MARIENHOSPITAL STUTTGART

Analkarzinome
definitive Radiochemotherapie
Phase II/III Daten 2012 - 2013

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Standard => kontinuierliche Evolution

Stadien I-III	simultane Radio-Chemotherapie 5-FU/MMC	
	T1 G1 N0 ggfls. Resektion oder alleinige Radiatio	
Heilung	begrenzte Tumorstadien	80-90 %
	fortgeschrittene Stadien	40-60 %
Rezidive	meist lokoregionär binnen 2-3Jahren	
Riskofaktor	Tumor >5cm, fixierter Tumor, Lymphknotenbefall	
ZV1	50-60 Gy in Abhängigkeit vom Tumorstadium	
ZV2	elektive Lymphknoten 36-45 Gy	

Grad 3/4 Toxizität

etwa 2/3 der Patienten benötigen eine Pause
Haut 50-75%, Darm 35-50%
IMRT Reduktion um die Hälfte

therapiebedingten Kolostomie

Spätfolge 5-10%
Korrelation mit Gesamtdosen > 55 Gy

Radiochemotherapie Phase III Fragestellung

Hämatotoxizität		60% 5/FU / MMC 10mg/m^2 d1+d29
Cancer specific mortality		40% durch Fernmetastasen
UK	ACT II	MMC durch DDP ersetzten
	2x2	adjuvante Chemotherapie 5FU/DDP
F	ACCORD 03	Induktionschemotherapie 5FU/DDP
	2x2	Boost ZVD intensivieren
USA	RTOG 98-11	MMC durch DDP ersetzten + Induktion

=> Colostomy failure rate
bedingt durch Progress, Rezidiv, Therapie

Radiochemotherapie 5-FU/Cisplatin – Phase III Design

Publikation	ACT II 2001-2008 2013, Abstr 2009	ACCORD 03 1999-2005 2012, Abstr 2009	RTOG 98-11 1998-2005 2012+2013, Abstr 2008
n	940, 25% aller Pat.	307	644
Stadium	cT1-4 cN0-2	cT2≥4cm, cTx cN+	cT2-4
Induktions-CHX		2x 5-FU800 / DDP80 vs. nihil	2x 5-FU1000 / DDP75
simultane RCT	DDP60 d1+d29 vs. MMC 12 d1 5-FU1000 d1-4+d29-32	2x 5-FU800 / DDP80	2x 5-FU1000 / MMC10 vs. 2x 5-FU1000 / DDP75
adj. CHX	2x DDP/5-FU vs. nihil		
elektive RTX	30,6 Gy GGF	45 Gy 3D/GGF	30,6 Gy 36 Gy 45Gy
obligate Pause		3 weeks	
Zielvolumen-dosis	50,4 Gy (19,8 Gy 3D)	60 Gy 65-70 Gy, v.a.BT	55-59Gy T3-4, N+, PR

Radiochemotherapie 5-FU/Cisplatin – Phase III Daten

	ACT II DDP vs MMC +/- adj CHX	ACCORD-03 +/- ICT +/- HDRT	RTOG 98-11 ICT DDP vs MMC
age	25% >65y	- 80y	- 88y
follow up	median 5y	median 5y	median 10y
endpoint	CR week 26	colostomy free survival	DFS
full CHX	sim. RCT 75%, 75% adj. CHX 41%, 46%	93-95% ICT 79-82% RCT after ICT 94-98% RCT alone	94% 95%
full RTX	91%, 92% no gap 75%, 78%	100% Boost 96%	88% 91% no gap 38%
Tox 3-4°	hem 16%, 26% other 17%,18%	17% ICT 37% RCT after ICT 29% RCT alone	hem 42 vs 61% p=.001 other 74%

Radiochemotherapie 5-FU/Cisplatin – Phase III

5 Jahres Daten	ACT II DDP vs MMC +/- adj CHX	ACCORD-03 +/- ICT +/- HDRT	RTOG 98-11 ICT DDP vs MMC
CR	week 26 89% 90% adj CHX 95% 94%	week 8 79%	
Subgruppen	DFS T1-2 83-80% T3-4 62-67% N- 76% N+ 68%	*LC 80/96/90/87%*	*LRF 26% 20% p=.087* *DM 18% 13%*
DFS	69% 69% adj CHX 70%	ICT-LD / HD 70% / 78% CRT-LD / HD 67% / 68%	58% 68% p=.006
colostomy free survival	67% 68%	ICT vs RCT 77% vs 75% RT vs HDRT 74% vs 78% ICT-LD vs HD 70% vs 82% CRT-LD vs HD 77% vs 73%	65% 72% p=.05
OS	77% 79%	ICT 74% CRT 71% p=.43	71% 78% p=.03

ACT II, EXTRA 2009 (UK)

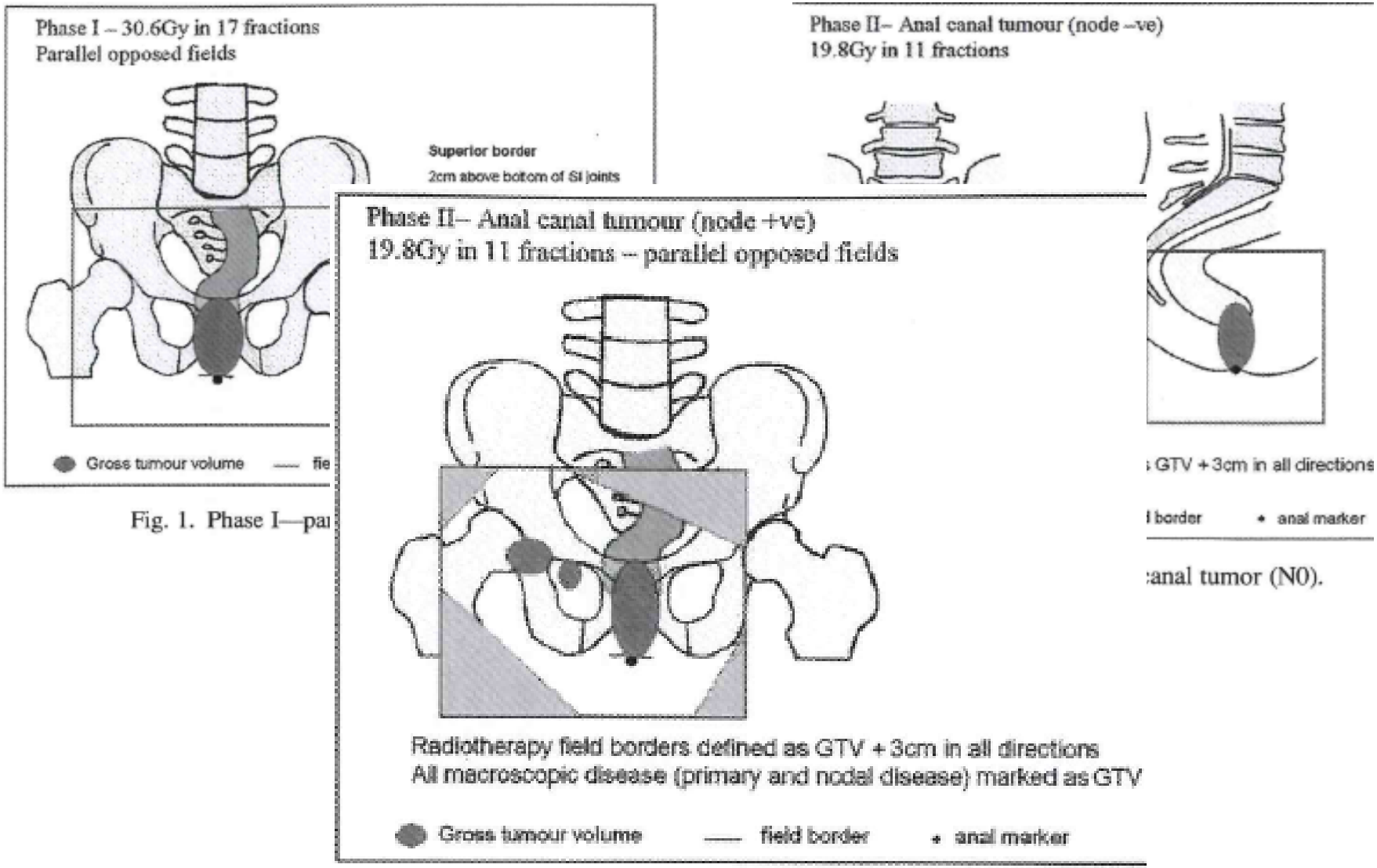


Fig. 1. Phase I—pa

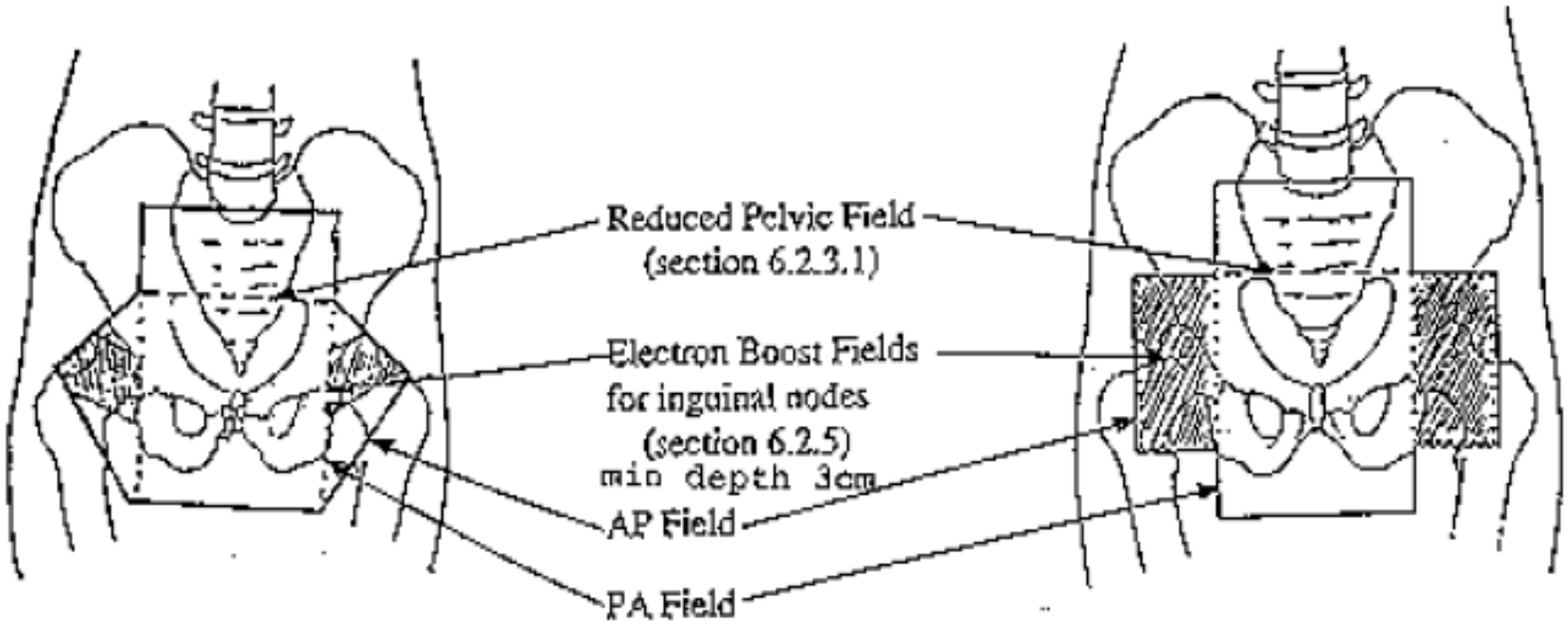
anal tumor (N0).

Fig. 3. Phase II—anal canal tumor (N+ve).

RTOG 98-11 Ajani 2008

Figure 1

Figure 2



Figures 1 & 2: Examples of acceptable AP/PA fields for N0 or N+ patients. The pelvis, anus, perineum and inguinal lymph nodes will be treated with either AP-PA fields or a 4-field *(Figures 3 & 4)* technique to include lateral inguinal nodes within AP/lateral fields but not PA field. Patient lies supine with a full bladder. Superior border reduced at 30.6 Gy level to level SI joint.

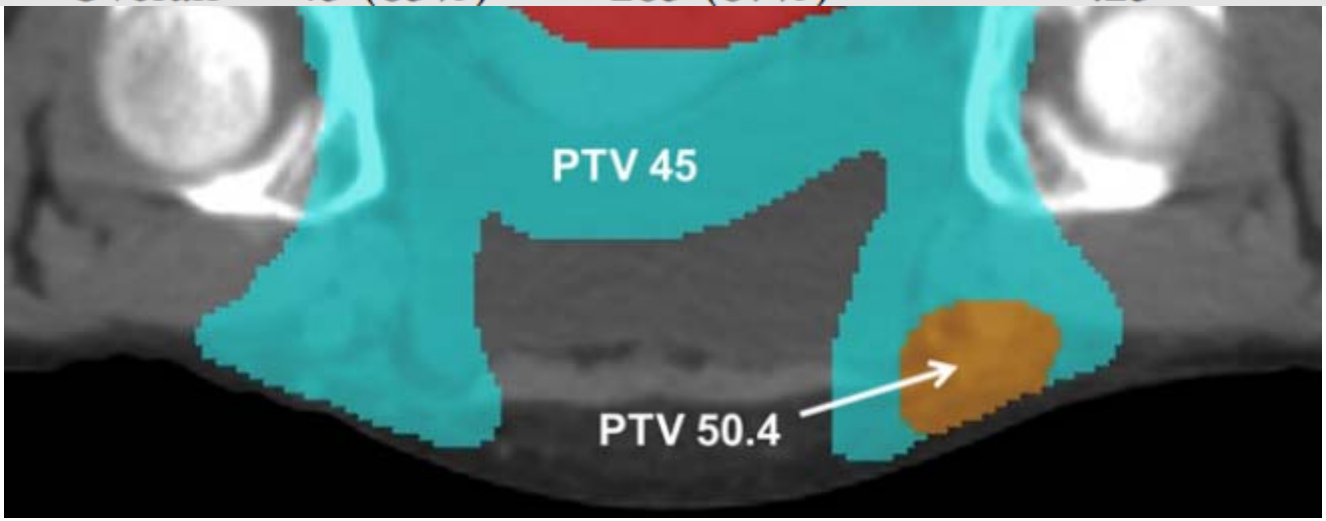
RTOG 0529 Phase II IMRT
fluenzmodulierte Strahlentherapie mit simultan integrierter boost

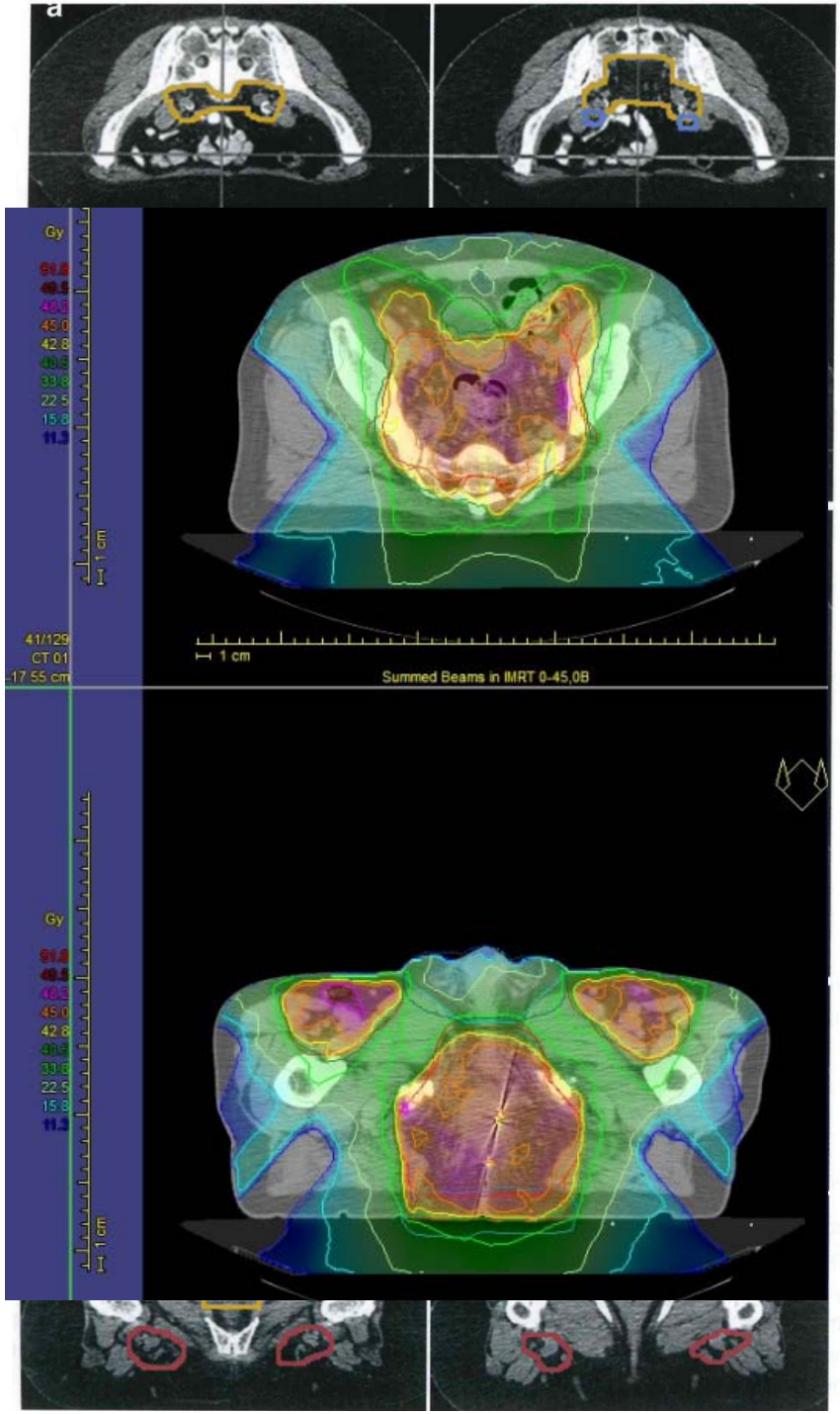
publ. 2013	12/2006 - 3/2008	
n	52/63 evaluable	
Stadium	T2-4 N0-3	
Radiochemotherapie	5 FU/MMC	
Zielvolumendosis	cT2 cN0	42 Gy elektiv 50,4 Gy makroskopischer Primärtumor (SIB)
	cT3-4 cN0-3	45 Gy elektiv 50,4Gy LK-Filia <3cm, 54 Gy LK Filia >3cm 54 Gy makroskopischer Primärtumor (SIB)
	no gap	
endpoint	reduce GI / GU Toxizität CTC ≥2°	≥15%
plan revision	80% replanning => guidelines	
gap	49% (RTOG 98-11 62%)	

RTOG 0529 Phase II IMRT

fluenzmodulierte Strahlentherapie mit simultan integrierter boost

Adverse events	0529 (n=52)	98-11 (Arm 1[†]) (n=325)	(1-sided proportions test[§])
Grade 3+			
GI/GU	11 (21%)	120 (37%)	.0052
Derm	12 (23%)	159 (49%)	<.0001
GI	11 (21%)	117 (36%)	.0082
GU	1 (2%)	11 (3%)	.32
Heme	30 (58%)	201 (62%)	.29
Overall	43 (83%)	283 (87%)	.23





OSP Stuttgart Leitlinie

NCCN consider PET/CT Staging cT2-4 cN+

RTOG consensus elective CTV

ZVD in Abhängigkeit vom Tumorstadium

elektive Lymphknotenstation	36,0-45,0 Gy
befallene LK-Station	50,4-60,0 Gy
Primärtumor	50,4-60,0 Gy

Supportivtherapie vermeidet Pausen

therapiebedingte Kolostomierate 5-10%
Korrelation mit Gesamtdosen >55 Gy

Brachytherapie boost
verbessert LC bei cT1-4 cN0-1

Interdisziplinäres follow up