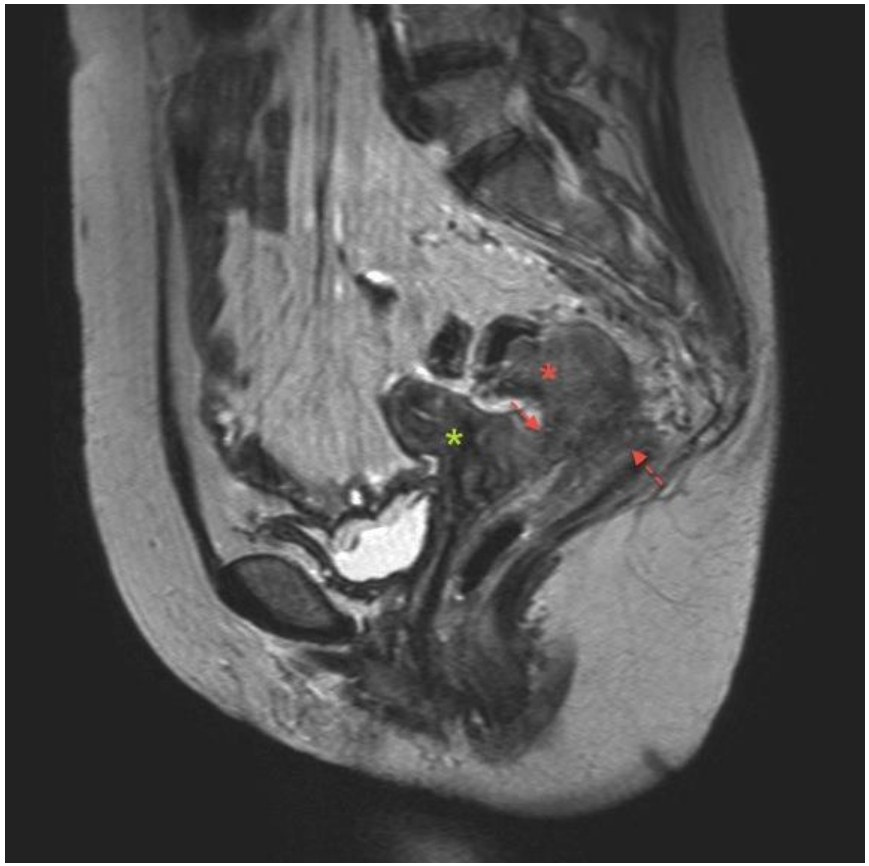
Cunningham D, Atkin W, Lenz HJ, Lynch HT, Minsky B, Nordlinger B, et al. Colorectal cancer. Lancet. 2010; **375**(9719): 1030-47.

Introduction



Introduction





Introduction

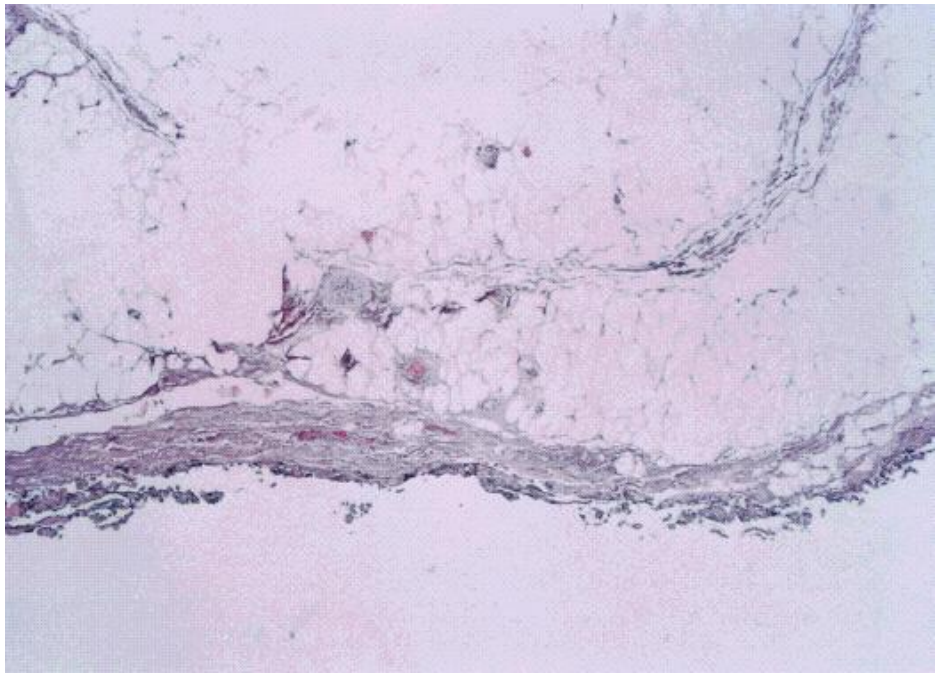
- Total Mesorectal Excision (TME) in the treatment of primary rectal cancer: the recurrence rate decreased.

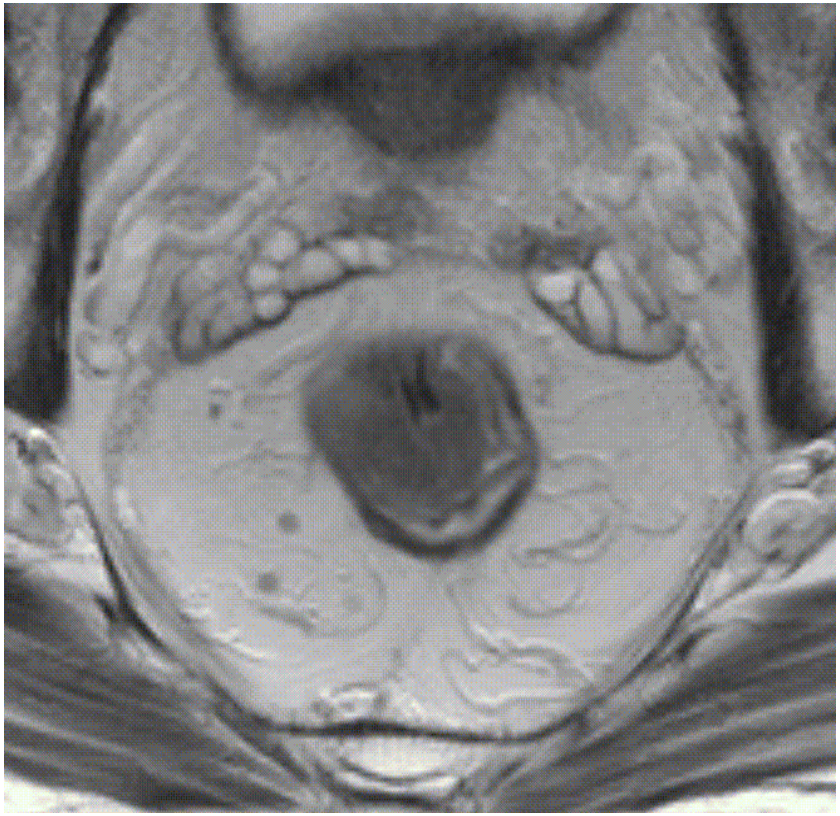
- Heald RJ. The 'Holy Plane' of rectal surgery. Journal of the Royal Society of Medicine. 1988; 81(9): 503-8.

Introduction

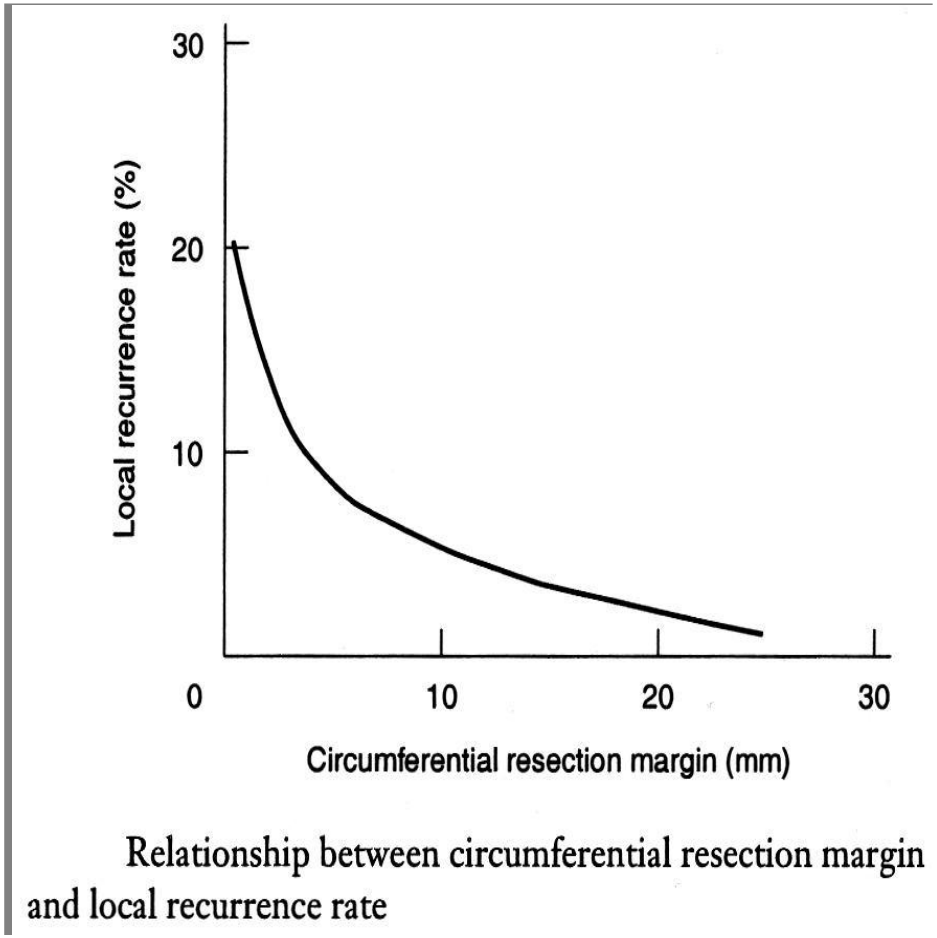
- TME
- CRM
- Neoadjuvant therapy

CRM

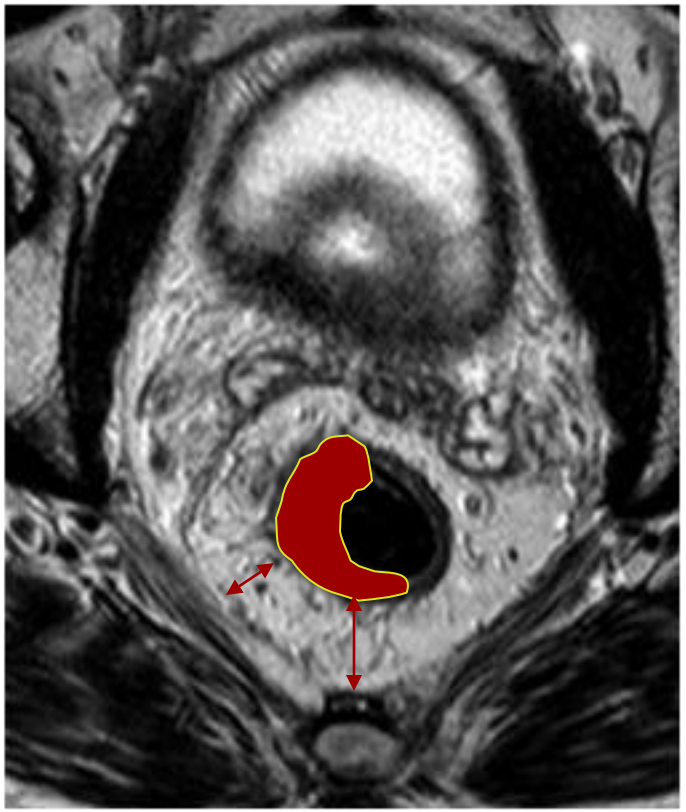




CRM



Relationship between circumferential resection margin and local recurrence rate



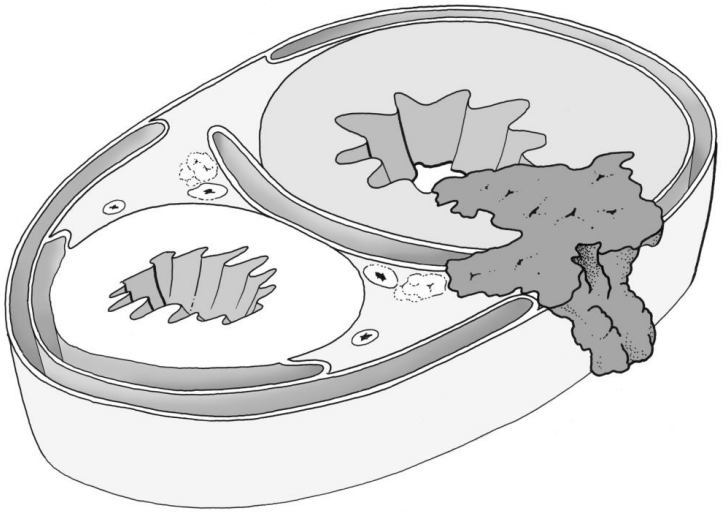
Wibe A, et al. Br J Surg 2002; 89:327-34.

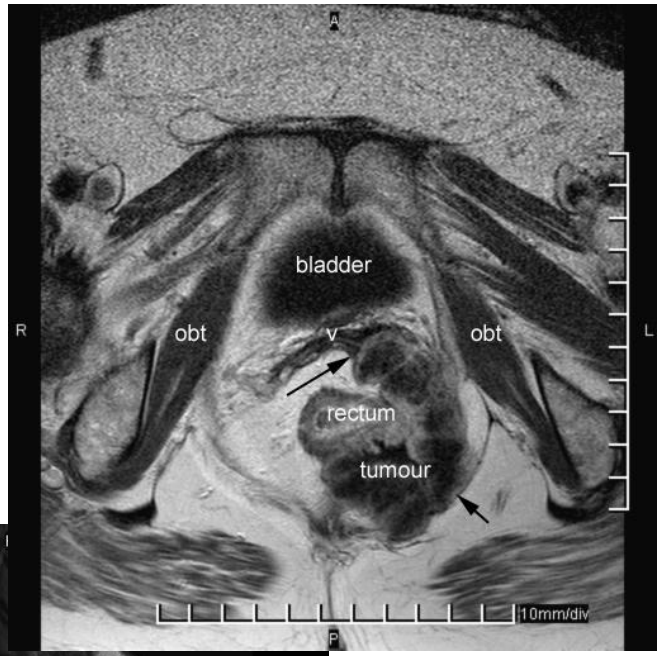
Introduction

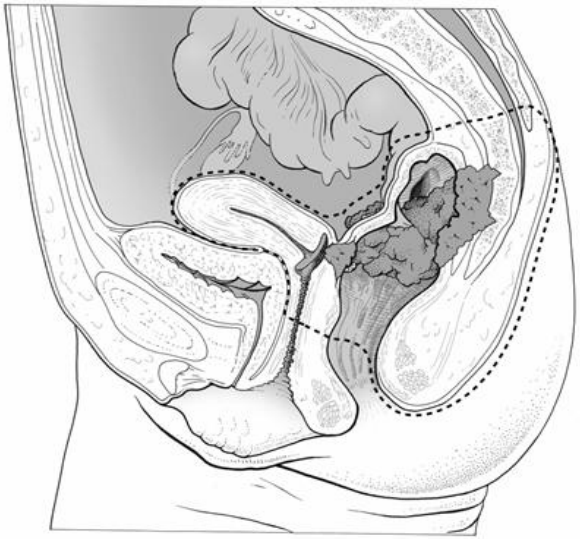
- T4a: penetration of the visceral peritoneum
- T4b: invasion into surrounding structures or organs

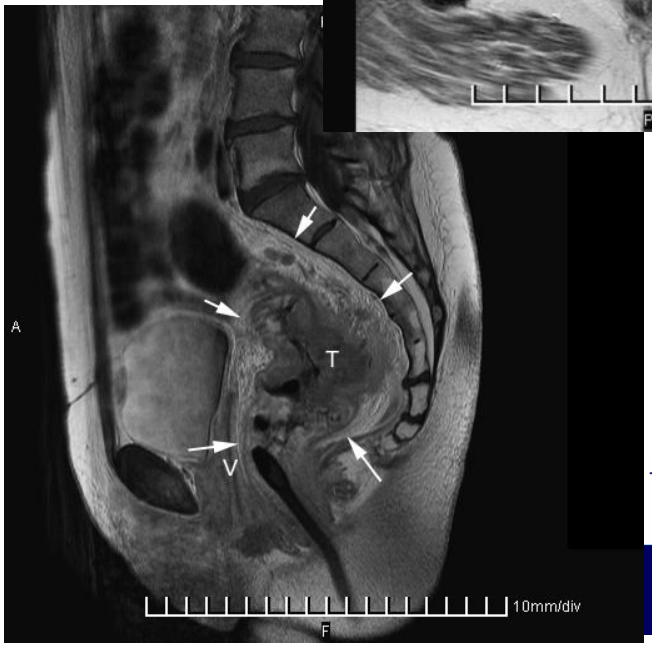
Introduction

Introduction



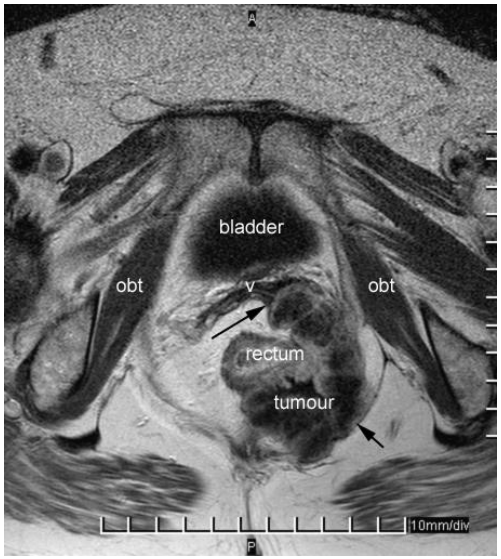


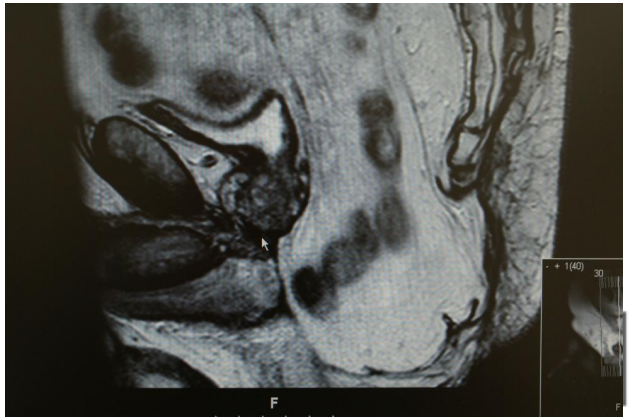




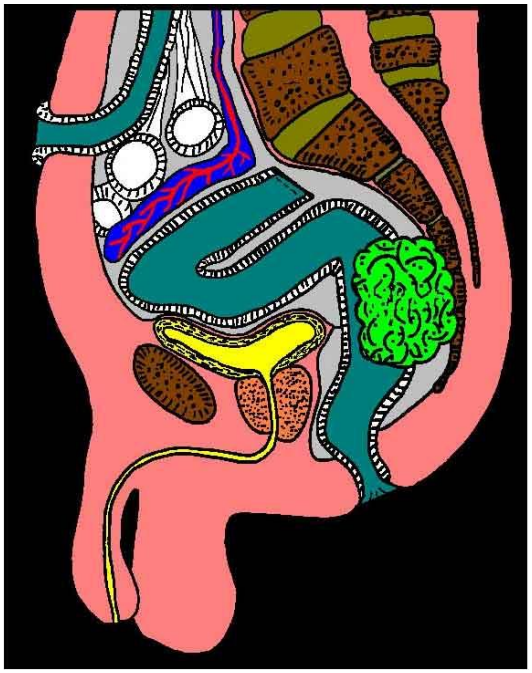
Locally Advanced Rectal Cancer

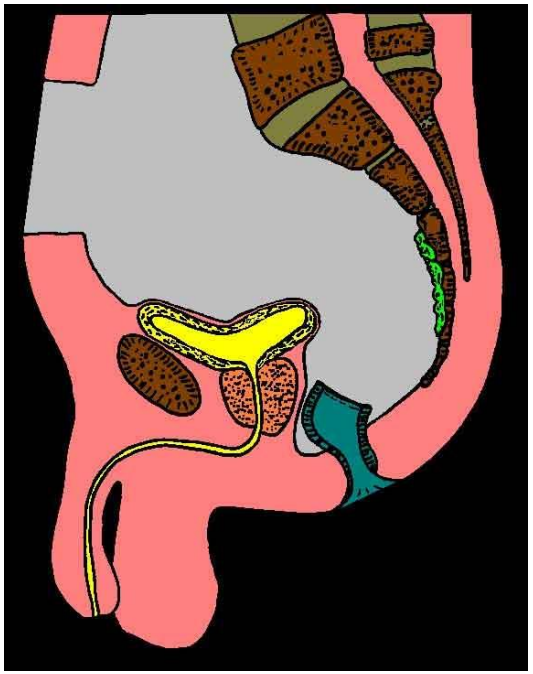
- Multimodality treatment
  - **Neoadjuvant chemoradiotherapy**
  - **(extra-anatomical) resection**
  - **Intra-Operative Radiotherapy**
  - **(Adjuvant Chemotherapy)**

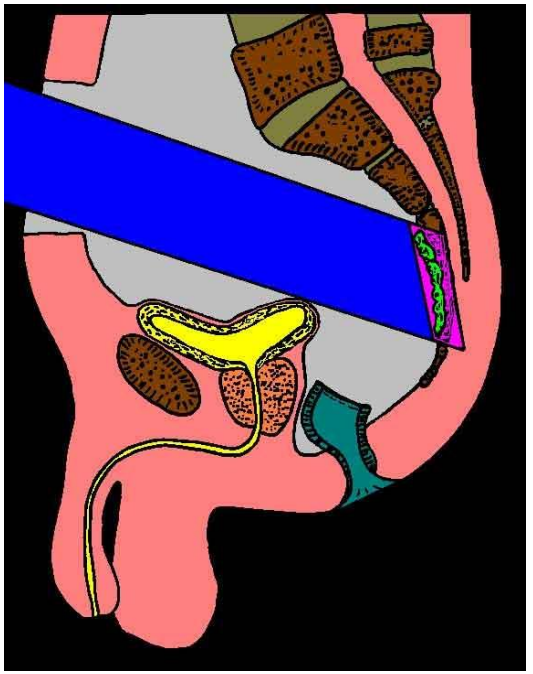




IORT

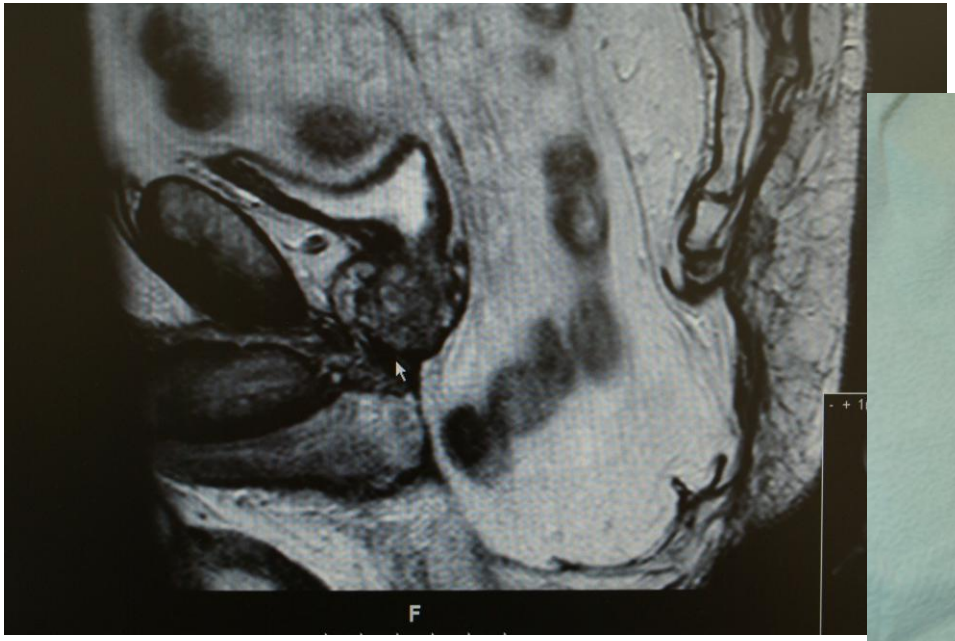


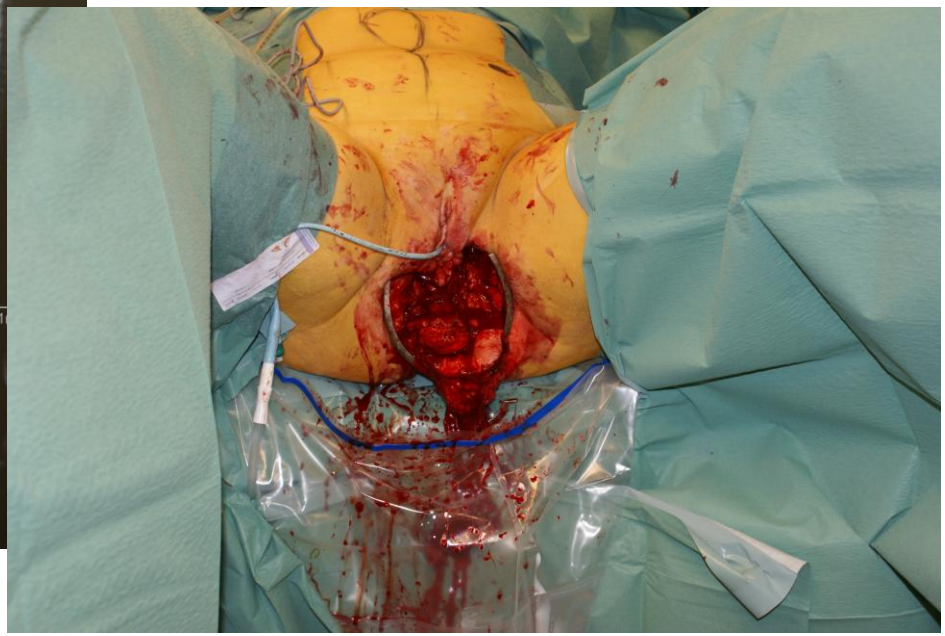




IORT

Locally Advanced Rectal Cancer

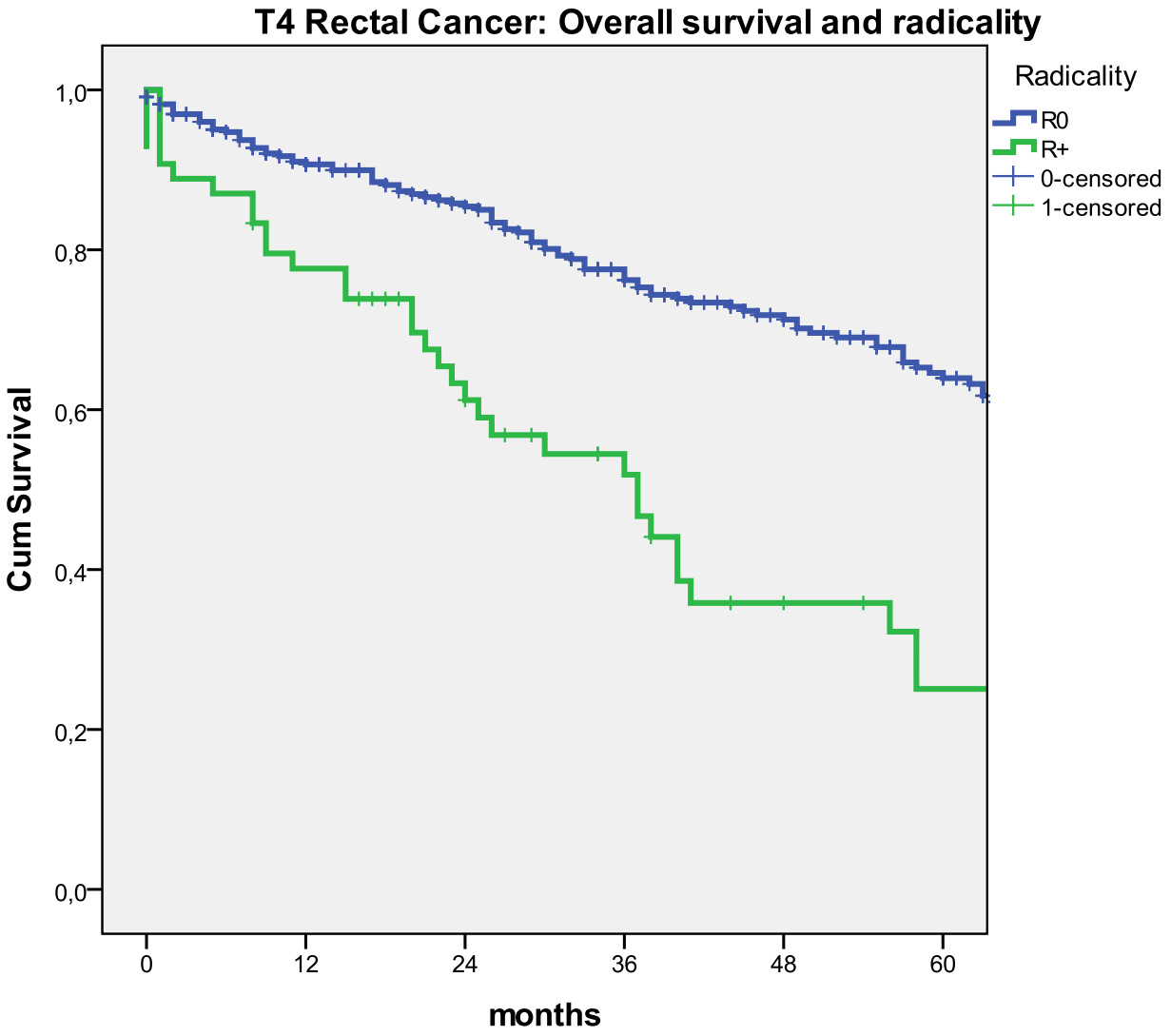


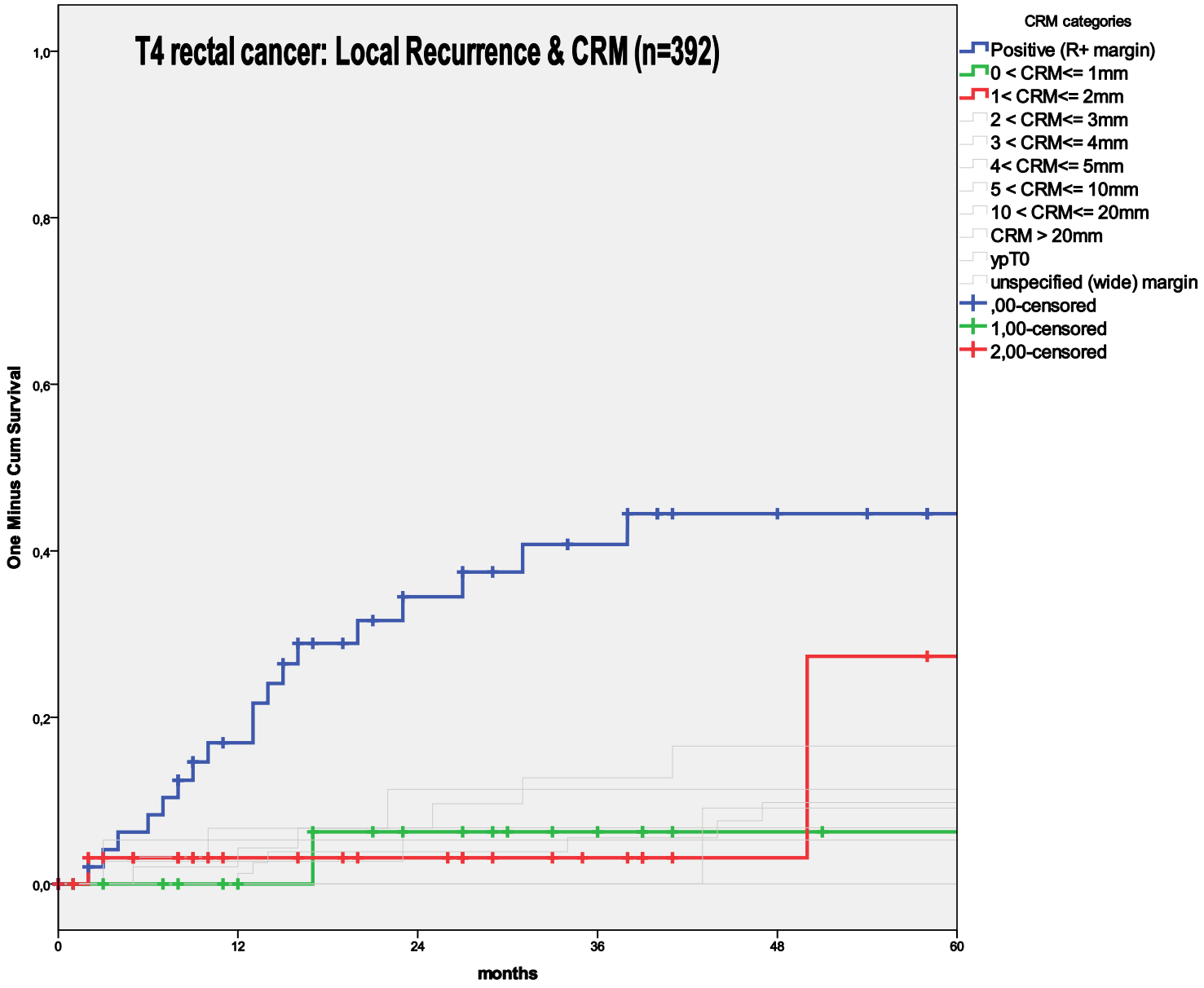


Locally Advanced Rectal Cancer

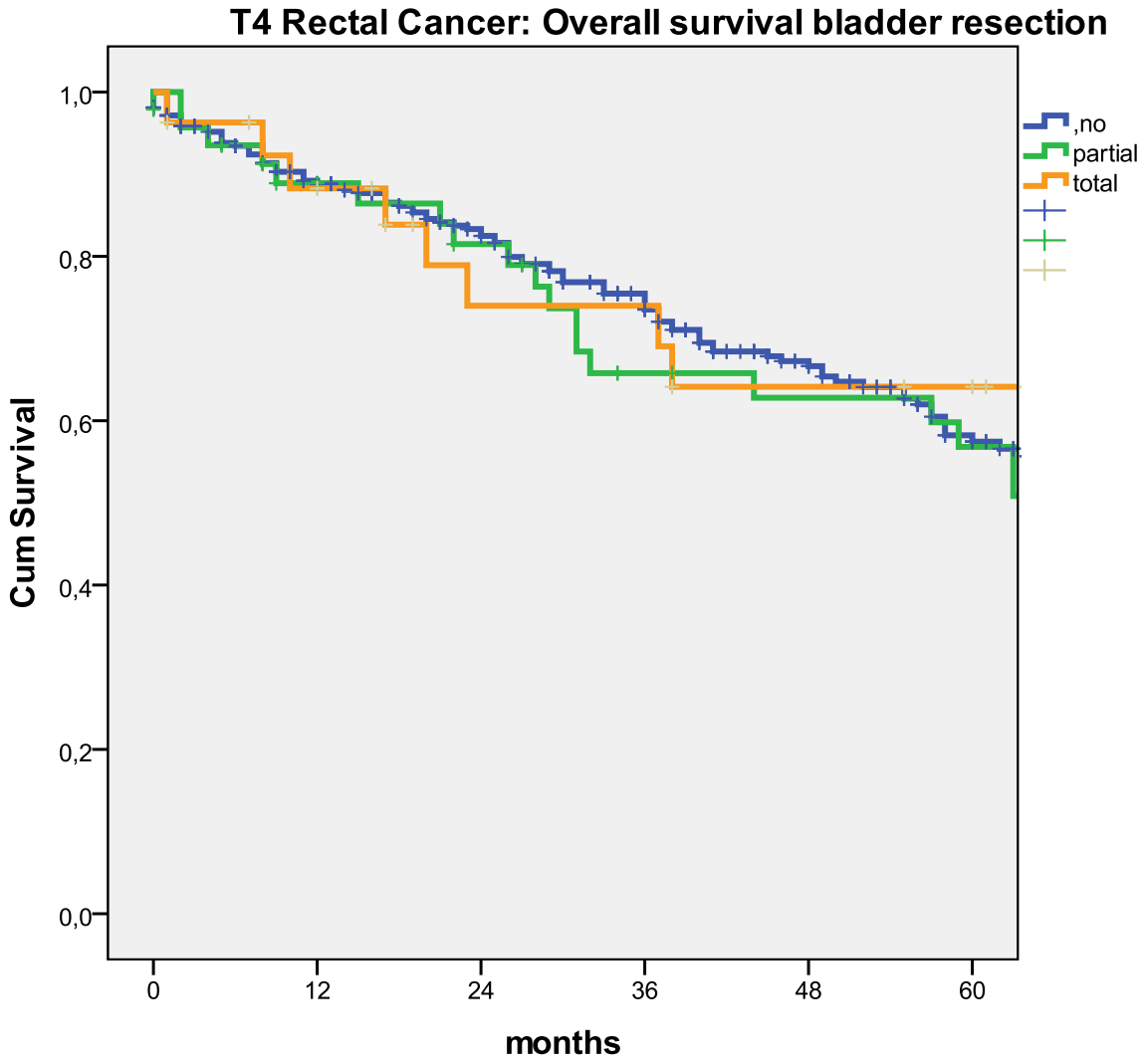
- Radical resection
- Neoadjuvant radiotherapy:
    - Downsizing
    - Local control and survival
- Neoadjuvant Chemoradiation:
    - Local control and survival
- IORT as element of multimodality treatment

Locally Advanced Rectal Cancer




T4 rectal cancer: Local Recurrence & CRM (n=392)
One Minus Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
12
24
36
48
60
months
CRM categories
Positive (R+ margin)
0 < CRM<= 1mm
1< CRM<= 2mm
2 < CRM<= 3mm
3 < CRM<= 4mm
4< CRM<= 5mm
5 < CRM<= 10mm
10 < CRM<= 20mm
CRM > 20mm
ypT0
unspecified (wide) margin
,00-censored
1,00-censored
2,00-censored

Locally Advanced Rectal Cancer



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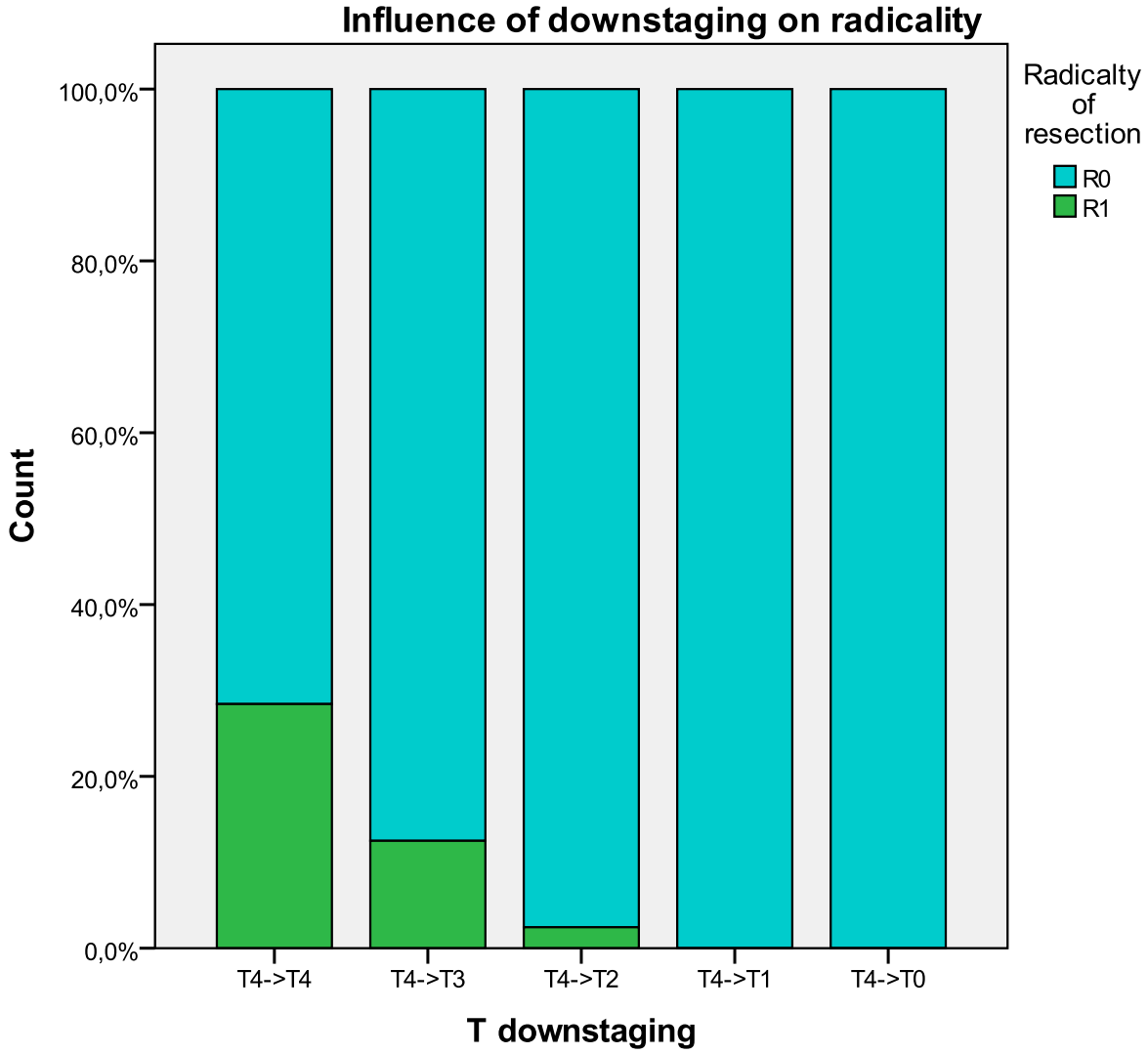
Locally Advanced Rectal Cancer



Locally Advanced Rectal Cancer

- 5 year survival up to 67%
- Radical resection most important prognostic factor

Kusters M, Valentini V, Calvo FA, Krempien R, Nieuwenhuijzen GA, Martijn H, et al. Results of European pooled analysis of IORT-containing multimodality treatment for locally advanced rectal cancer: adjuvant chemotherapy prevents local recurrence rather than distant metastases. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2010; 21(6): 1279-84.
Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2008; 26(2): 303-12.

Locally Advanced Rectal Cancer

- Radical resection
- Neoadjuvant Chemoradiation:
    - Downsizing
    - Local control and survival
- IORT as element of multimodality treatment

Locally Advanced Rectal Cancer
IORT: RCT's

Masaki T, Takayama M, Matsuoka H, Abe N, Ueki H, Sugiyama M, et al. Intraoperative radiotherapy for oncological and function-preserving surgery in patients with advanced lower rectal cancer. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie. 2008; **393**(2): 173-80.

Dubois JB, Bussieres E, Richaud P, Rouanet P, Becouarn Y, Mathoulin-Pelissier S, et al. Intra-operative radiotherapy of rectal cancer: results of the French multi-institutional randomized study. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology. 2011; **98**(3): 298-303

Locally Advanced Rectal Cancer
IORT: RCT's

- Masaki et al, 2008
- 19 patients with LARC treated with surgery and IORT vs 22 patients with surgery alone
- No difference was found
- T1/2 included

Locally Advanced Rectal Cancer
IORT: RCT's

- Dubois et al, 2011
- 142 patients with T3/4 or N+ randomized for neoadjuvant EBRT, surgery and IORT vs neoadjuvant EBRT and surgery
- No difference was found
- 90% 5 year local control
- Complete resection minimizes the of effect of IORT

Locally Advanced Rectal Cancer
IORT: non randomized trials

- Ferenschild et al, 2006
- LARC with or without IORT
- R0: No difference in local control
- R1/2 resection: improved local control in IORT group

- Valentini et al, 2009
- Improved local control

Locally Advanced Rectal Cancer
IORT: non randomized trials

- Willet et al, 1991
- Improved local control

- Ratto et al, 2003
- Improved local control

Locally Advanced Rectal Cancer
IORT: non comparative studies

- Kusters M, Valentini V, Calvo FA, Krempien R, Nieuwenhuijzen GA, Martijn H, Doglietto GB, del Valle E, Roeder F, Buchler MW, C. J. H. van de Velde CJH, Rutten HJT. Results of European pooled analysis of IORT-containing multimodality treatment for locally advanced rectal cancer: adjuvant chemotherapy prevents local recurrence rather than distant metastases. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2010; **21**(6): 1279-84.

- Mathis KL, Nelson H, Pemberton JH, Haddock MG, Gunderson LL. Unresectable colorectal cancer can be cured with multimodality therapy. Annals of surgery. 2008; **248**(4): 592-8.

Locally Advanced Rectal Cancer
IORT: non randomized trials

- Kusters et al, 2009
- 431 (CRM threathened) T3
- 174 T4
- 5 year OS rate: 67%
- 5 year LR rate: 12%

- 55% of patients with an irradical resection remained free of LR

Locally Advanced Rectal Cancer
IORT: non randomized trials

- Mathis et al, 2008
- 146 T4 (colon and rectum)
- 5 year OS: 52%

- 5 year LR: 14%
- Sign reduced rates of LR in the IORT field

Locally Advanced Rectal Cancer

Table 1
Studies reporting oncological outcomes following IORT for locally advanced colorectal cancer.

Author, year, location	Time frame	*N*	Cancer type (%)	Clinical T stage (%)	Type of IORT	IORT dose (Gy)	PR-RT (%)	CT (%)	PO-RT (%)	Follow up (months)	Resection margin	5-year LC (%)	In-field LC (%)	5-year OS (%)	5-year DFS (%)
Willett et al., 1991, USA [23] ς	1978–1989	42	R	–	IOERT	10–20 ϕ	100	–	0	26 (6–120)§	R0 R1 R2	88 69 50	–	–	53 47 17
Huber et al., 1996, Germany [24]	1989–1993	38	R	T3 (50) T4 (50)	HDR-IORT	15	50	NA (50) A (50)	50	25.5 ‡	R0/R1/R2	T3 (84) T4 (90)	100	28ғ	–
Nakfoor et al., 1998, USA [37] ς	1978–1996	73	R	–	IOERT	10–20 ϕ	100	–	0	53 ‡	R0 R1/R2	89 65	–	–	63 32
Mannaerts et al., 2000, Netherlands [25] Φ	1994–1998	38	R	–	IOERT	10–17.5 ϕ	100	–	–	21 (1–57) §	R0/R1/R2	82*	92*	72*	65*
Ratto et al., 2003, Italy [28] ϖ	1990–1997	19	R	T1–T3 N3 (7) T4Nx (93)	IOERT	10–15 ϕ	–	–	–	74 (27–120) §	–	91	95	61	47
Sadahiro et al., 2004, Japan [26]	1991–2001	99	R	T1/T2 (29) T3 (59) T4 (12)	IOERT	17.3 ‡	100	NA (53)	0	67 Ω	–	98	–	79	71
Nuyttens et al., 2004, Netherlands [27] ¡	1997–2000	18	R	T1–T4 LN +ve (16) T3N0 (66) T4N0 (16)	HDR-IORT	10	100	0	0	34 Ω	–	81*	94*	61*	–
Diaz-Gonzalez et al., 2006, Spain [38]	1995–2001	115	R	T1/T2 (8) T3 (95) T4 (12)	IOERT	12.5 Ω	100	NA (100) A (57)	0	37 (6–83) §	–	94*	98*	74*	74*
Krempien et al. 2006, Germany [39] Φ	1991–2003	210	R	T1/T2 (6) T3 (72) T4 (22)	IOERT	10 (8–18) §	93	93	42	61 (4–177) §	R0 R1/R2	93 77	98	74 55	68 0
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Roeder et al., 2007, Germany [41] Φ	1991–2004	243	R	T1/T2 (14) T3 (66) T4 (20)	IOERT	10.4 ‡	50	36	0	59 Ω	R0 R1/R2	94 72	97	–	–
Masaki et al., 2008, Japan [29]	2000–2007	19	R	T1/T2 (11) T3 (89)	IOERT	18–20 ϕ	–	A (37)	–	34 §	–	95	–	64	60
Mathis et al., 2008, USA [30] Φ	1981–2007	146	C (27) R (73)	T4 (100)	IOERT	12.5 (7.5–25) §	100	NA (5) A (40)	0	44 Ω	R0/R1/R2	86	98	52	43
Valentini et al., 2009, Italy [31] Φ ϖ	1991–2006	29	R	T4 (100)	IOERT	10–15 ϕ	100	100	0	31 (4–136) §	R0	100	100	–	–
Kusters et al., 2010, Netherlands [42]	–	605	R	T3 (71) T4 (29)	IOERT	–	R (36)	A (42)	0	–	R0/R1/R2	88	–	67	–
Dubois et al., 2011, France [32] ¢	1993–2001	68	R	T3/T4 (100)	IOERT	18 Œ	100	A (25)	–	60 (10–112) §	–	92	96	77	62

PR-RT: pre-operative radiotherapy; **CT**: chemotherapy; **PO-RT**: post-operative radiotherapy; **LC**: local control; **OS**: overall survival; **DFS**: disease-free survival; **R**: rectal; **ς**: all patients having IORT had obvious residual cancer or positive/<5 mm margins on frozen section; **ϕ**: range reported with no mean/median; §: median; ‡: mean; **ғ**: overall survival reported for T3 and T4 cancers combined; **Φ**: all patients received IORT irrespective of frozen section outcome but dose was increased where margins were positive or close; **ϖ**: overlapping patient populations; *: 3-year local control/survival reported; **LN**: lymph node; **¡**: IORT used in cases where resection margin was found to be positive or <2 mm on intraoperative frozen section.
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Locally Advanced Rectal Cancer

T3 (50)
T4 (50)
–

–

T1–T3 N3 (7)
T4Nx (93)
T1/T2 (29)
T3 (59)
T4 (12)
T1–T4
LN +ve (16)
T3N0 (66)
T4N0 (16)
T1/T2 (8)
T3 (95)
T4 (12)
T1/T2 (6)
T3 (72)
T4 (22)
T3

T1/T2 (14)
T3 (66)
T4 (20)
T1/T2 (11)
T3 (89)
T4 (100)

T4 (100)

T3 (71)
T4 (29)
T3/T4 (100)

Locally Advanced Rectal Cancer

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Willett et al., 1991, USA [23] ç	1978–1989	42	R	–	IOERT	10–20 ϕ	100	–	0	26 (6–120)§	R0 R1 R2	88 69 50	–	–	53 47 17
Huber et al., 1996, Germany [24]	1989–1993	38	R	T3 (50) T4 (50)	HDR-IORT	15	50	NA (50) A (50)	50	25.5 ‡	R0/R1/R2	T3 (84) T4 (90)	100	28ŕ	–
Nakfoor et al., 1998, USA [37] ç	1978–1996	73	R	–	IOERT	10–20 ϕ	100	–	0	53 ‡	R0 R1/R2	89 65	–	–	63 32
Mannaerts et al., 2000, Netherlands [25] Φ	1994–1998	38	R	–	IOERT	10–17.5 ϕ	100	–	–	21 (1–57) §	R0/R1/R2	82*	92*	72*	65*
Ratto et al., 2003, Italy [28] ϖ	1990–1997	19	R	T1–T3 N3 (7) T4Nx (93)	IOERT	10–15 ϕ	–	–	–	74 (27–120) §	–	91	95	61	47
Sadahiro et al., 2004, Japan [26]	1991–2001	99	R	T1/T2 (29) T3 (59) T4 (12)	IOERT	17.3 ‡	100	NA (53)	0	67 Ω	–	98	–	79	71
Nuyttens et al., 2004, Netherlands [27] ¡	1997–2000	18	R	T1–T4 LN +ve (16) T3N0 (66) T4N0 (16)	HDR-IORT	10	100	0	0	34 Ω	–	81*	94*	61*	–
Diaz-Gonzalez et al., 2006, Spain [38]	1995–2001	115	R	T1/T2 (8) T3 (95) T4 (12)	IOERT	12.5 Ω	100	NA (100) A (57)	0	37 (6–83) §	–	94*	98*	74*	74*
Krempien et al. 2006, Germany [39] Φ	1991–2003	210	R	T1/T2 (6) T3 (72) T4 (22)	IOERT	10 (8–18) §	93	93	42	61 (4–177) §	R0 R1/R2	93 77	98	74 55	68 0
Ferenschild et al., 2006, Netherlands [40] ¡	1987–2002	30	R	T3	HDR-IORT	10	100	–	0	25 (1–136) §	R0 R1/R2	72 58	–	66 38	–
Roeder et al., 2007, Germany [41] Φ	1991–2004	243	R	T1/T2 (14) T3 (66) T4 (20)	IOERT	10.4 ‡	50	36	0	59 Ω	R0 R1/R2	94 72	97	–	–
Masaki et al., 2008, Japan [29]	2000–2007	19	R	T1/T2 (11) T3 (89)	IOERT	18–20 ϕ	–	A (37)	–	34 §	–	95	–	64	60
Mathis et al., 2008, USA [30] Φ	1981–2007	146	C (27) R (73)	T4 (100)	IOERT	12.5 (7.5–25) §	100	NA (5) A (40)	0	44 Ω	R0/R1/R2	86	98	52	43
Valentini et al., 2009, Italy [31] Φ ϖ	1991–2006	29	R	T4 (100)	IOERT	10–15 ϕ	100	100	0	31 (4–136) §	R0	100	100	–	–
Kusters et al., 2010, Netherlands [42]	–	605	R	T3 (71) T4 (29)	IOERT	–	R (36)	A (42)	0	–	R0/R1/R2	88	–	67	–
Dubois et al., 2011, France [32] ¢	1993–2001	68	R	T3/T4 (100)	IOERT	18 Œ	100	A (25)	–	60 (10–112) §	–	92	96	77	62

PR-RT: pre-operative radiotherapy; **CT**: chemotherapy; **PO-RT**: post-operative radiotherapy; **LC**: local control; **OS**: overall survival; **DFS**: disease-free survival; **R**: rectal; **ç**: all patients having IORT had obvious residual cancer or positive/<5 mm margins on frozen section; **ϕ**: range reported with no mean/median; §: median; ‡: mean; **ŕ**: overall survival reported for T3 and T4 cancers combined; **Φ**: all patients received IORT irrespective of frozen section outcome but dose was increased where margins were positive or close; **ϖ**: overlapping patient populations; *: 3-year local control/survival reported; **LN**: lymph node; **¡**: IORT used in cases where resection margin was found to be positive or <2 mm on intraoperative frozen section.
Ω: median reported without range; **NA**: neo-adjuvant chemotherapy; **A**: adjuvant chemotherapy; **¢**: randomised controlled trial; **Œ**: one patient received dose of 15 Gy.

Results

	No	T	5 yr OS
Diaz-Gonzales	115	T1/2 T3 T4	74
Kusters	605	T3 T4	67
Ferenschild	30	T3	66
Dubois	100	T3 T4	77

Results of IOERT-containing multimodality treatment for T4 rectal cancer

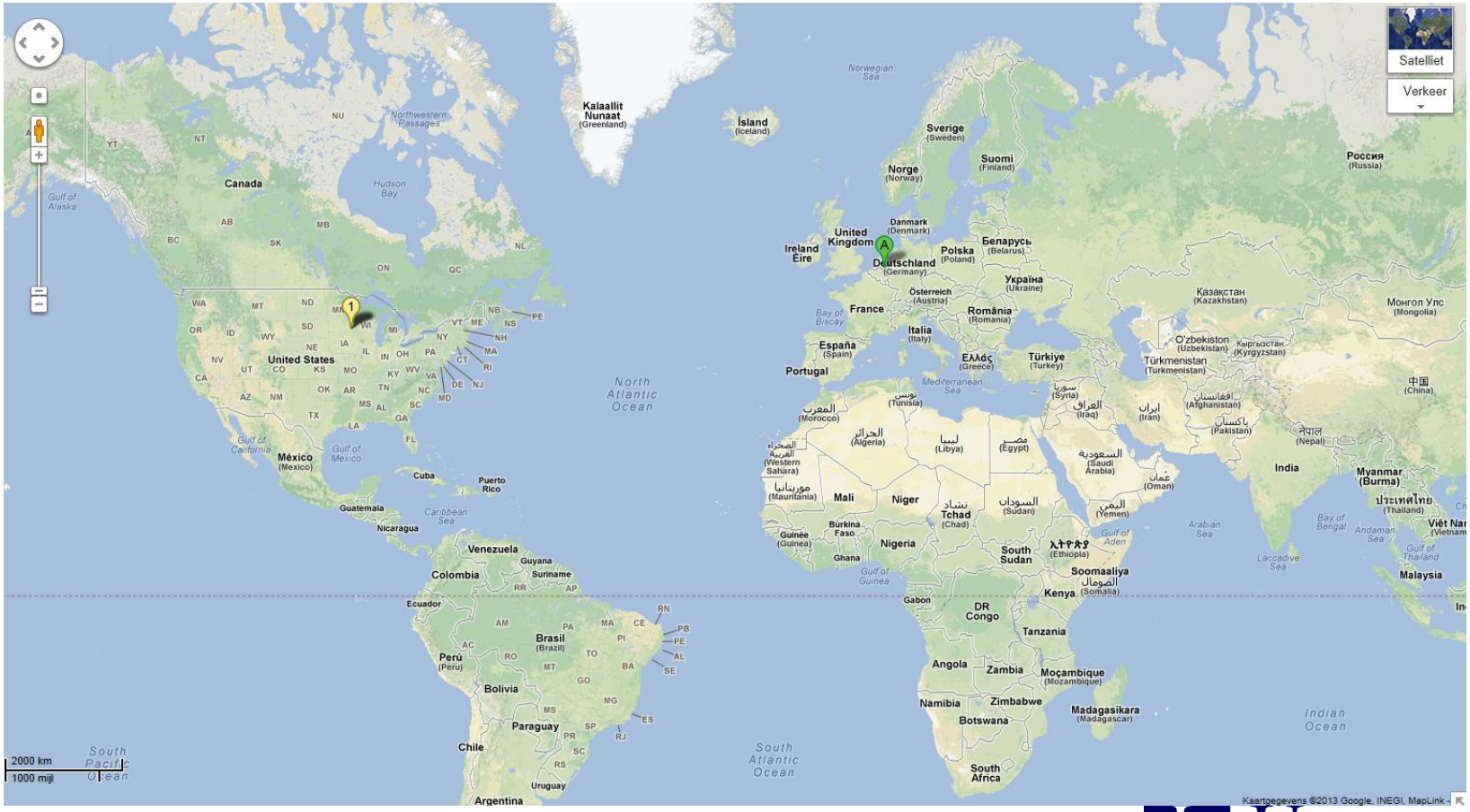
A pooled analysis of the Mayo Clinic and Catharina Hospital

Locally Advanced Rectal Cancer

- Pooled analysis
- 505 patients
- T4 rectal carcinomas
- Mayo Clinic, Rochester, Minnesota, USA
  1981-2010
- Catharina Ziekenhuis Eindhoven
  1994-2010

F.A. Holman, M Kusters, M. Haddock, H.J.M. Rutten, G.A.P. Nieuwenhuijzen, H. Nelson. A pooled analysis of multimodality treatment of locally advanced rectal cancer: results of 505 patients of two major treatment centers.(submitted).

Locally Advanced Rectal Cancer



Locally Advanced Rectal Cancer

	All N = 505
Mean age, years (range)	61 ± 12.0 (19-89)
Mean follow-up, months (range)	49.6 ± 36.5 (0-234)
Gender Male Female	 294 (58%) 211 (42%)
Preoperative treatment No Therapy Radiotherapy Chemoradiotherapy	 13 (3%) 97 (19%) 395 (78%)
Postoperative treatment No therapy Radiotherapy Chemotherapy Chemoradiotherapy	 394 (78%) 17 (3%) 83 (17%) 11 (2%)

Locally Advanced Rectal Cancer

	Radical (R0)	Irradical (R1/R2)	P-value
Age			**0.382**
Up to 69 years	299 (77%)	88 (23%)	
70 years or older	89 (75%)	29 (25%)	
Gender			**0.086**
Male	219 (75%)	75 (25%)	
Female	169 (80%)	42 (20%)	
Preoperative treatment			**0.023**
No Therapy	7 (54%)	6 (46%)	
Radiotherapy	70 (72%)	27 (28%)	
Chemoradiotherapy	311 (79%)	84 (21%)	
Waiting Time			**0.001**
Up to 56 days	**176 (72%)**	**69 (28%)**	
57 days and longer	**200 (84%)**	**39 (19%)**	

Locally Advanced Rectal Cancer

	Local recurrence			Distant metastasis			Cancer-specific survival			Overall survival		
	HR	CI	P	HR	CI	P	HR	CI	P	HR	CI	P
Age			0.442			0.646			0.524			**0.000**
Up to 69 years	1.00			1.00			1.00			1.00		
70 years or older	1.240	0.717-2.145		0.908	0.600-1.374		1.138	0.769-1.685		1.744	1.305-2.331	
Gender			0.964			0.174			0.699			**0.806**
Male	1.00			1.00			1.00			1.00		
Female	0.964	0.619-1.580		1.252	0.906-1.731		1.065	0.775-1.463		0.967	0.742-1.261	
Preoperative treatment			0.724			0.385			0.161			**0.112**
No therapy	1.00			1.00			1.00			1.00		
Radiotherapy	0.971	0.271-3.474		0.758	0.324-1.774		0.685	0.318-1.473		0.850	0.421-1.715	
Chemoradiotherapy	0.781	0.237-2.576		0.625	0.285-1.369		0.537	0.266-1.084		0.634	0.328-1.225	
Waiting Time			0.025			0.359			0.794			**0.506**
Up to 56 days	1.00			1.00			1.00			1.00		
57 days and longer	2.058	1.093-3.873		1.221	0.796-1.872		1.057	0.697-1.603		1.121	0.801-1.568	
Radicality of the resection			0.000			0.019			0.000			**0.000**
R0	1.00			1.00			1.00			1.00		
R1	3.521	2.144-5.782		1.712	1.185-2.473		2.368	1.673-3.351		2.131	1.590-2.855	
R2	4.019	0.926-17.445		1.605	0.496-5.180		2.925	1.045-8.184		3.162	1.361-7.348	
Postoperative treatment			0.714			0.961			0.564			**0.111**
No therapy	1.00			1.00			1.00			1.00		
Chemotherapy	0.567	0.137-2.349		0.877	0.383-2.008		0.646	0.262-1.593		0.722	0.353-1.476	
Radiotherapy	0.837	0.439-1.597		0.904	0.582-1.405		0.860	0.554-1.335		0.633	0.422-0.949	
Chemoradiotherapy	1.416	0.427-4.702		1.030	0.413-2.571		1.332	0.608-2.917		0.945	0.436-2.045	
Adjuvant Chemotherapy			**0.682**			**0.781**			**0.457**			**0.015**
No	**1.00**			**1.00**			**1.00**			**1.00**		
Yes	**0.880**	**0.473-1.636**		**0.942**	**0.617-1.439**		**0.852**	**0.555-1.309**		**0.627**	**0.422-0.932**	

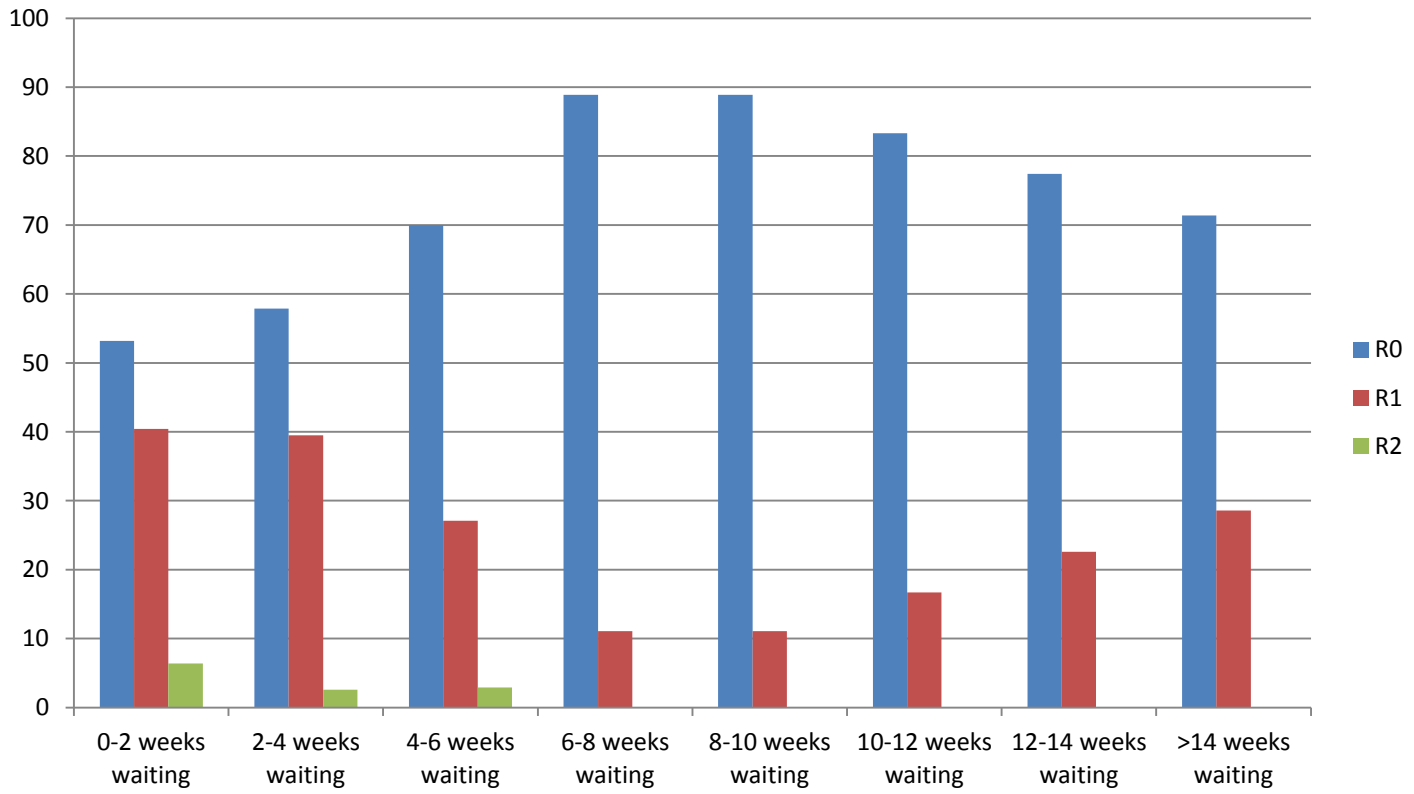
Locally Advanced Rectal Cancer

	Local recurrence			Distant metastasis			Cancer-specific survival			Overall survival		
	HR	CI	P	HR	CI	P	HR	CI	P	HR	CI	P
Age			0.442			0.646			0.524			**0.000**
Up to 69 years	1.00			1.00			1.00			1.00		
70 years or older	1.240	0.717-2.145		0.908	0.600-1.374		1.138	0.769-1.685		1.744	1.305-2.331	
Gender			0.964			0.174			0.699			**0.806**
Male	1.00			1.00			1.00			1.00		
Female	0.964	0.619-1.580		1.252	0.906-1.731		1.065	0.775-1.463		0.967	0.742-1.261	
Preoperative treatment			0.724			0.385			0.161			**0.112**
No therapy	1.00			1.00			1.00			1.00		
Radiotherapy	0.971	0.271-3.474		0.758	0.324-1.774		0.685	0.318-1.473		0.850	0.421-1.715	
Chemoradiotherapy	0.781	0.237-2.576		0.625	0.285-1.369		0.537	0.266-1.084		0.634	0.328-1.225	
Waiting Time			0.025			0.359			0.794			**0.506**
Up to 56 days	1.00			1.00			1.00			1.00		
57 days and longer	2.058	1.093-3.873		1.221	0.796-1.872		1.057	0.697-1.603		1.121	0.801-1.568	
Radicality of the resection			0.000			0.019			0.000			**0.000**
R0	1.00			1.00			1.00			1.00		
R1	3.521	2.144-5.782		1.712	1.185-2.473		2.368	1.673-3.351		2.131	1.590-2.855	
R2	4.019	0.926-17.445		1.605	0.496-5.180		2.925	1.045-8.184		3.162	1.361-7.348	
Postoperative treatment			0.714			0.961			0.564			**0.111**
No therapy	1.00			1.00			1.00			1.00		
Chemotherapy	0.567	0.137-2.349		0.877	0.383-2.008		0.646	0.262-1.593		0.722	0.353-1.476	
Radiotherapy	0.837	0.439-1.597		0.904	0.582-1.405		0.860	0.554-1.335		0.633	0.422-0.949	
Chemoradiotherapy	1.416	0.427-4.702		1.030	0.413-2.571		1.332	0.608-2.917		0.945	0.436-2.045	
Adjuvant Chemotherapy			**0.682**			**0.781**			**0.457**			**0.015**
No	**1.00**			**1.00**			**1.00**			**1.00**		
Yes	**0.880**	**0.473-1.636**		**0.942**	**0.617-1.439**		**0.852**	**0.555-1.309**		**0.627**	**0.422-0.932**	

Locally Advanced Rectal Cancer

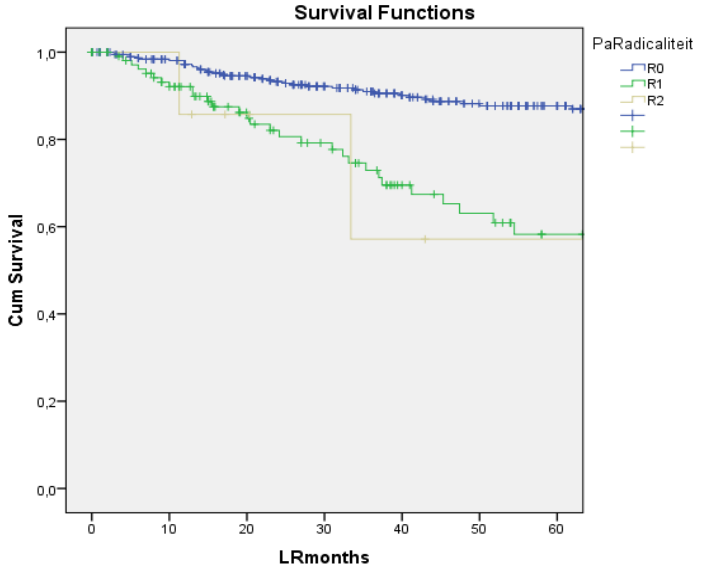
	Local recurrence			Overall survival		
	HR	CI	P	HR	CI	P
Age						**0.000**
Up to 69 years	n.a.			1.00		
70 years or older				1.695	1.263-2.276	
Waiting Time			0.020			
Up to 56 days	1.00			**n.a.**		
57 days and longer	2.146	1.129-4.076				
Radicality of the resection			0.000			**0.000**
R0	1.00			1.00		
R1	3.226	1.938-5.369		2.064	1.538-2.796	
R2	2.413	0.320-18.222		3.170	1.362-7.378	
Adjuvant Chemotherapy						**0.193**
No	**n.a.**			**1.00**		
Yes				**0.764**	**0.509-1.146**	

Locally Advanced Rectal Cancer



Locally Advanced Rectal Cancer
Local recurrence

- 18,4% 5 yr local recurrence rate
- Radical resection most important prognostic factor
- R0 resection: 12% 5 yr local recurrence rate
- R1/R2 resection: 42% 5 yr local recurrence rate



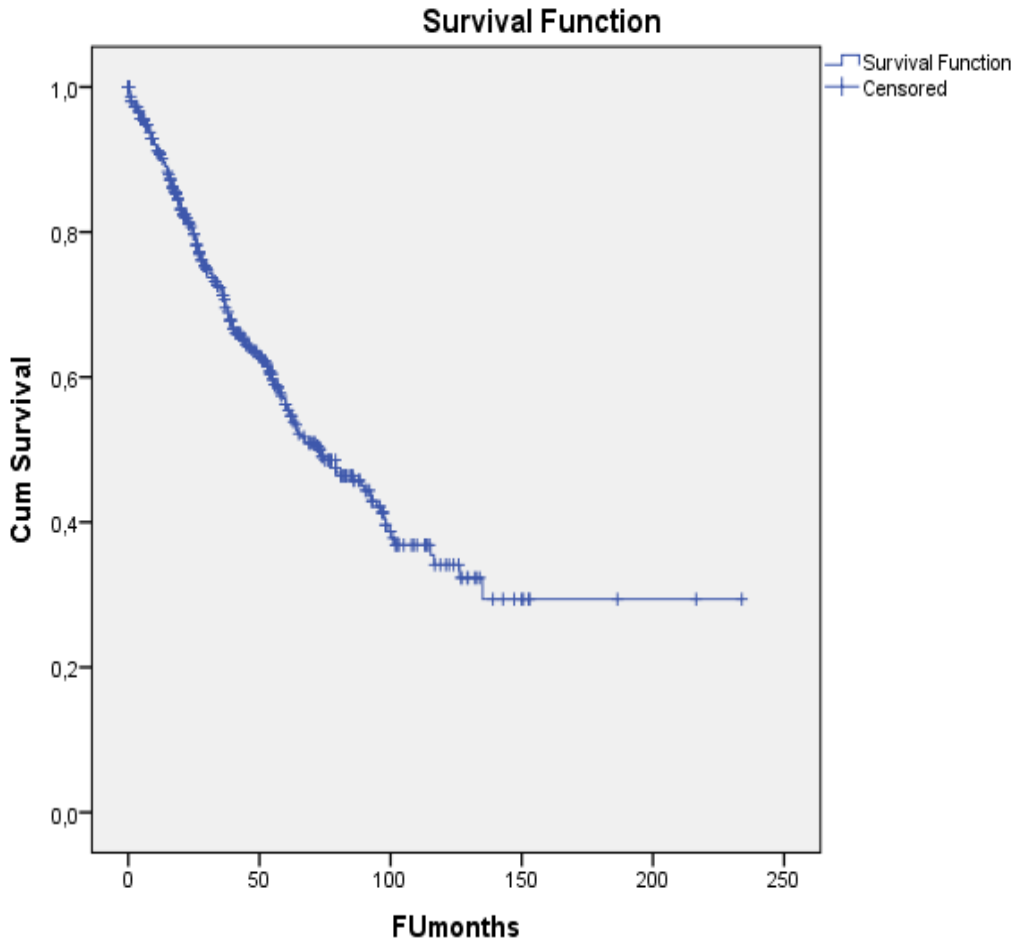
Locally Advanced Rectal Cancer
Distant metastases

- 34% 5 yr distant metastases rate
- Radical resection most important prognostic factor

- R0 resection: 29% 5 yr distant metastases rate

- R1/R2 resection: 53% 5 yr distant metastases rate
- No effect adjuvant therapy

Locally Advanced Rectal Cancer
Overall Survival



Locally Advanced Rectal Cancer
Overall Survival

Overall 5 yr survival: 57,3%

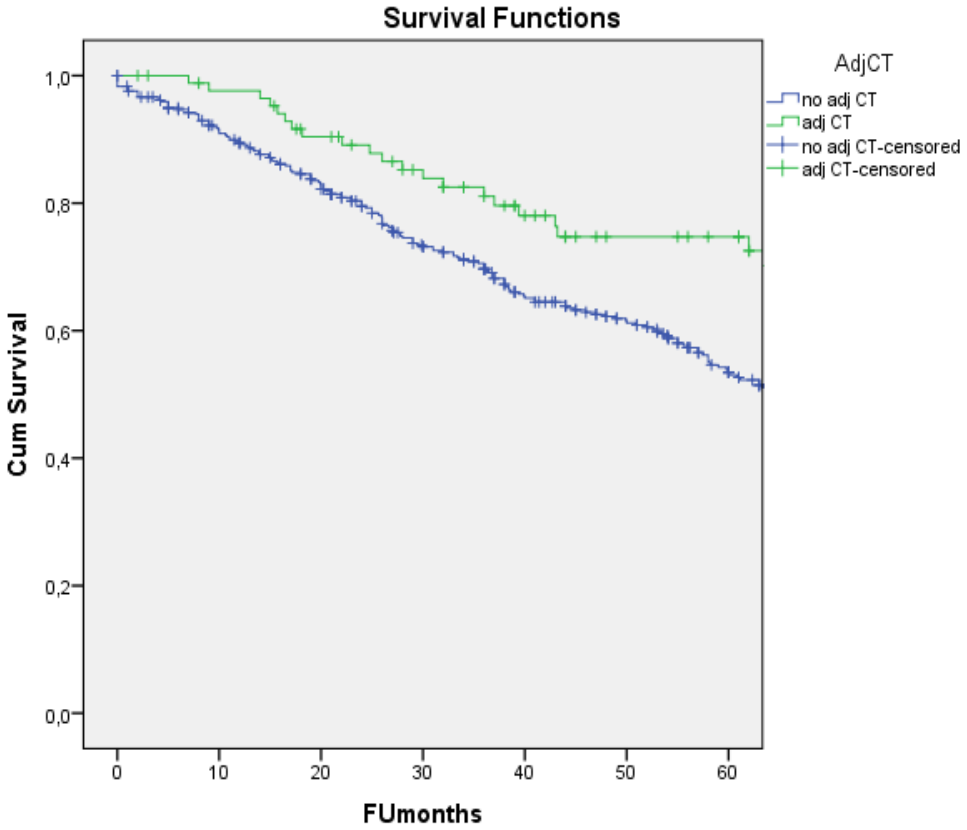
Overall 10 yr survival: 34,6%

R0 resection: 5 yr 65,1%, 10 yr 38,1%

R1/2 resection: 5 yr 33,8%

Multivariate analysis: factors influencing survival were age($p<0.001$), margin status ($p<0.001$) and neoadjuvant therapy ($p = 0,040$)

Adjuvant Therapy



IORT for primary Locally Advanced Rectal Cancer

Conclusion

- A radical resection is the most important prognostic factor
- Neoadjuvant Chemoradiation improves radicality
- A waiting period of 6-10 weeks improves radicality
- IORT improves local control

IORT for primary Locally Advanced Rectal Cancer