



MSc Medizinische Strahlenwissenschaften Radioonkologie Lungenkrebs

D. Zips

Universitätsklinik für Radioonkologie Tübingen

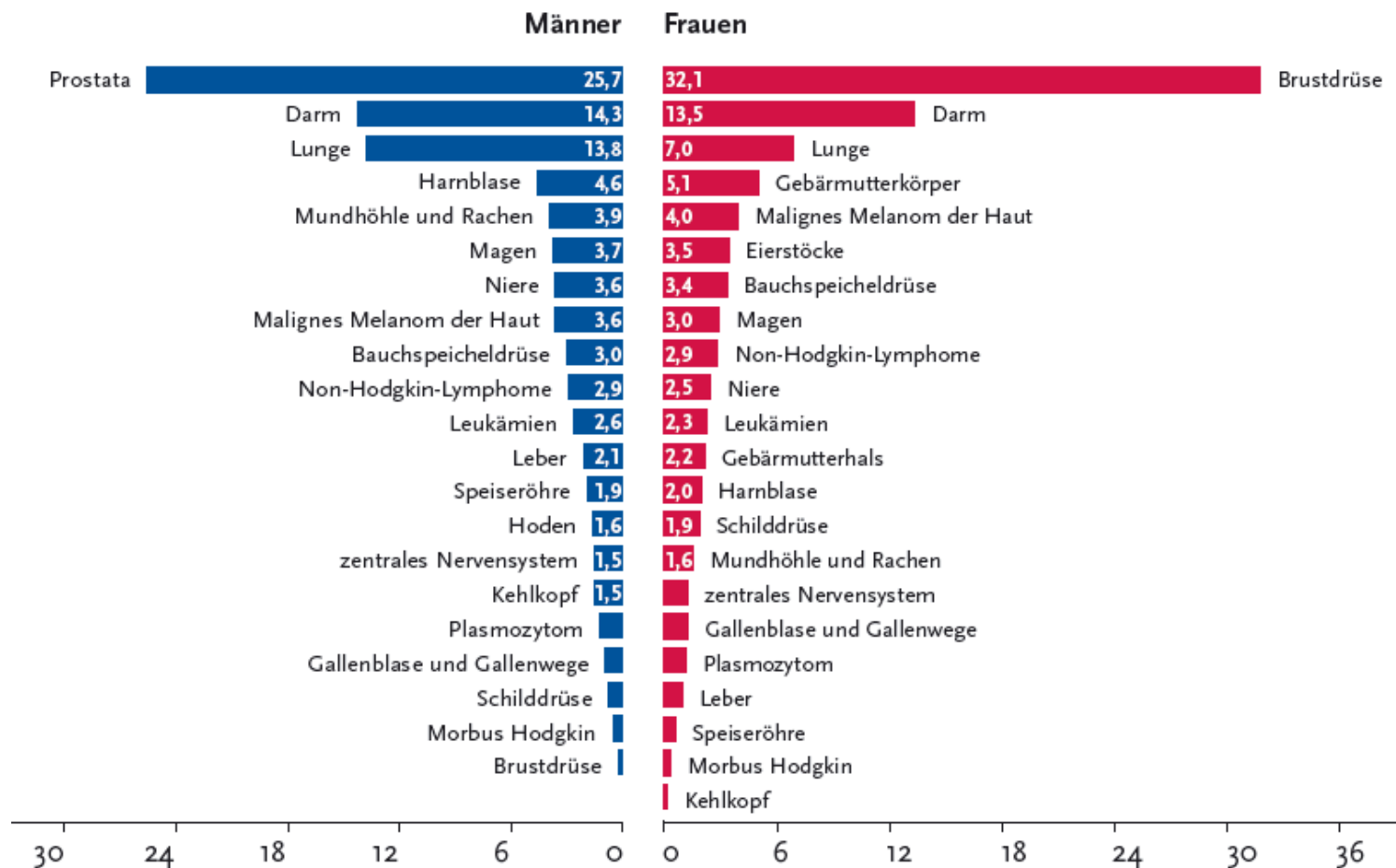


Lernziele Lungenkrebs

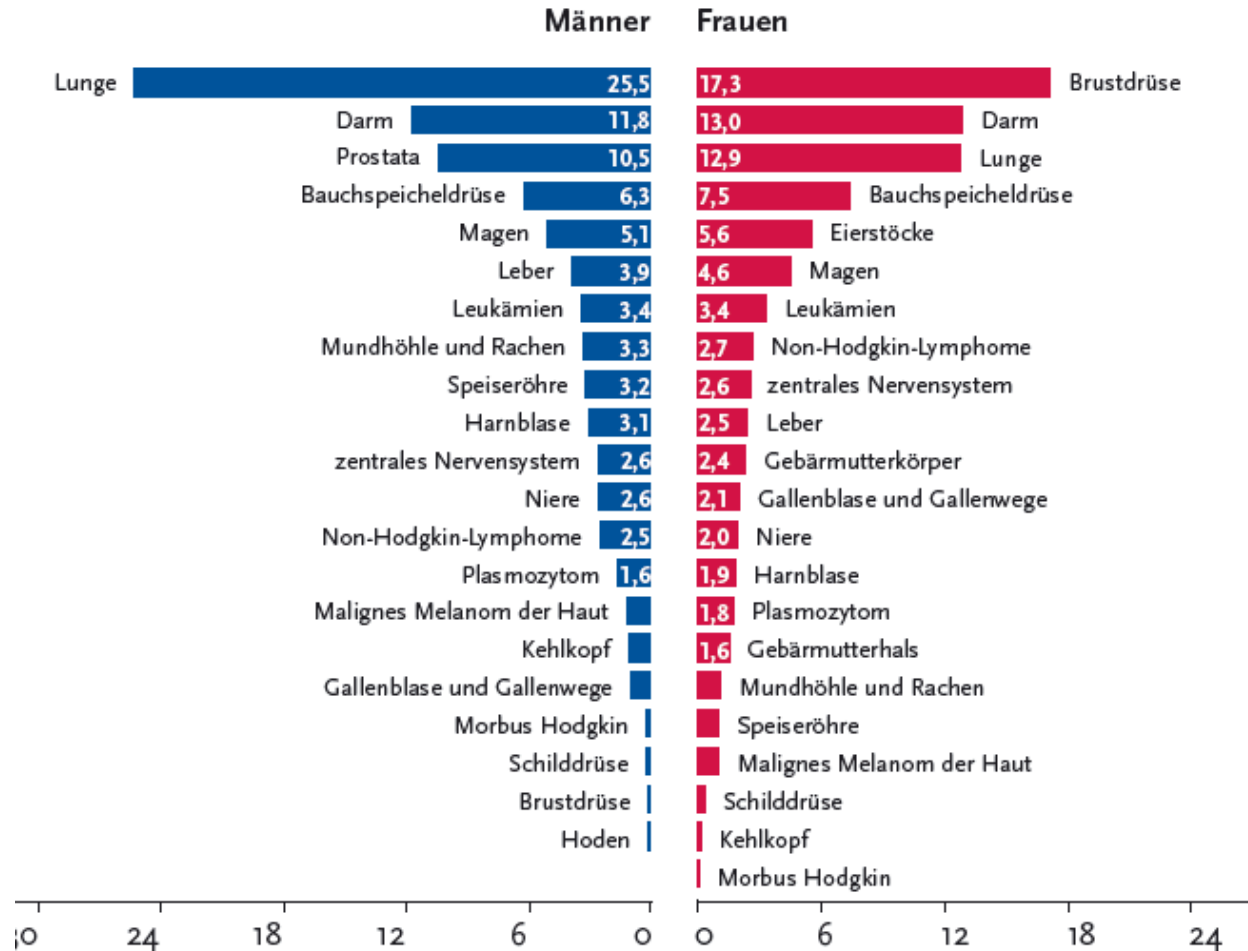
- Häufigkeit
- Therapieprinzipien
- Strahlentherapie-Indikationen, Ergebnisse
- Strahlentherapiedosis
- Grundlagen der Bestrahlungsplanung
- Nebenwirkungen



Neuerkrankung: 470.000/ Jahr



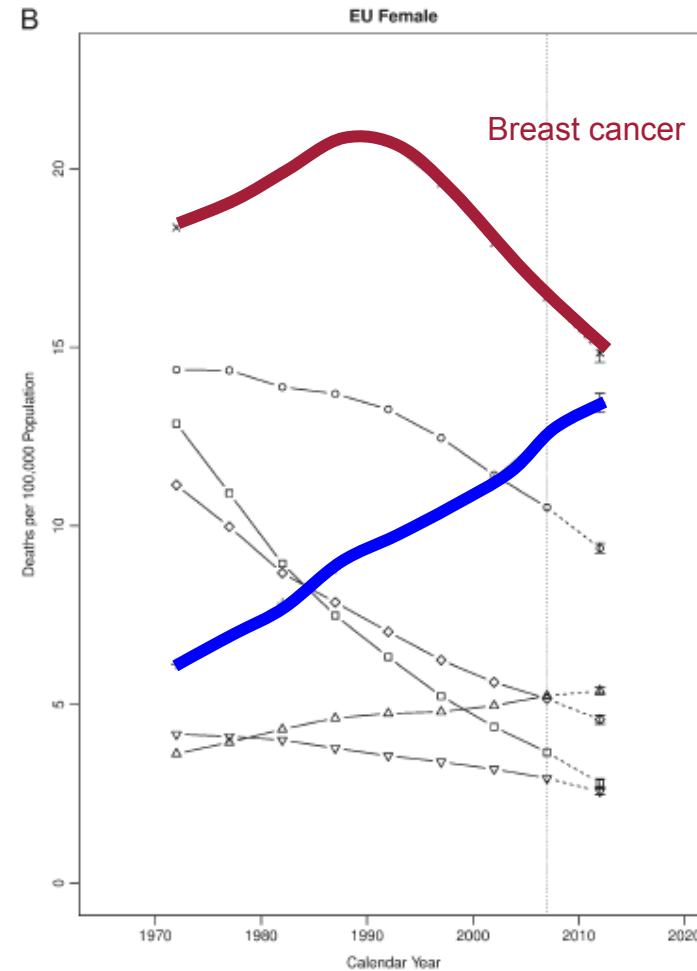
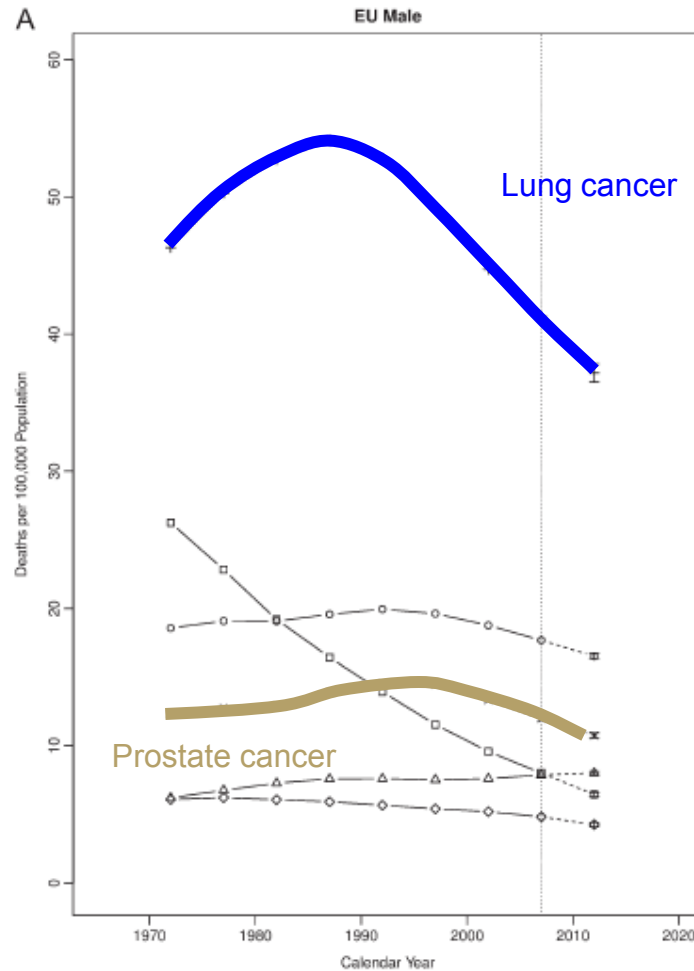
Krebssterbefälle: 215.000/Jahr



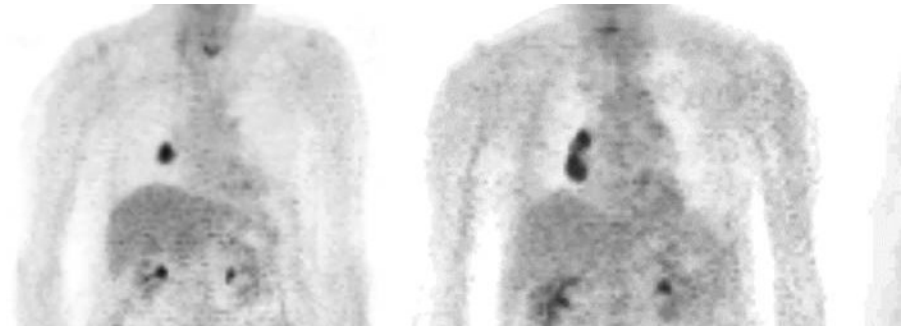
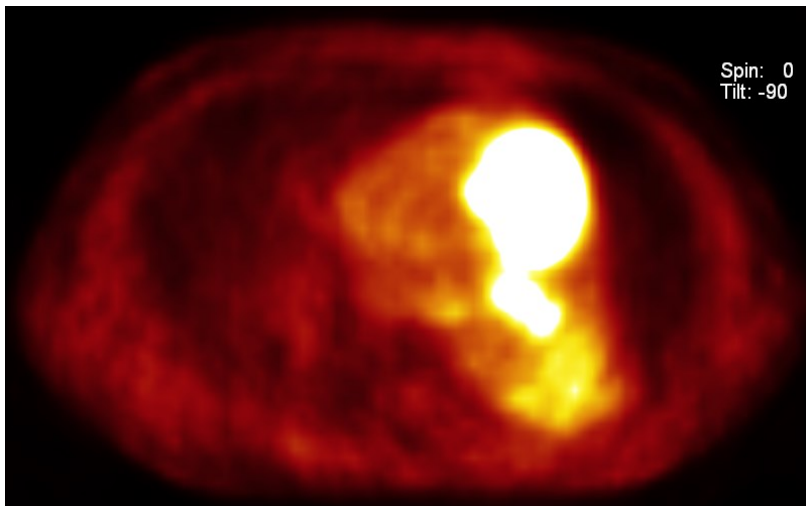
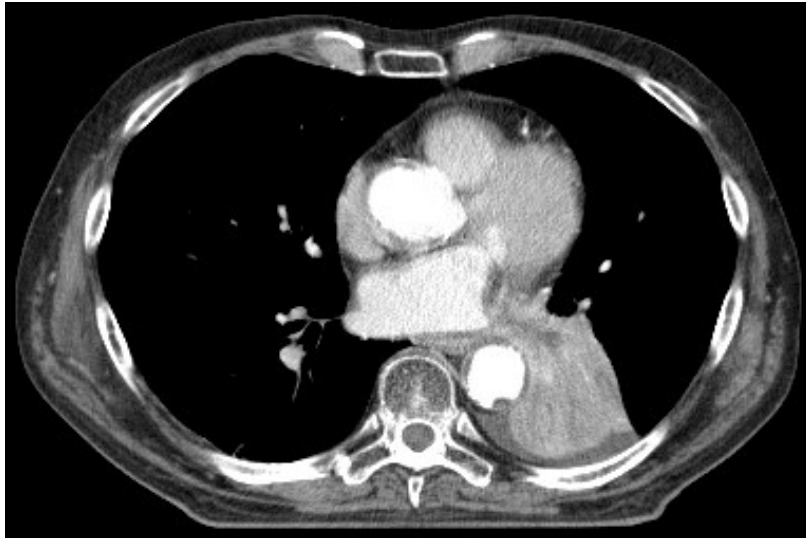
Krebs in Deutschland 2007/2008, RKI 2012



Lung cancer

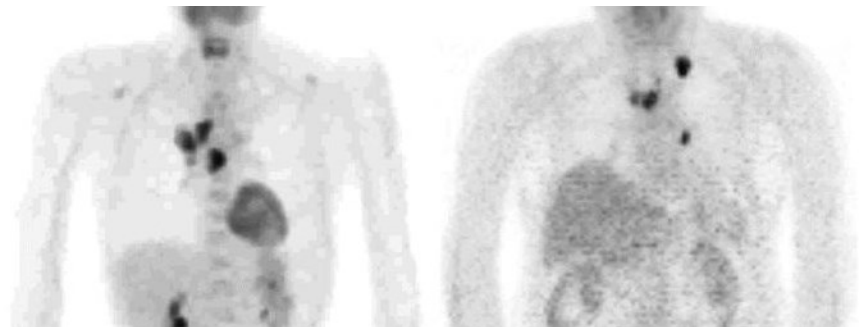


FDG PET/CT for treatment planning



N0

N1



N2

N3



Stadienadaptierte Therapie: Lungenkrebs

Stadium IA	T1N0M0	kurativ: OP sonst (CTx)RT
Stadium IB	T2N0M0	
Stadium IIA	T1N1M0	
Stadium IIB	T2N1M0	
	T3N0M0	
Stadium IIIA	T1-2N2M0	kurativ: (CTx)RT, OP+RT, CTx(RT) +OP
	T3N1-2M0	
Stadium IIIB	T4 u./o. N3M0	palliativ: CTx, RT
Stadium IV	M1	palliativ: CTx, RT

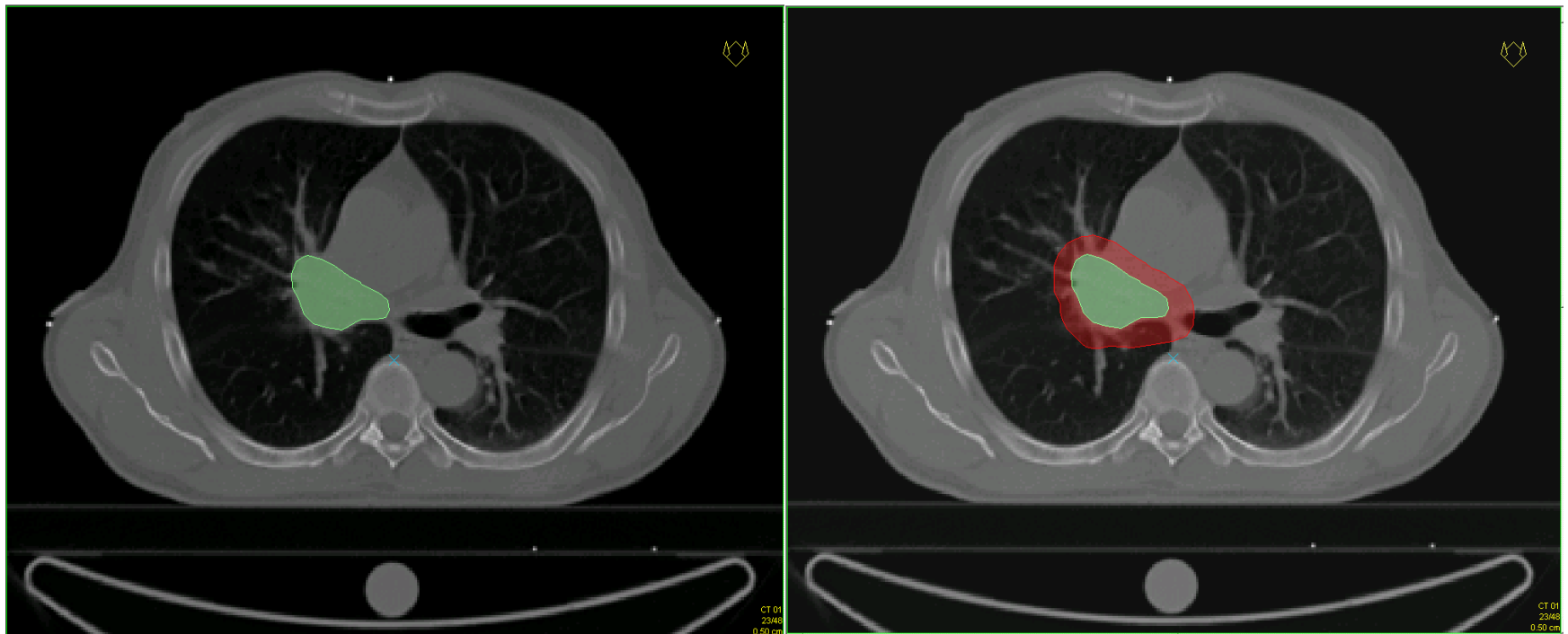
Prinzipien der Bestrahlungsplanung

Festlegung der Lagerung/ Immobilisation



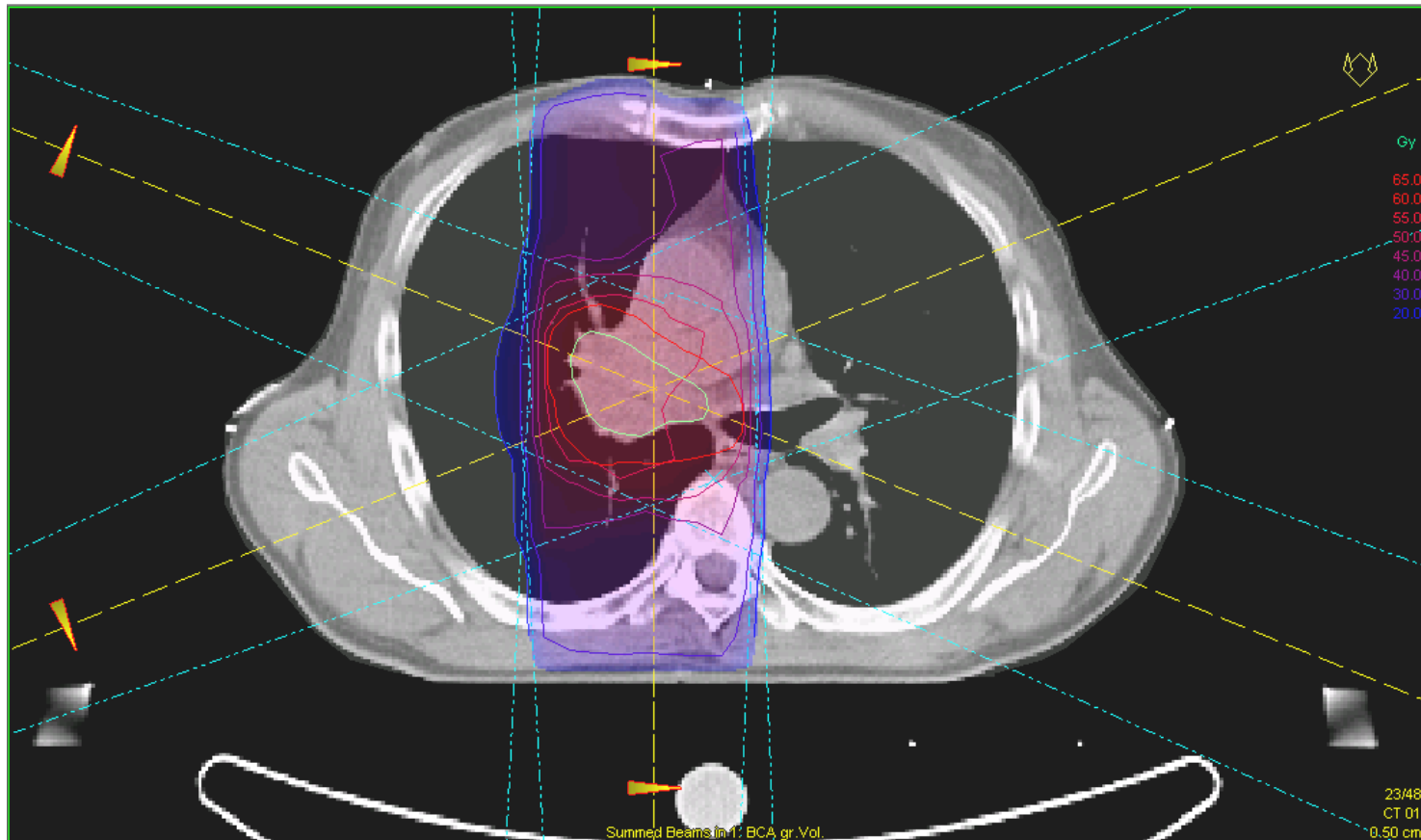
Prinzipien der Bestrahlungsplanung

Festlegung der Zielvolumina im Planungs-CT



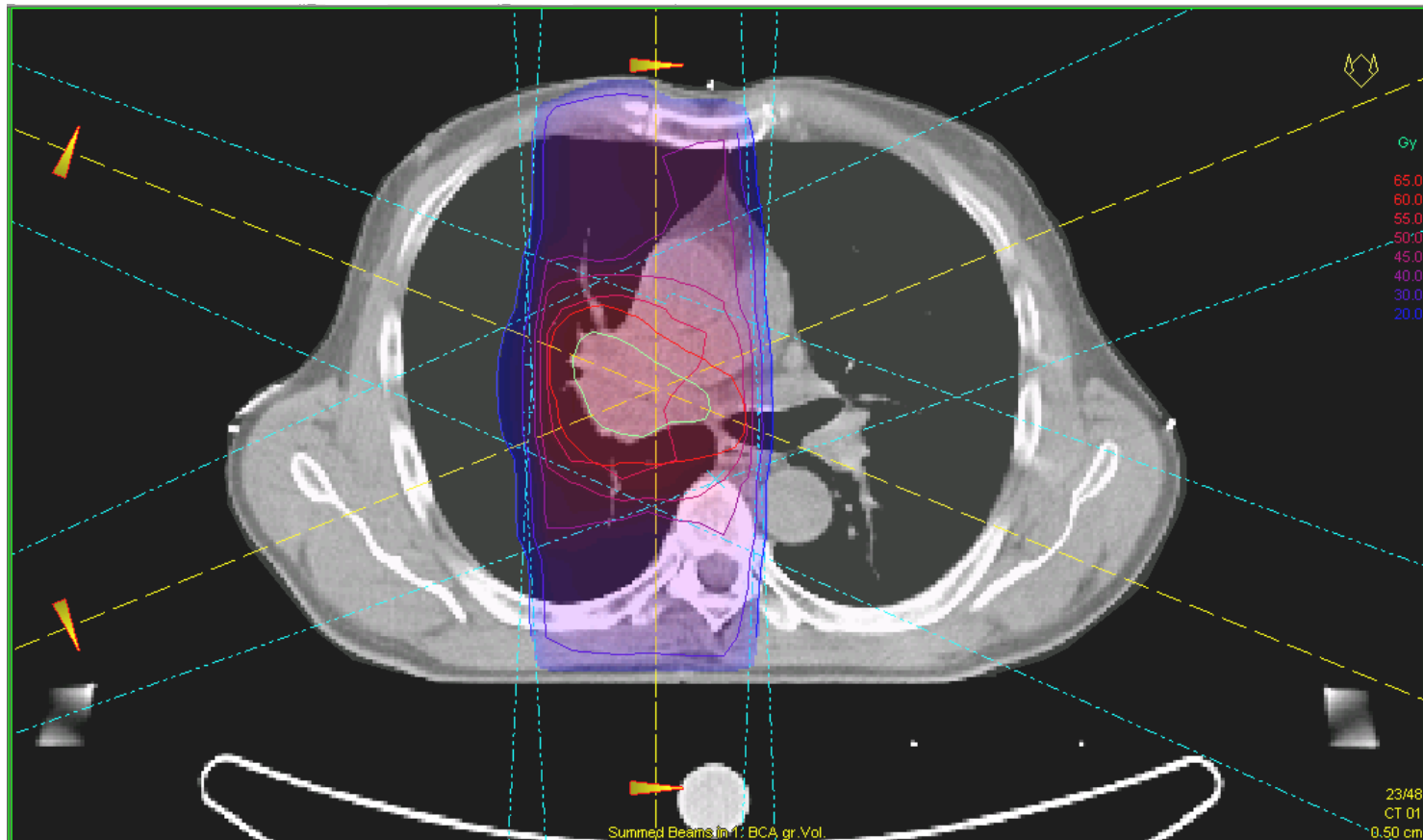
Prinzipien der Bestrahlungsplanung

Festlegung der Bestrahlungsfelder



Prinzipien der Bestrahlungsplanung

Festlegung der Bestrahlungsfelder/ Optimierung





Strahlentherapie NSCLC: Indikation

postoperativ

- R1/2-Resektion
- pN2/3

primär (+CTx)

- Inoperabilität
- Palliation



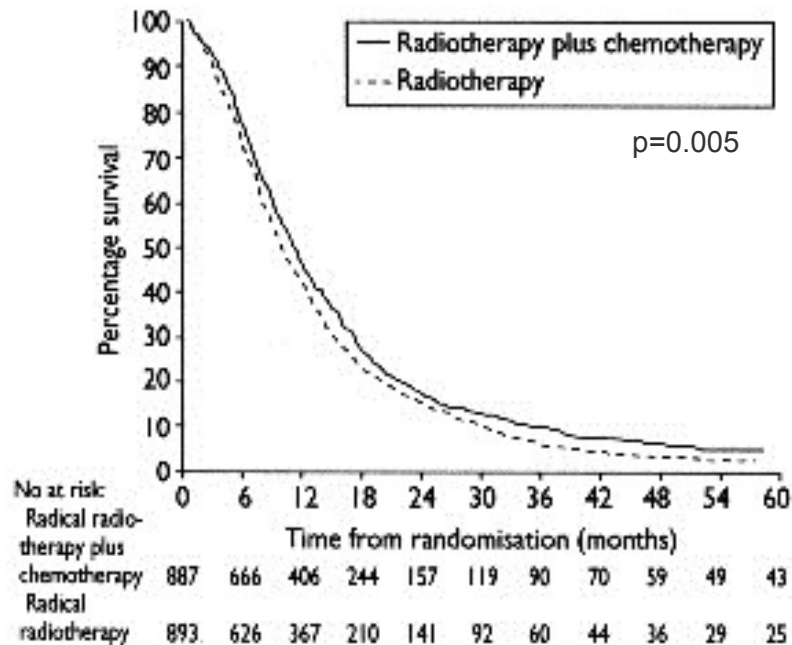
Strahlentherapie NSCLC

Konventionelle Therapie

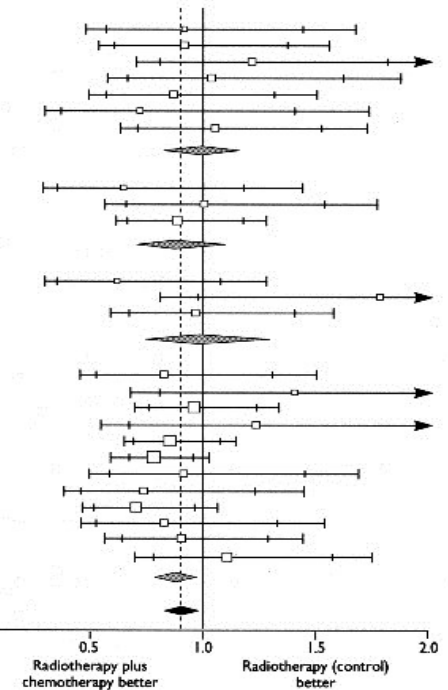
- Dosis 60-70 Gy
post-OP 50Gy
- D/fx 1.8-2.0 Gy
1fx/d, 5fx/w
- Dauer 6-7 w
- 3D-CT-Planung



RTx vs RTx/CTx Metaanalyse

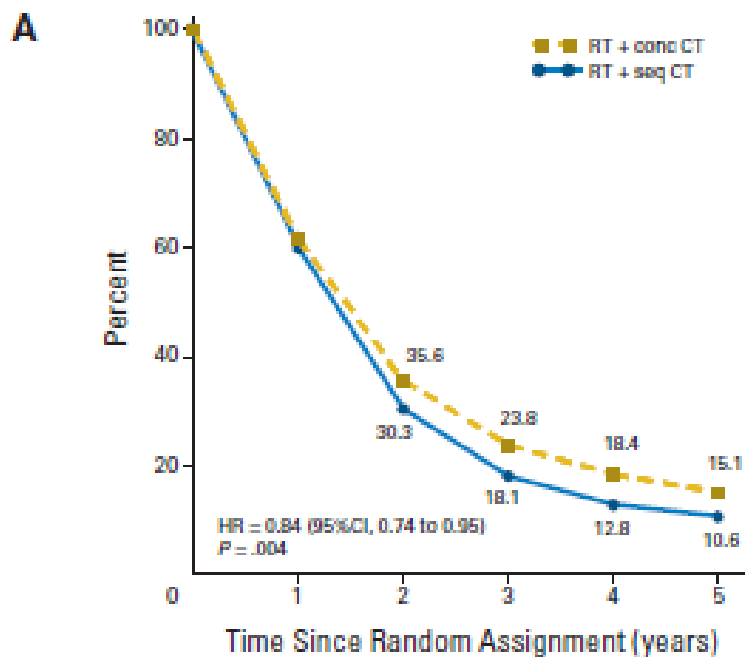


Trial	No of events/ No of patients entered		Observed - expected deaths	Variance
	Radiotherapy plus chemotherapy	Radiotherapy		
Long term alkylating agents:				
NRH NSC-26271	36/36	38/38	-1.63	17.55
EORTC 08742	45/53	51/64	-1.91	23.36
RTOG 7302a	52/55	48/56	4.58	23.23
RTOG7302b	38/46	43/50	0.84	19.31
RTOG7302c	38/47	53/57	-3.08	22.19
MCL-I	16/25	19/27	-2.79	8.49
Aviano	47/49	61/62	1.15	26.09
Subtotal	272/311	313/354	-2.83	140.23
Vinca alkaloids/etoposide:				
AZ-OC-1-80	22/27	23/25	-4.56	10.35
Gwent 3	40/41	43/44	-0.06	20.25
SECSG 81 LUN375	94/107	97/105	-5.94	47.21
Subtotal	156/175	163/174	-10.55	77.80
Other drugs:				
Gwent 1	23/26	30/30	-6.11	12.47
SWOG 7635	25/30	23/32	6.04	10.44
NCCTG 822451	54/58	59/63	-1.03	28.04
Subtotal	102/114	112/125	-1.10	50.95
Cisplatin based:				
Buenos Aires	43/43	35/38	-3.57	18.26
Brussels	25/31	29/34	4.18	12.31
FLCSG 2	124/125	126/127	-2.49	62.14
Essen	21/22	22/26	2.09	9.80
SLCSG	159/163	161/164	-12.39	77.92
CEBI 138	166/176	173/177	-21.95	82.68
WSLCRG/FI	37/40	35/39	-1.61	17.82
Perugia	32/33	32/33	-4.45	14.84
CALGB 8433	73/89	80/91	-13.39	37.13
EORTC 08842	36/38	37/37	-3.23	17.70
SWOG 8300a	62/64	62/64	-3.07	30.19
SWOG 8300b	63/63	63/63	2.81	30.38
Subtotal	841/887	855/893	-57.08	411.18
Total	1371/1487	1443/1546	-71.56	680.16

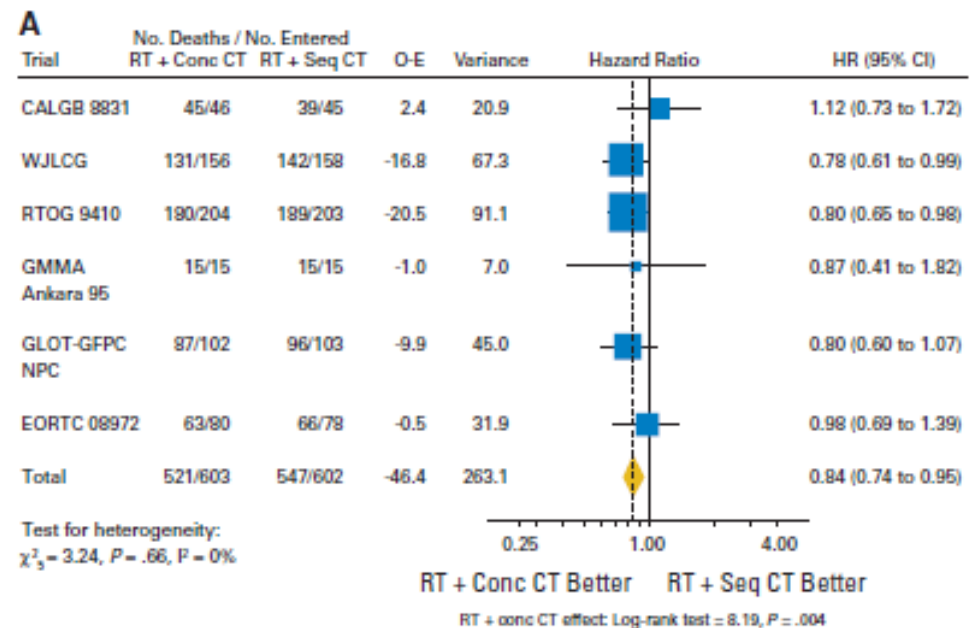


NSCLC Collaborative Group
BMJ 311: 899 (1995)

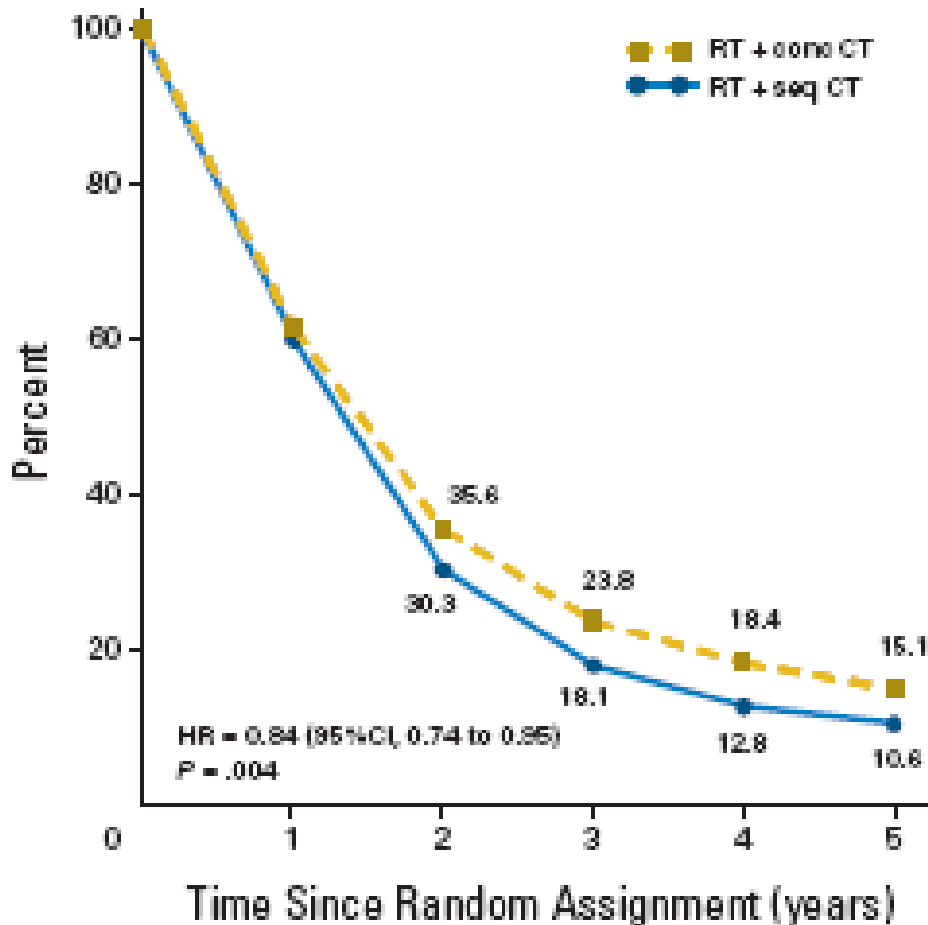
Metaanalyse RCTx NSCLC simultan vs. sequentiell



	Deaths/Person-Years by Period				
	0y-1y	1y-2y	2y-3y	3y-4y	> 4y
RT+ conc CT (n = 603)	240/498	147/276	67/171	30/116	37/186
RT+ seq CT (n = 602)	253/491	171/242	70/129	30/83	23/126



Metaanalyse RCTx NSCLC simultan vs. sequentiell



OS

HR 0.84 [0.74;0.95], p=0.004

5.7% at 3 yrs

Loco-regional control

HR 0.77 [0.62;0.95], p=0.01, 6% at 3 yrs

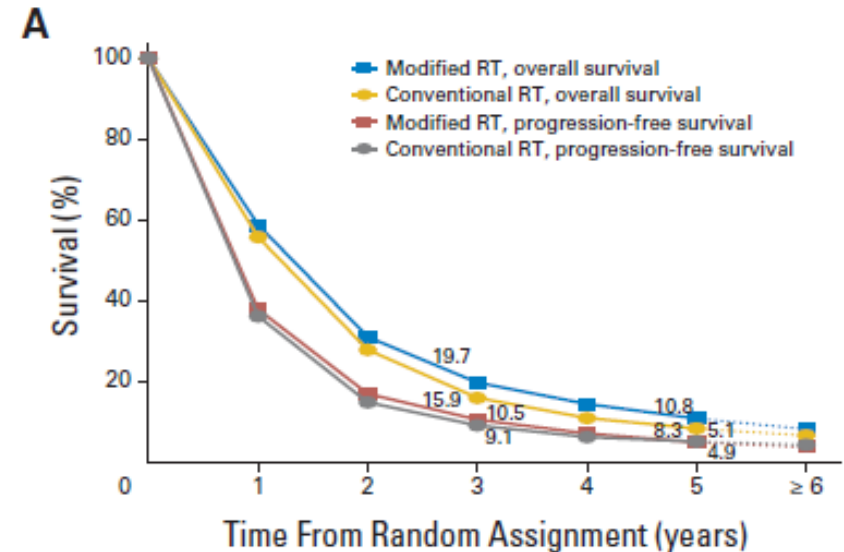
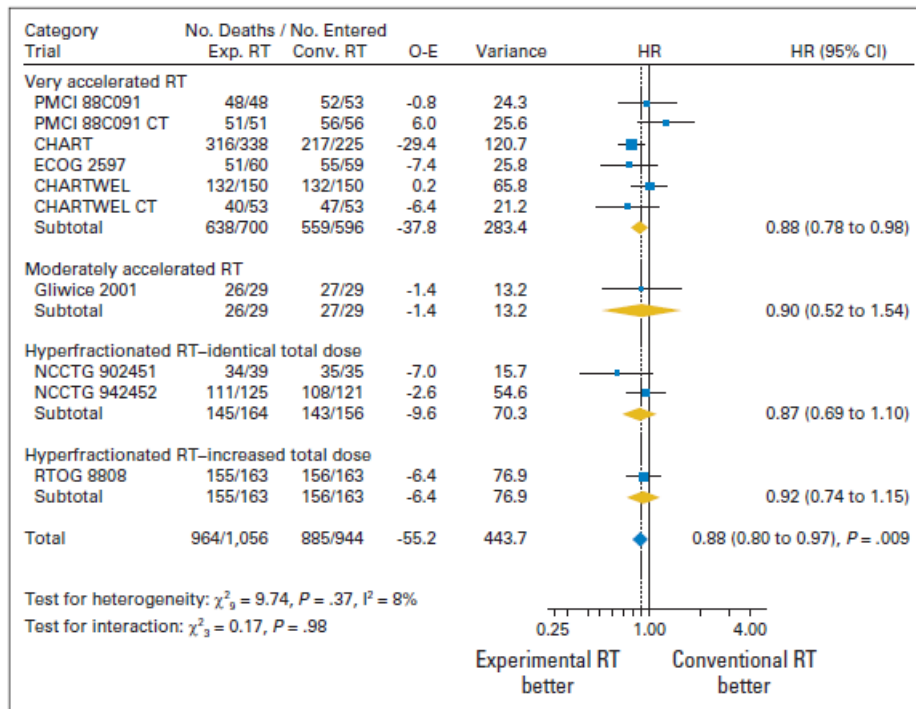
DM

HR 1.04 [0.86;1.25], p=0.69

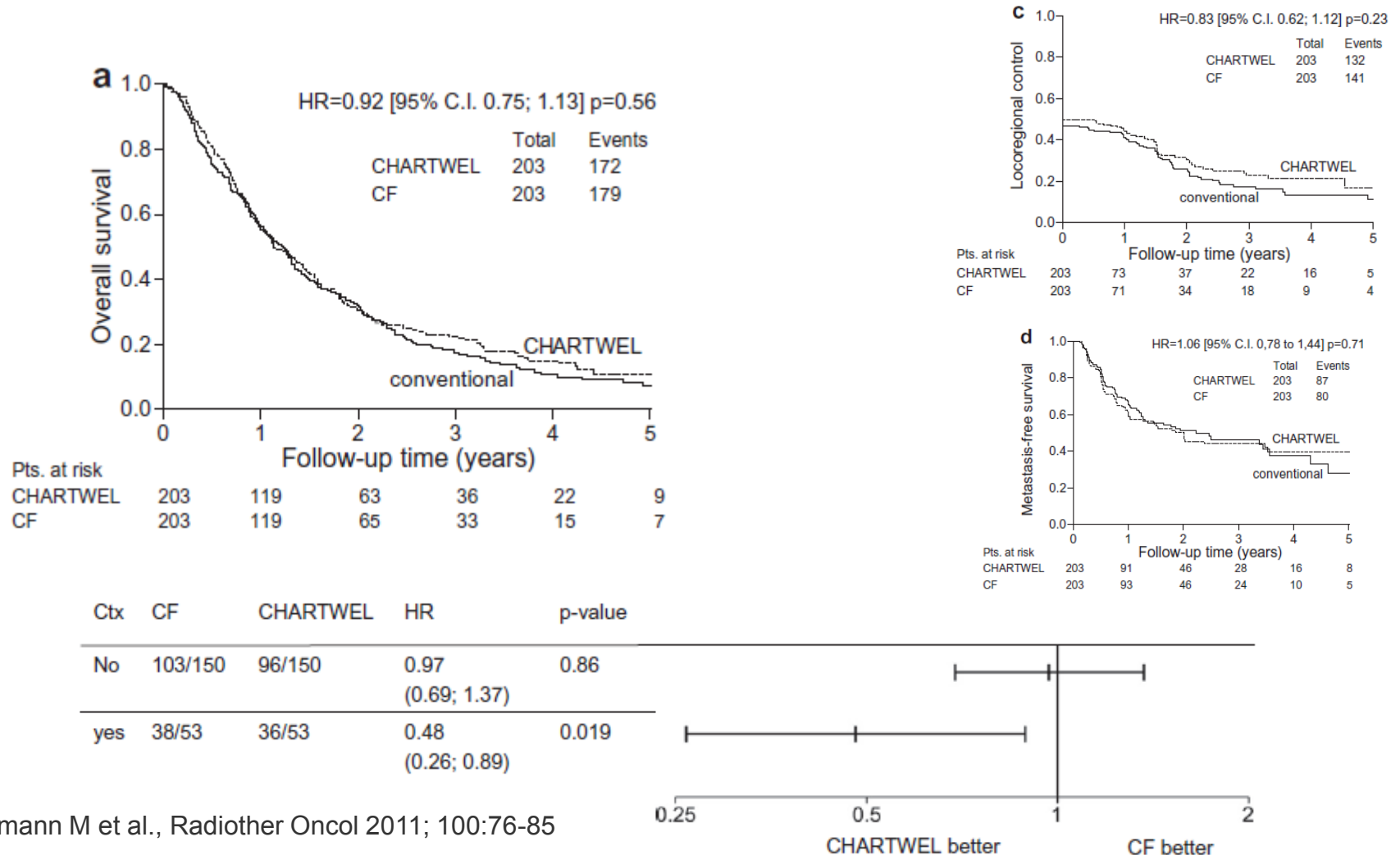
39.5 vs 39.1% at 3 yrs

Higher toxicity with conc CRT

Modifizierte Fraktionierung NSCLC



Modifizierte Fraktionierung NSCLC: CHARTWEL



Strahlentherapie SCLC: Indikation

kurativ

- Stadium limited disease (=M0)
- Immer CTx + (+OP) +RTx

palliativ

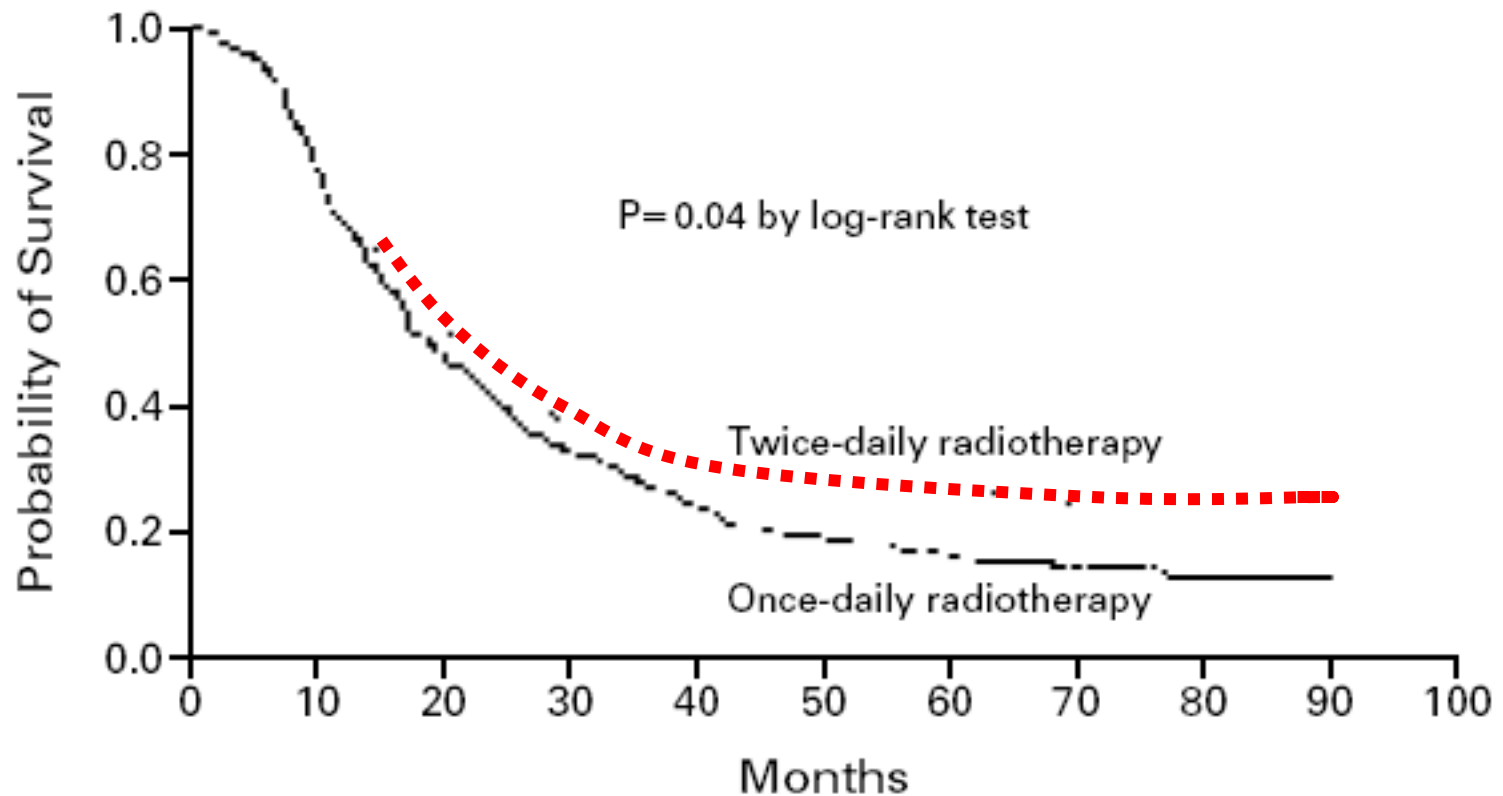
- RTx bei Symptomatik



Radiochemotherapie beim SCLC

- Dosis 45-60 Gy
- Dosis/Fraktion 1.5-2.0 Gy
1 Fraktion oder 2 Fraktionen/d
- Therapiedauer 3-6 Wochen
- Planung PET/CT-Planung, 3D-konformal, Tumor und Lymphabfluß
- Hirnbestrahlung prophylaktisch 30 Gy/ 3W

Radiochemotherapie beim SCLC: Ergebnisse



TREATMENT GROUP	0–20 Mo	20–40 Mo	40–60 Mo	60–80 Mo	80–100 Mo
	no. of deaths/no. at risk				
Once daily	108/206	48/96	15/47	4/21	0/5
Twice daily	100/211	47/109	7/62	5/42	1/14



SBRT im Stadium I NSCLC

5 Zentren, n=483 Pat., 78% inoperable, 64% histologisch gesichert, mittleres GTV 2.6cm (0.9-8.5 cm), 63% Stadium IA, 33% IB

2-Jahres-Ergebnisse	IA (T1N0M0)	IB (T2N0M0)
Lokale Kontrolle	96%	92%
Regionäre Kontrolle	90%	90%
Distante Kontrolle	85%	63%

7% $\geq$ Grad 2 Pneumonitis , 2% $\geq$ Grad 3 Pneumonitis, n=1 Grad 5 Pneumonitis, 8% Rippenfrakturen (5% Grad 1)

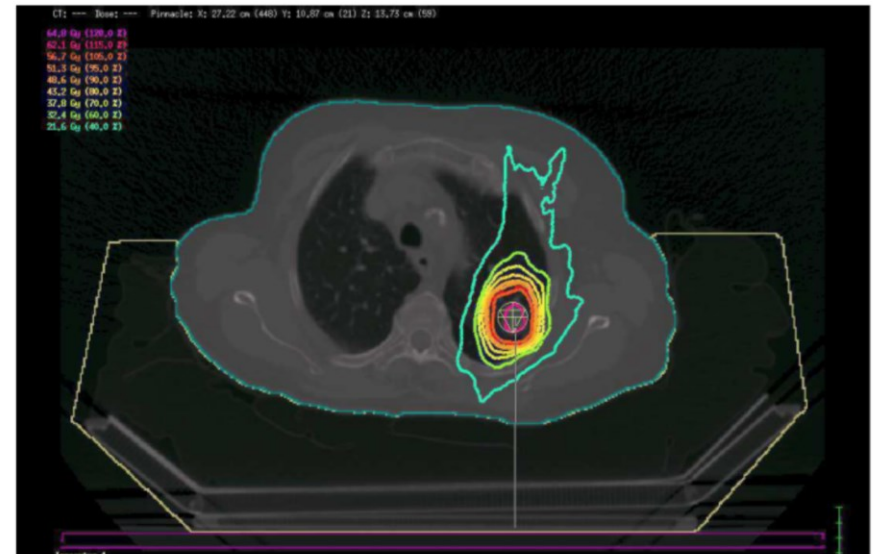
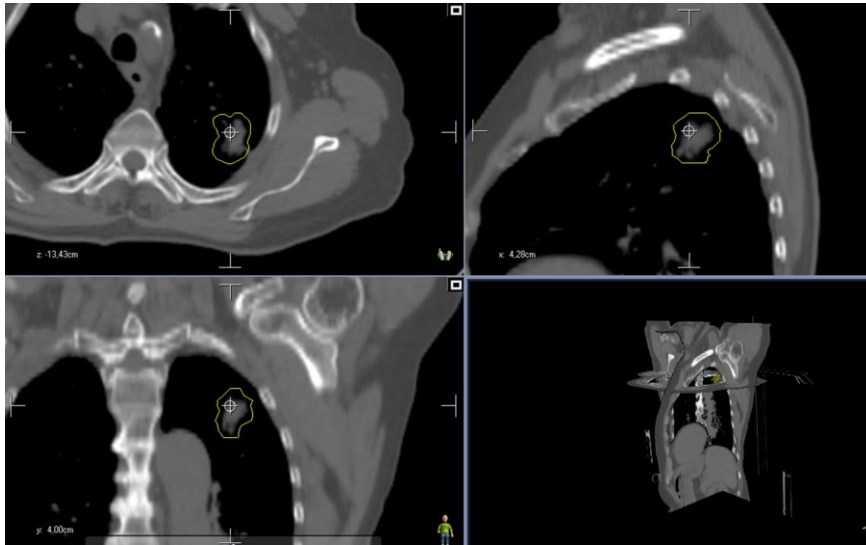
SBRT im Stadium I NSCLC

76 jährige Patientin, ED im Rahmen einer Lungenentzündung rechts, TTF1-positives Adenokarzinom, Stadium: cT1b (28 mm) cN0 cM0, FEV1 1.3 l, DLCOc SB 67%, Z.n. schwerer Pneumonie, pAVK, hypertrophe Kardiomyopathie, Polyarthrit, Z.n. Vulva-Ca, Z.n. MammaCa Therapie 3 x 18 Gy

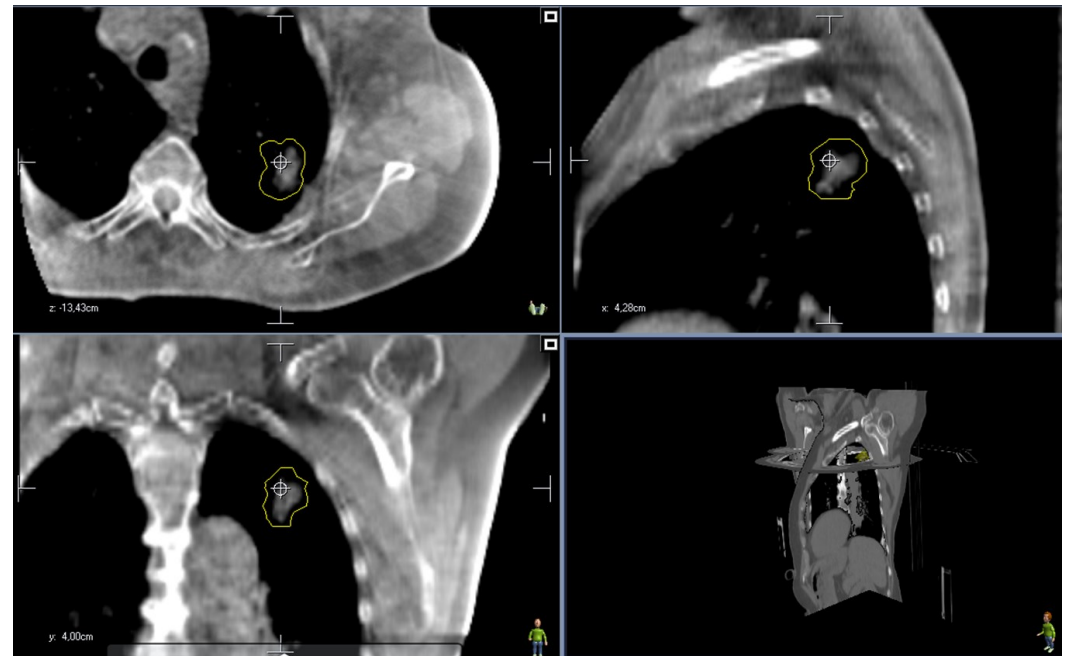


FDG-PET/CT
06/17

4D Planungs-CT/ VMAT-IMRT



4D Cone-Beam CT (4D-IGRT)





Strahlentherapie Lungenkrebs: Akute Nebenwirkungen

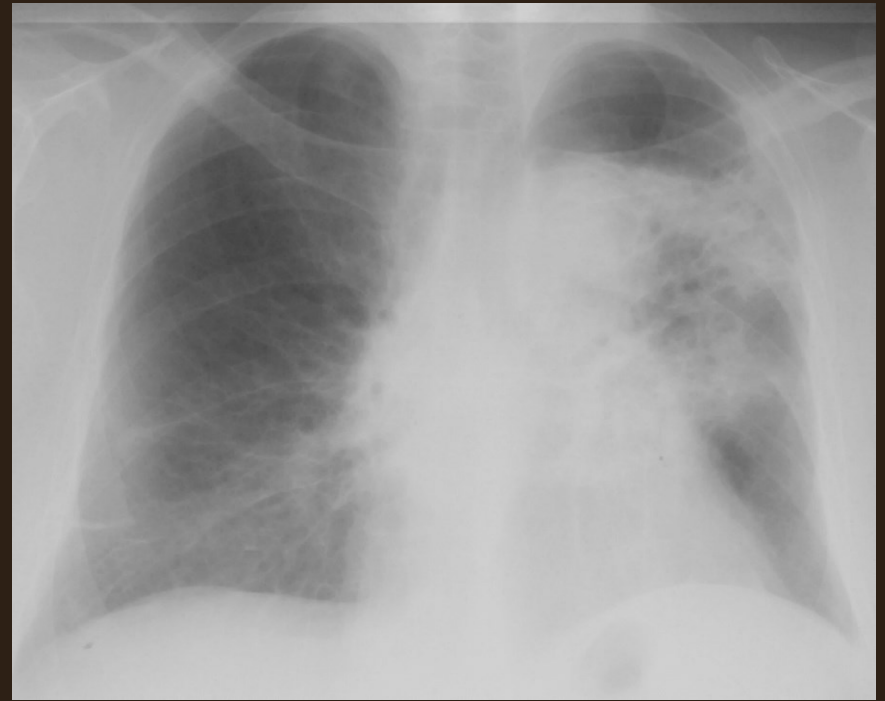
Haut	Erythem, feuchte Schuppung
Ösophagitis	Schluckbeschwerden, Inappetenz, Gewichtsverlust
Pneumonitis	Dyspnoe, Fieber, AZ ↓
Herz	Rhythmusstörungen

Radiogene Pneumonitis

vor RT



6 Wochen nach 66 Gy/ 2 Gy





Parameter der Strahlentherapie

- Feldgröße / DVH
- Fraktionierung
- Gesamtdosis
- Applikationsort der Dosis

Table 4. Incidence of radiation pneumonitis according to V_{dose} in patients treated with radiotherapy for lung cancer

Reference	Severity of pneumonitis	V_{dose}	Observed rate
Armstrong <i>et al.</i> , 1995 (45)	Grade ≥ 3	$V_{25} > 30\%$	38%
		$V_{25} < 30\%$	4%
Graham <i>et al.</i> , 1999 (46)	Grade ≥ 2	$V_{20} < 22\%$	0%
		$V_{20} 22\% - 31\%$	7%
		$V_{20} 32\% - 40\%$	13%
		$V_{20} > 40\%$	36%
Hernando <i>et al.</i> , 2001 (34)	Grade ≥ 1	$V_{30} < 22\%$	6%
		$V_{30} 22\% - 31\%$	24%
		$V_{30} 32\% - 40\%$	18%
		$V_{30} > 40\%$	29%
Claude <i>et al.</i> , 2004 (36)	Grade ≥ 1	$V_{10} > 33\%$	53%
		$V_{20} > 18\%$	56%
		$V_{30} > 13\%$	56%
		$V_{40} > 10\%$	56%
		$V_{50} > 5\%$	53%

QUANTEC: Quantitative Analysis of Normal Tissue Effects in the Clinic

- In the QUANTEC report, a mean lung dose ≤ 20 Gy is recommended to limit the incidence rate of pneumonitis in a population to $\leq 20\%$

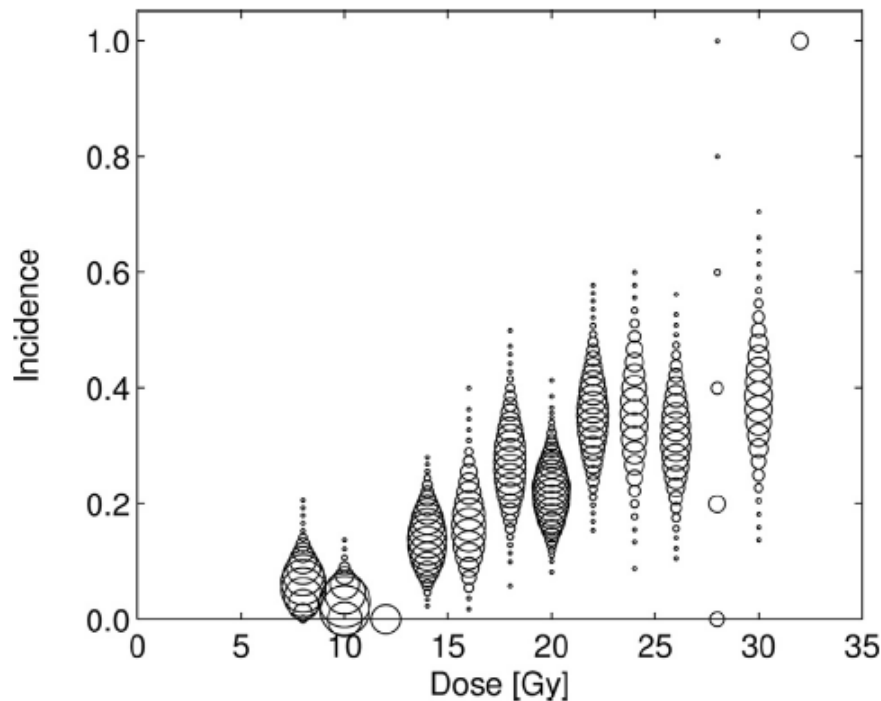


Fig. 2. The incidence rate calculated separately in each of the bootstrap replicates in 2-Gy bins for the pneumonitis data. The data points are weighted by the number of bootstrap occurrences and the number of patients in each dose bin.

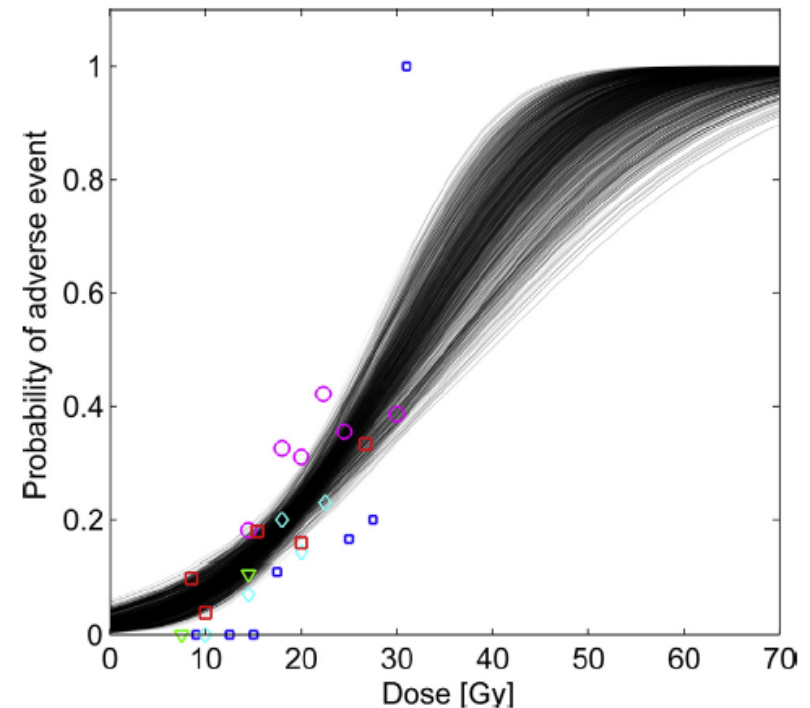
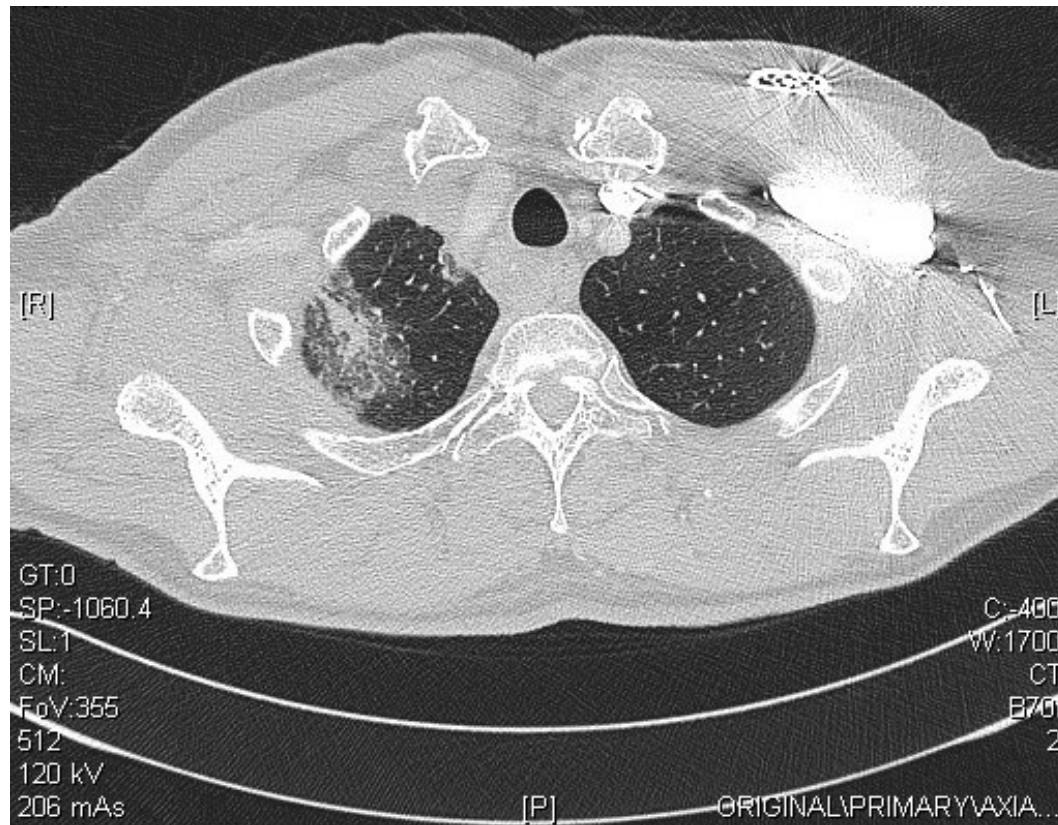


Fig. 3. Dose-response curves shown for $2 \cdot 10^3$ bootstrap replicates of the original pneumonitis incidence data. The Lyman dose-response model was used. The original data points are weighted by the number of patients, N : $N < 10$ blue squares, $10 \leq N < 20$ cyan diamonds, $20 \leq N < 30$ green triangles, $30 \leq N < 50$ magenta circles, $N \geq 50$ red squares.

Radiogene Pneumonitis



Strahlentherapie Lungenkrebs: Chronische Nebenwirkungen

Lungenfibrose

dauerhafte Schluckbeschwerden

erhöhtes Risiko für Herzinfarkt
