



MSc Medizinische Strahlenwissenschaften Radioonkologie Lungenkrebs

D. Zips

Universitätsklinik für Radioonkologie Tübingen

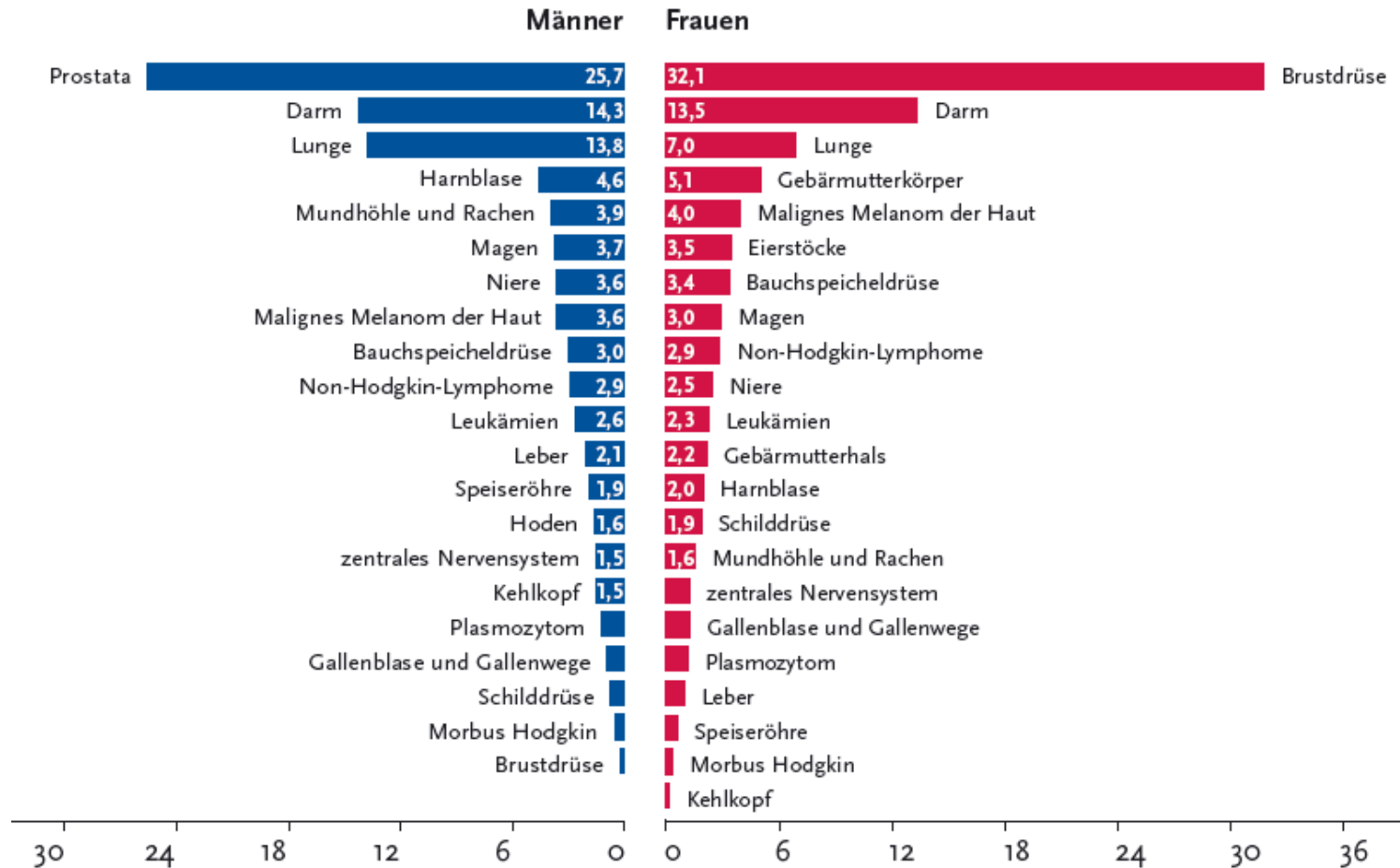


Lernziele Lungenkrebs

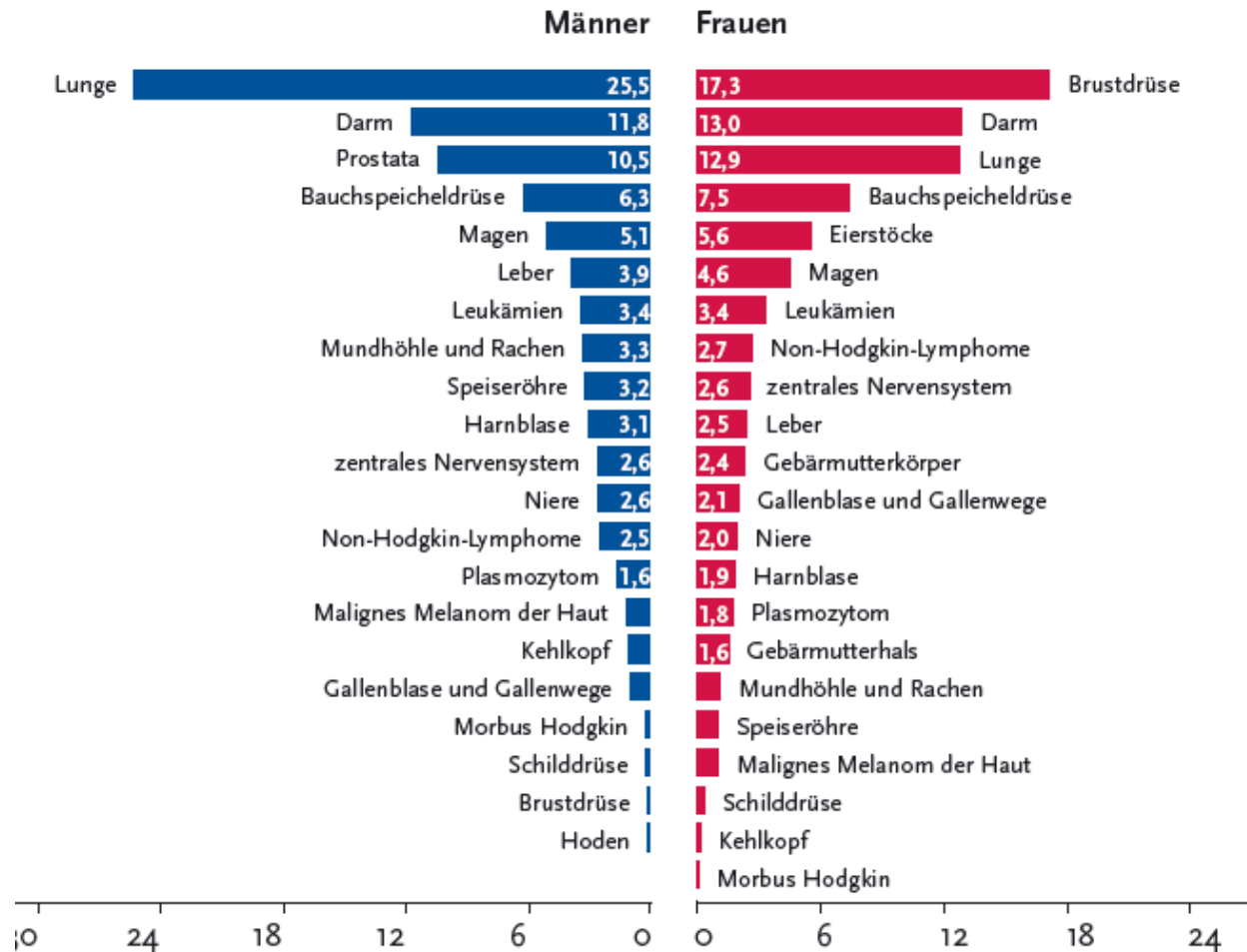
- Häufigkeit
- Therapieprinzipien
- Strahlentherapie-Indikationen, Ergebnisse
- Strahlentherapiedosis
- Grundlagen der Bestrahlungsplanung
- Nebenwirkungen



Neuerkrankung: 470.000/ Jahr



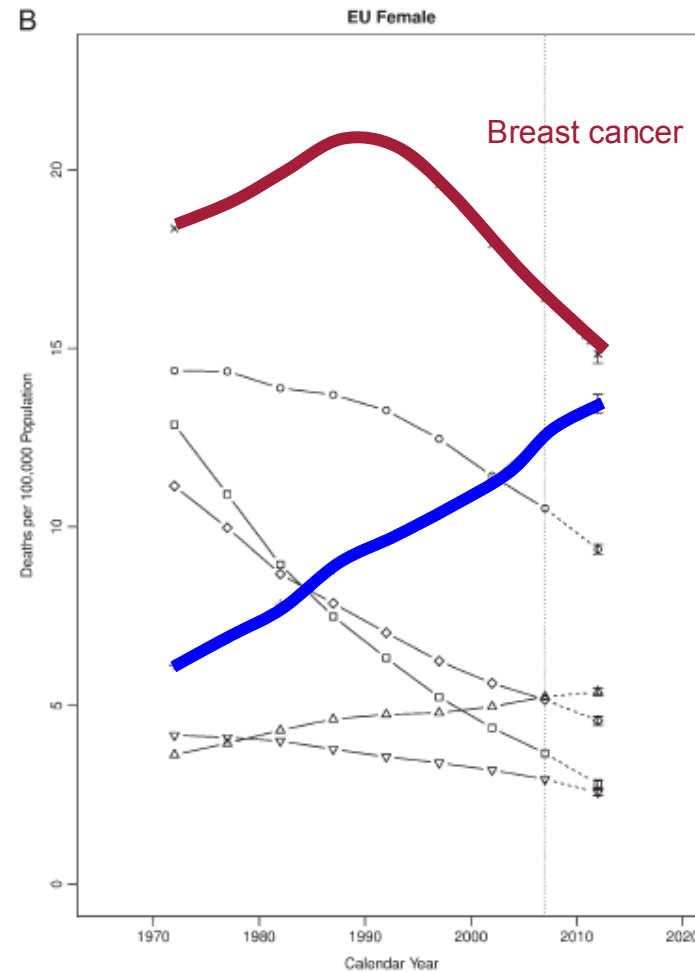
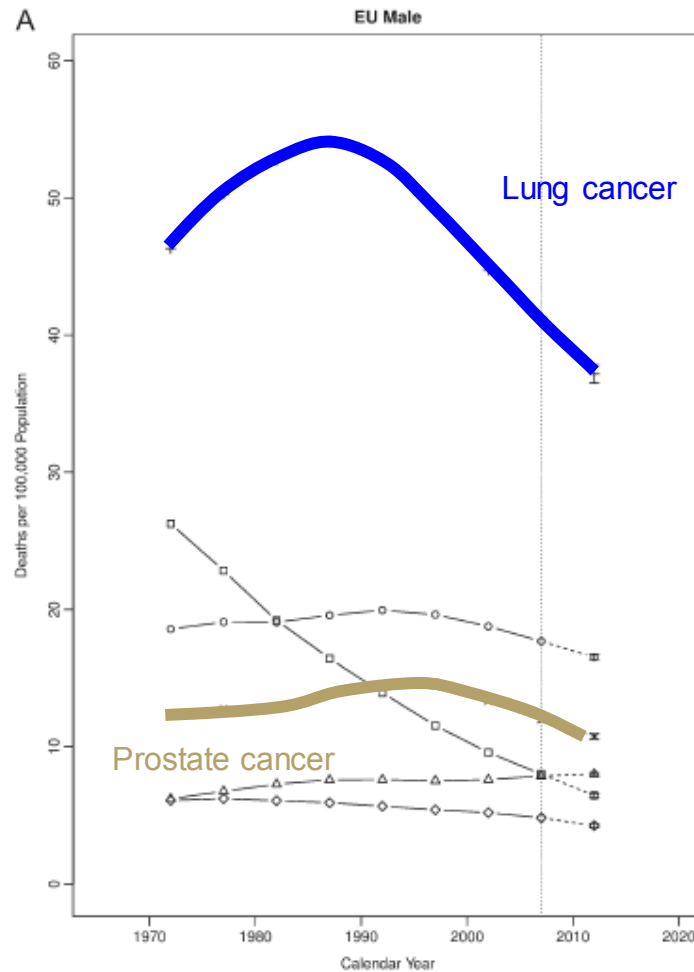
Krebssterbefälle: 215.000/Jahr



Krebs in Deutschland 2007/2008, RKI 2012



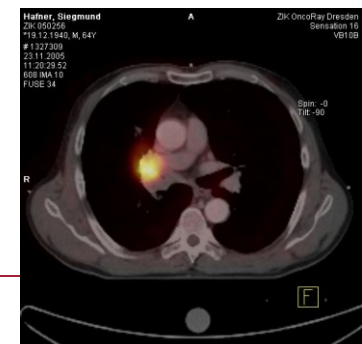
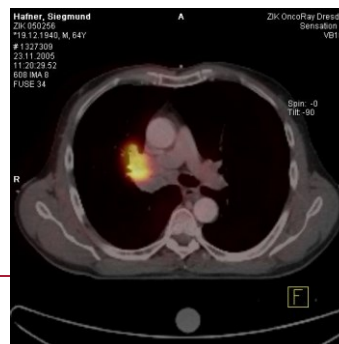
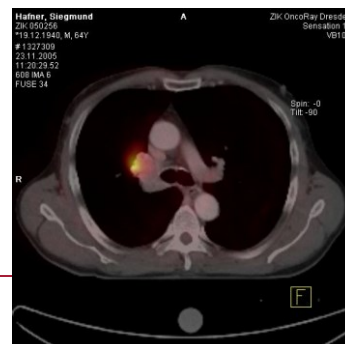
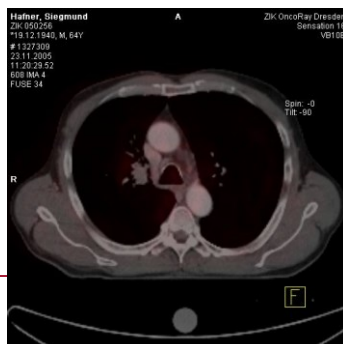
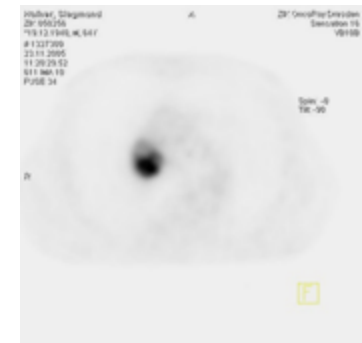
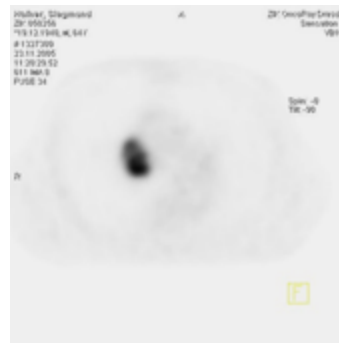
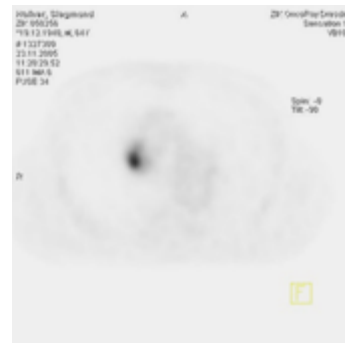
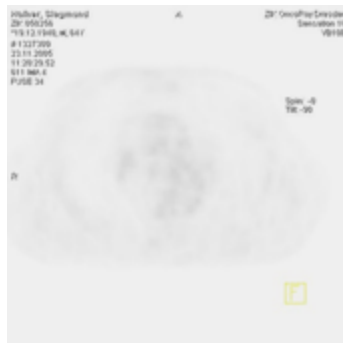
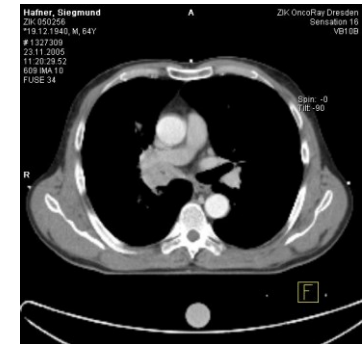
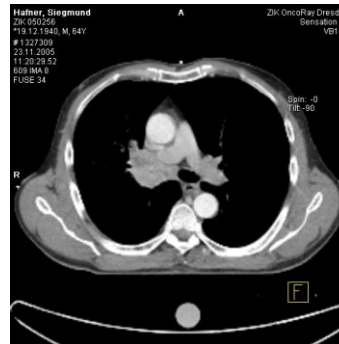
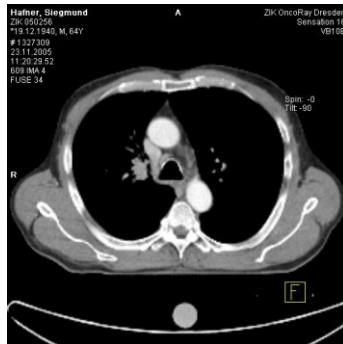
Lung cancer



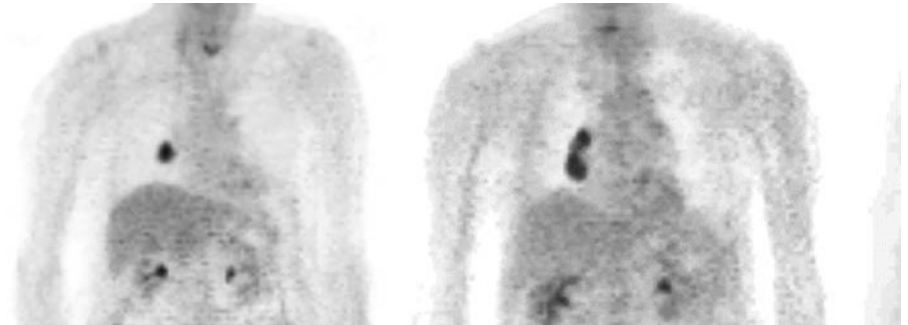
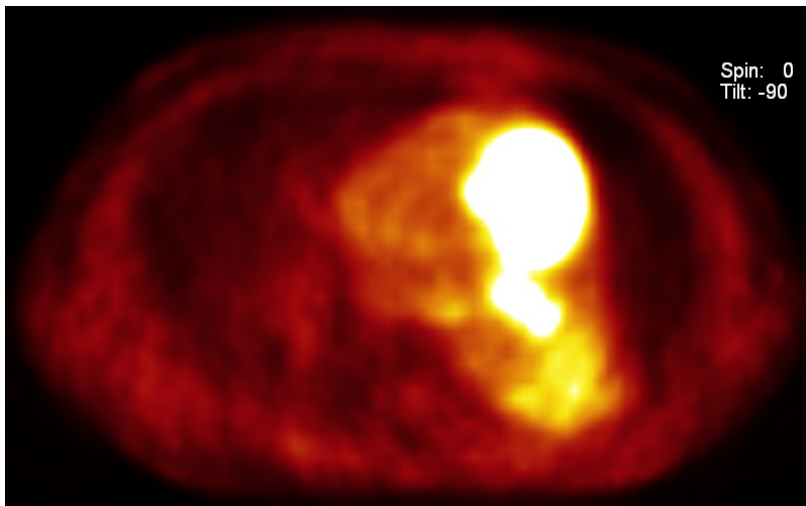
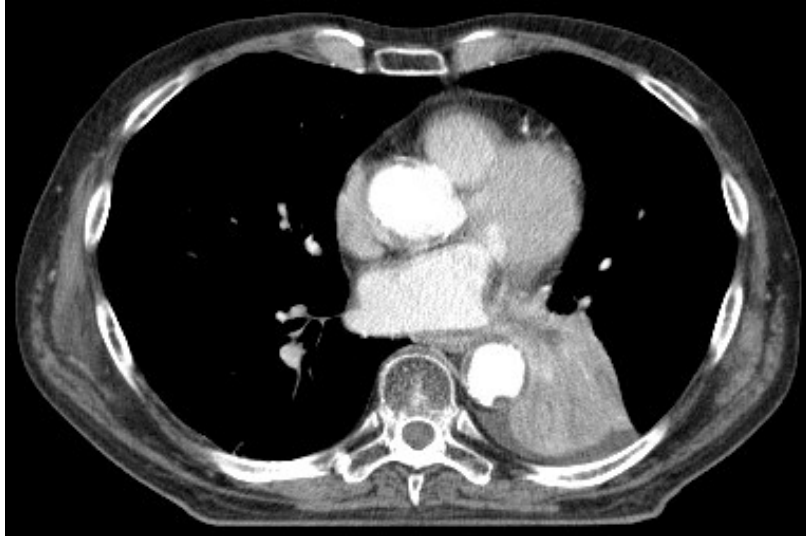
Stadienadaptierte Therapie: Nichtkleinzelliger Lungenkrebs

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 palliativ: Immuntherapie, molekulares Targeting, CTx, RT
	T3N1-2M0		
Stadium IIIB	T4 u./o. N3M0		
Stadium IV	M1		palliativ: Immuntherapie, molekulares Targeting, CTx, RT

Lungenkrebs: Diagnostik/ PET/CT

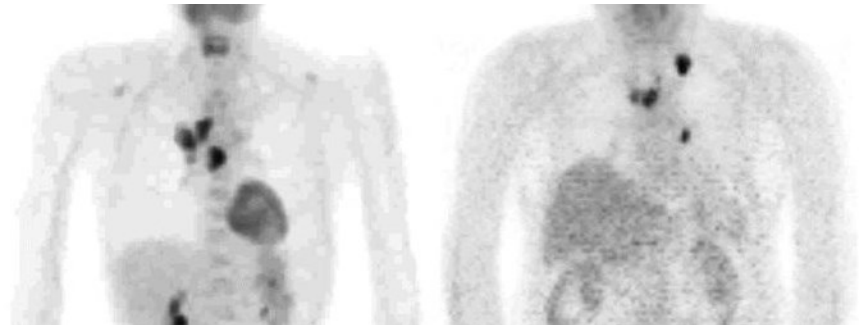


FDG PET/CT for treatment planning



N0

N1

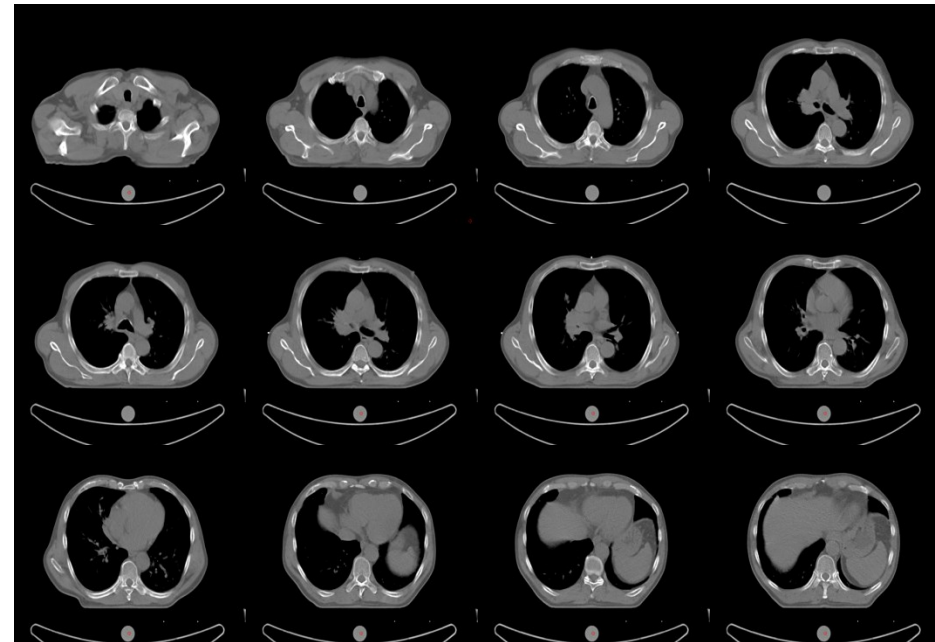


N2

N3

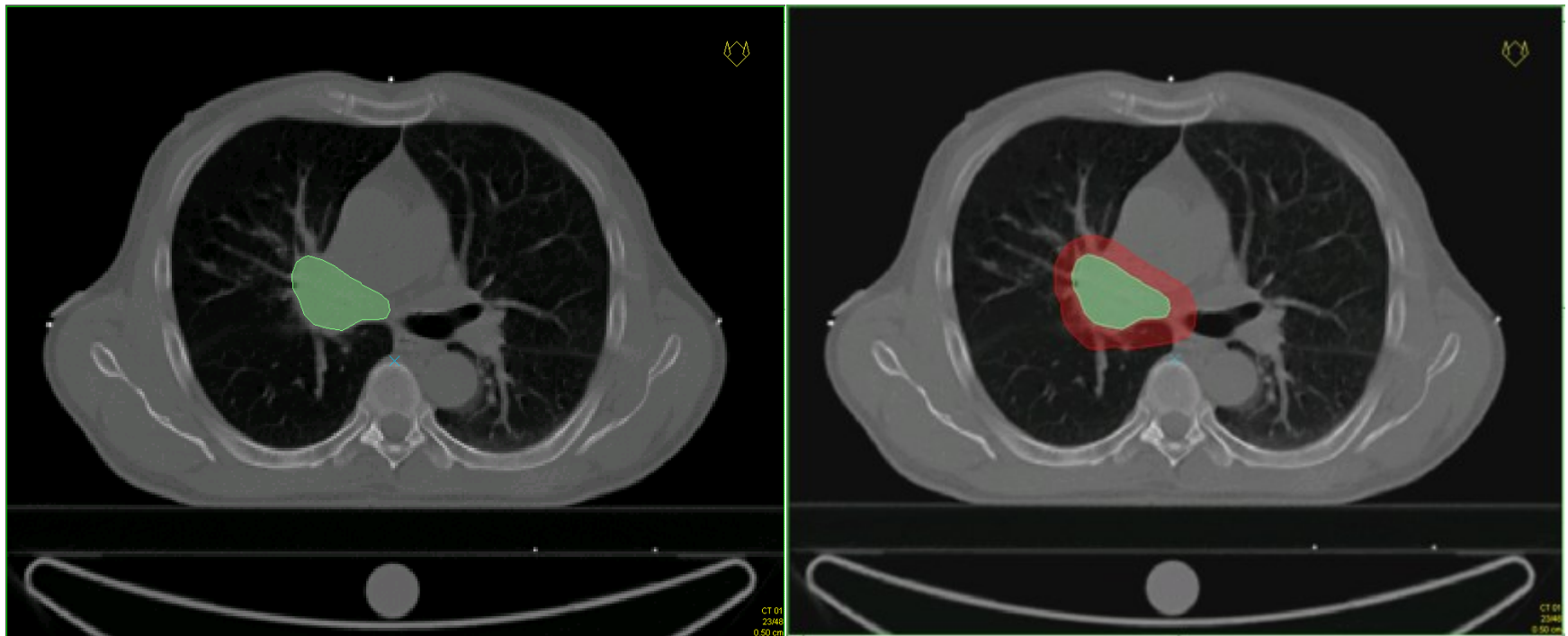
Prinzipien der Bestrahlungsplanung

Planungs-CT



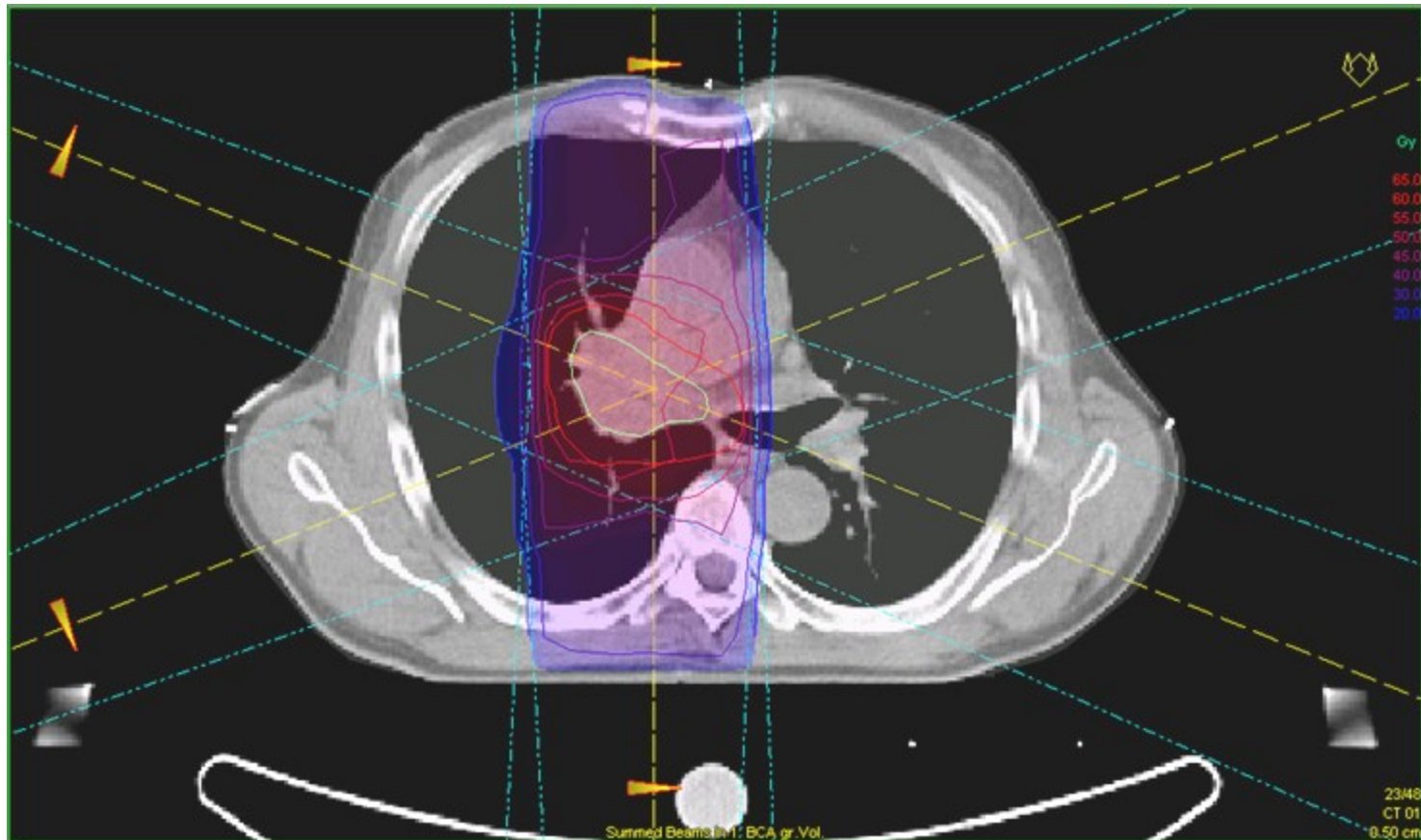
Prinzipien der Bestrahlungsplanung

Festlegung der Zielvolumina im Planungs-CT



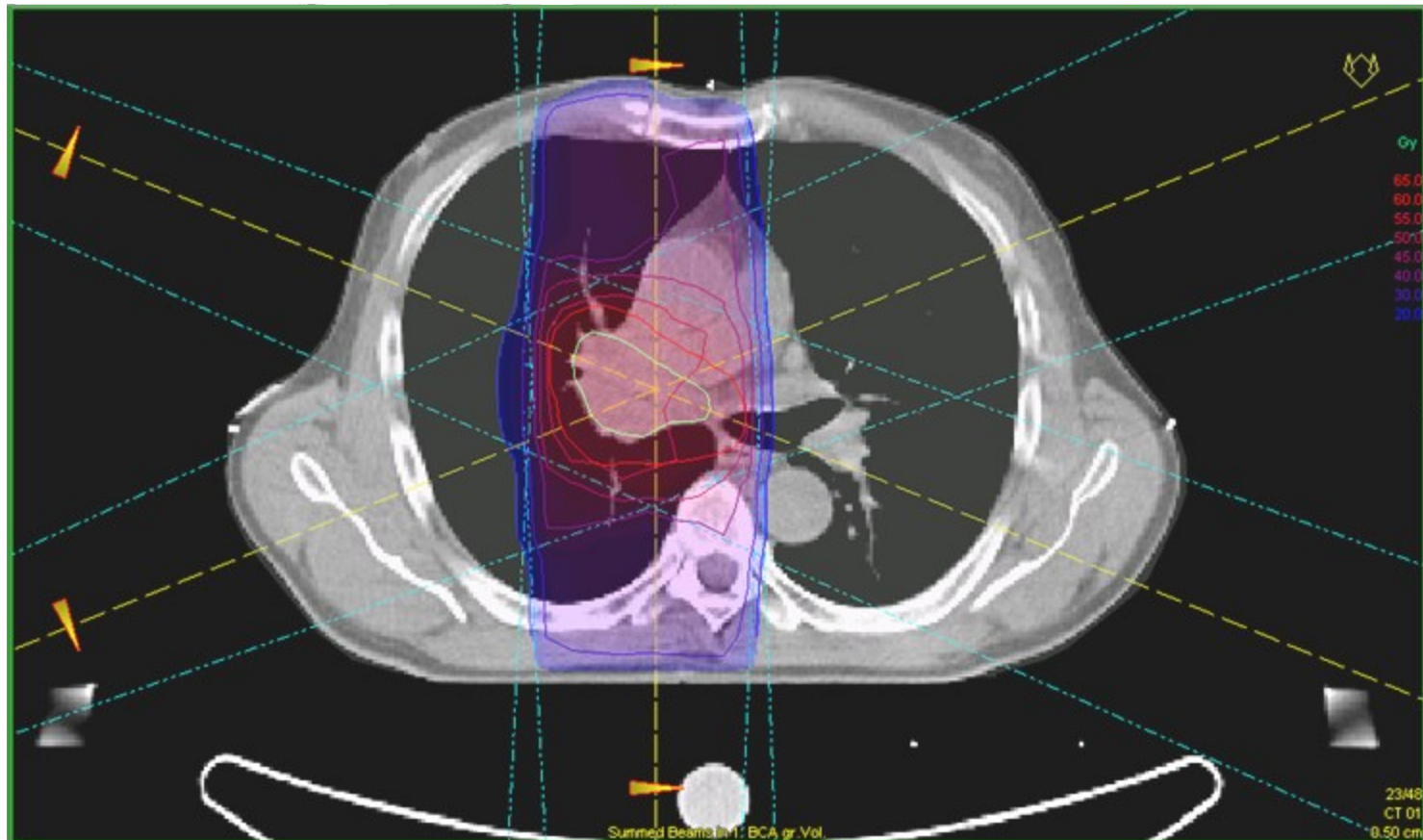
Prinzipien der Bestrahlungsplanung

Festlegung der Bestrahlungsfelder



Prinzipien der Bestrahlungsplanung

Festlegung der Bestrahlungsfelder/ Optimierung





Strahlentherapie NSCLC: Indikation

postoperativ

- R1/2-Resektion
- pN2/3

primär (+CTx)

- Inoperabilität
- Palliation



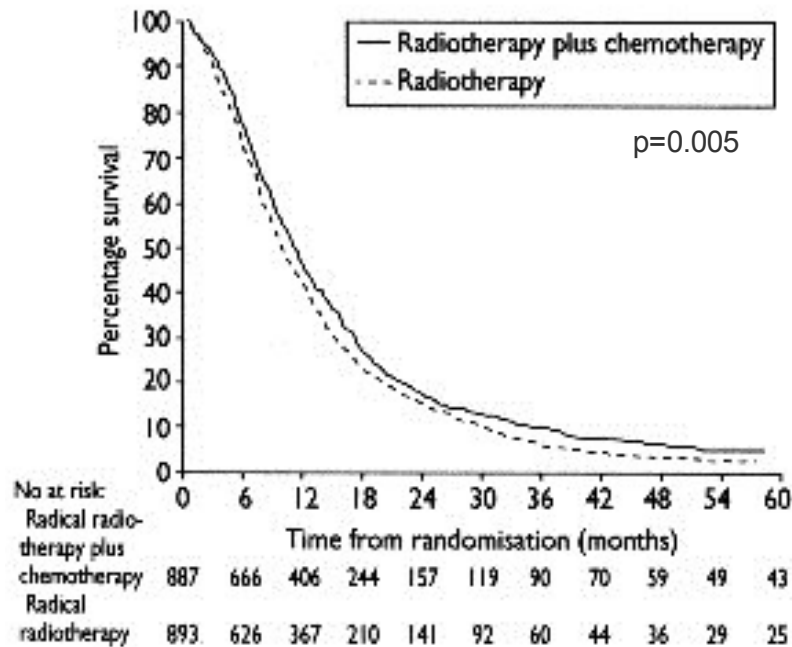
Strahlentherapie NSCLC

Konventionelle Therapie

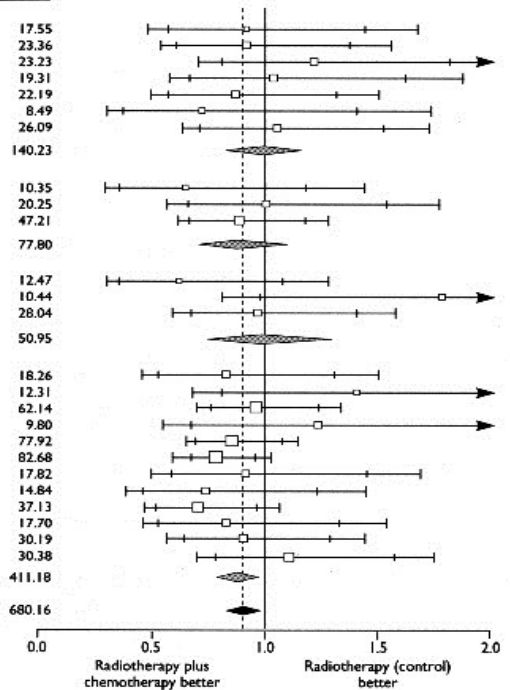
- Dosis 60-70 Gy
post-OP 50Gy
- D/fx 1.8-2.0 Gy
1fx/d, 5fx/w
- Dauer 6-7 w
- 4D-CT-Planung



RTx vs RTx/CTx Metaanalyse

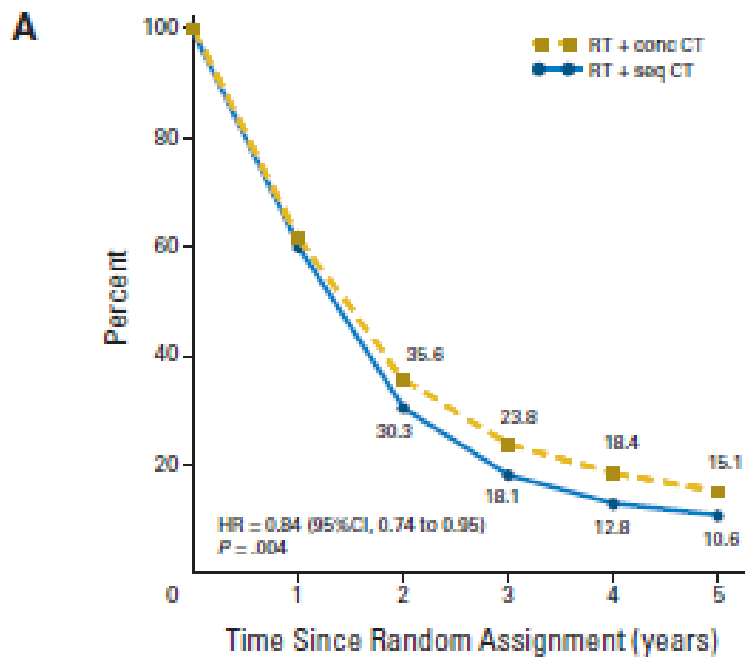


Trial	No of events/ No of patients entered		Observed - expected deaths	Variance
	Radiotherapy plus chemotherapy	Radiotherapy		
Long term alkylating agents:				
NRH NSC-26271	36/36	38/38	-1.63	17.55
EORTC 08742	45/53	51/64	-1.91	23.36
RTOG 7302a	52/55	48/56	4.58	23.23
RTOG7302b	38/46	43/50	0.84	19.31
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

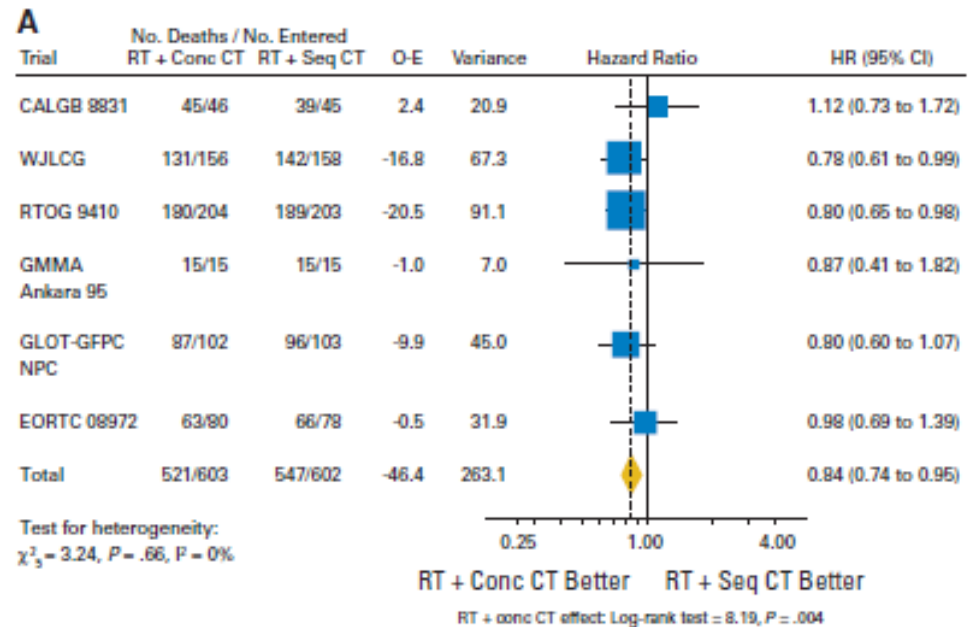


NSCLC Collaborative Group
BMJ 311: 899 (1995)

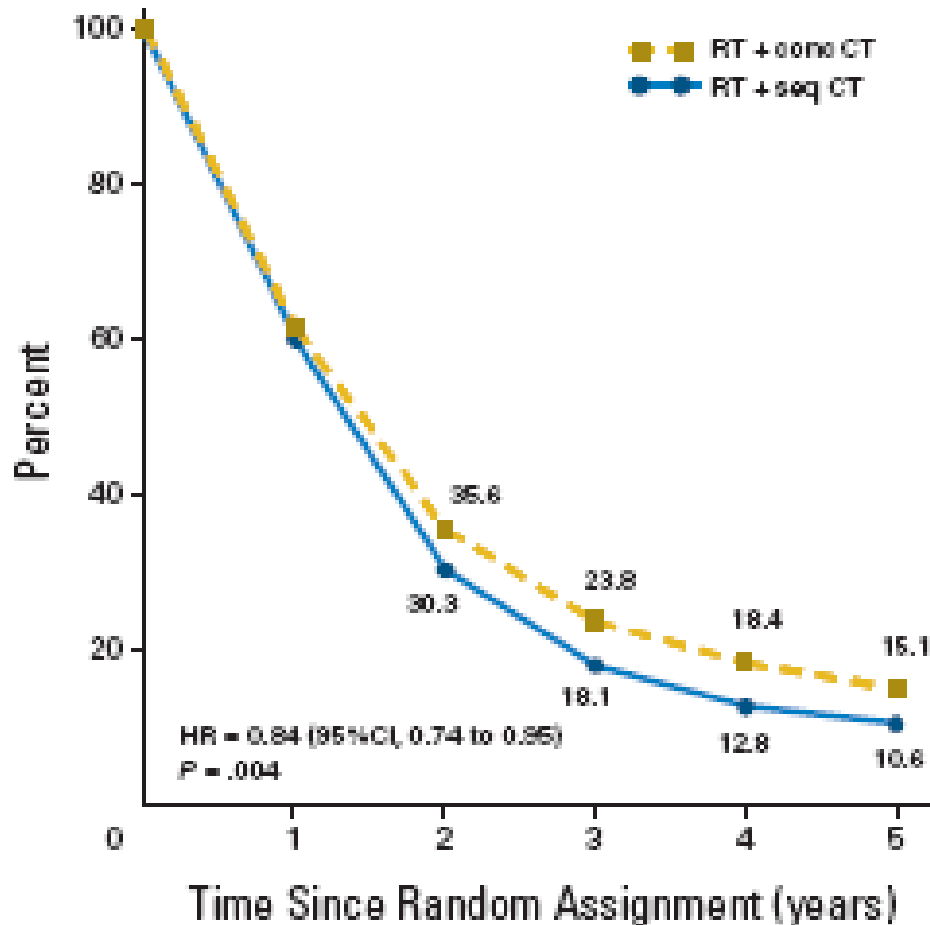
Metaanalyse RCTx NSCLC simultan vs. sequentiell



	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	37/166
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

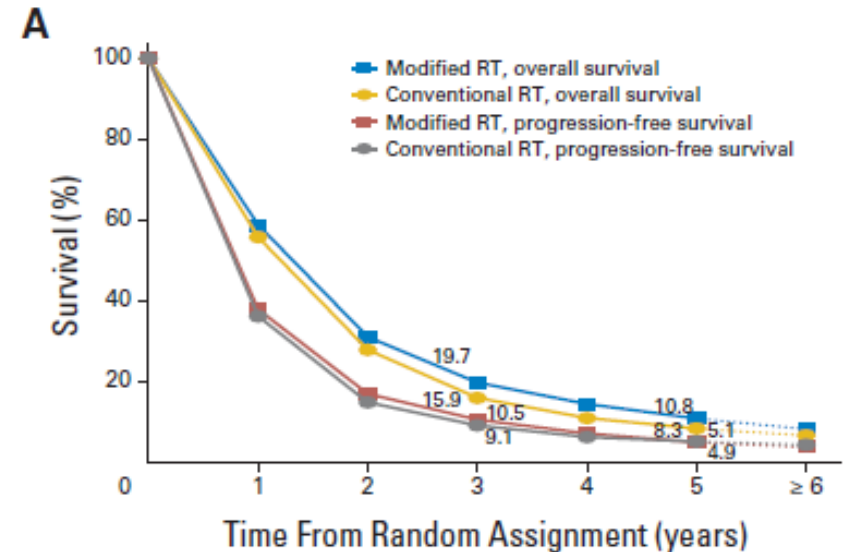
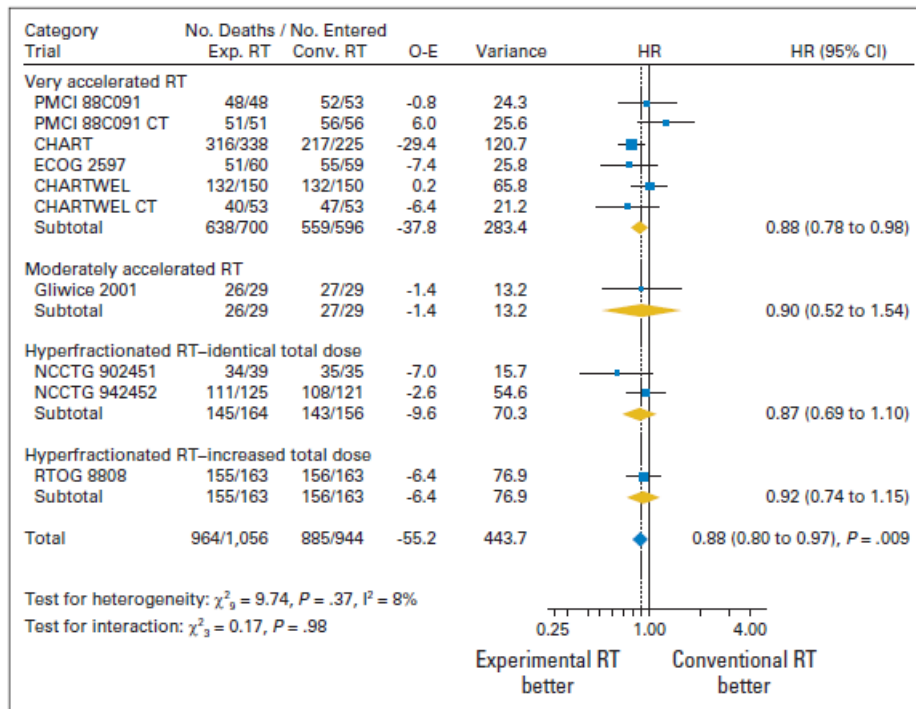
DM

HR 1.04 [0.86;1.25], $p=0.69$

39.5 vs 39.1% at 3 yrs

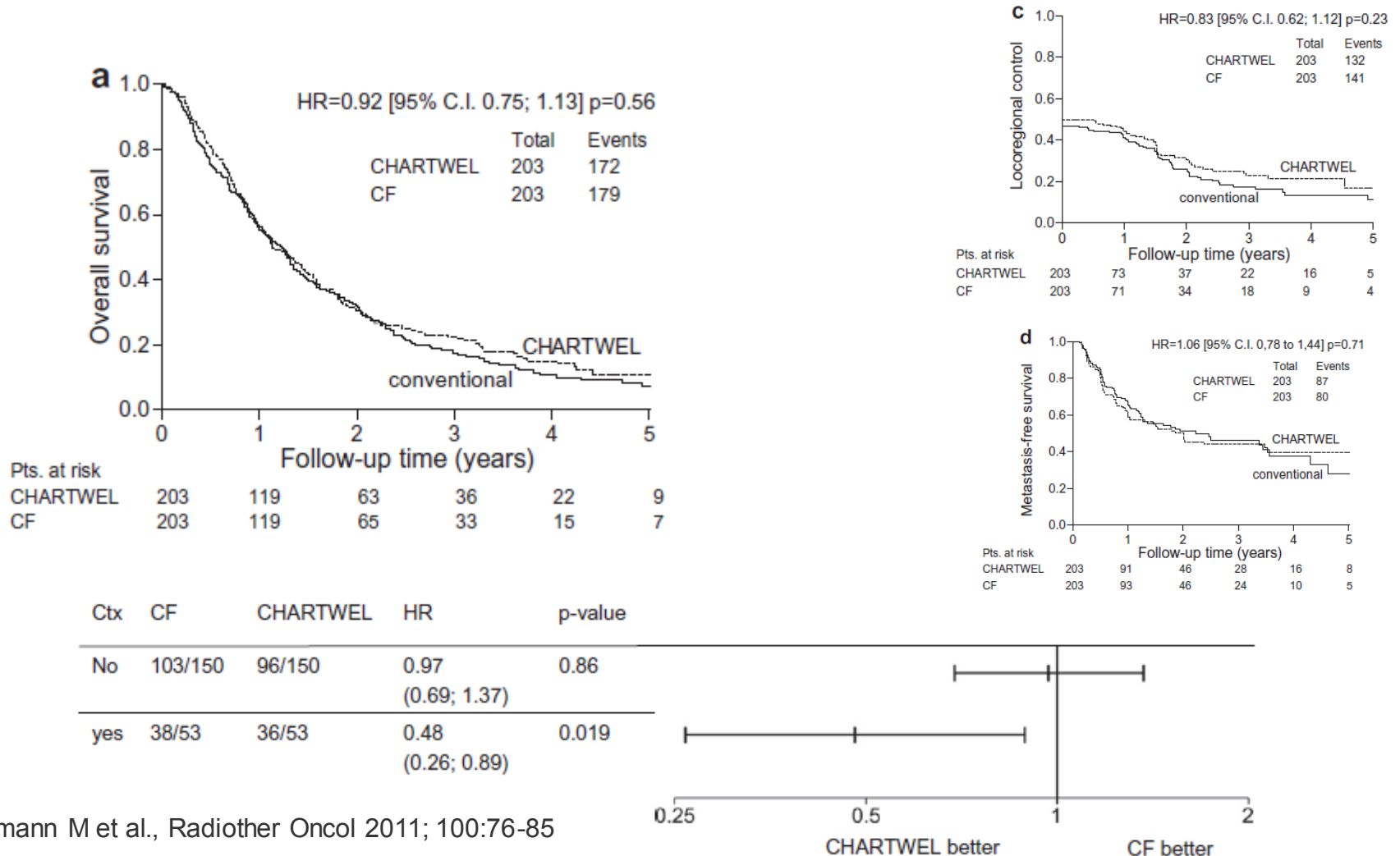
Higher toxicity with conc CRT

Modifizierte Fraktionierung NSCLC

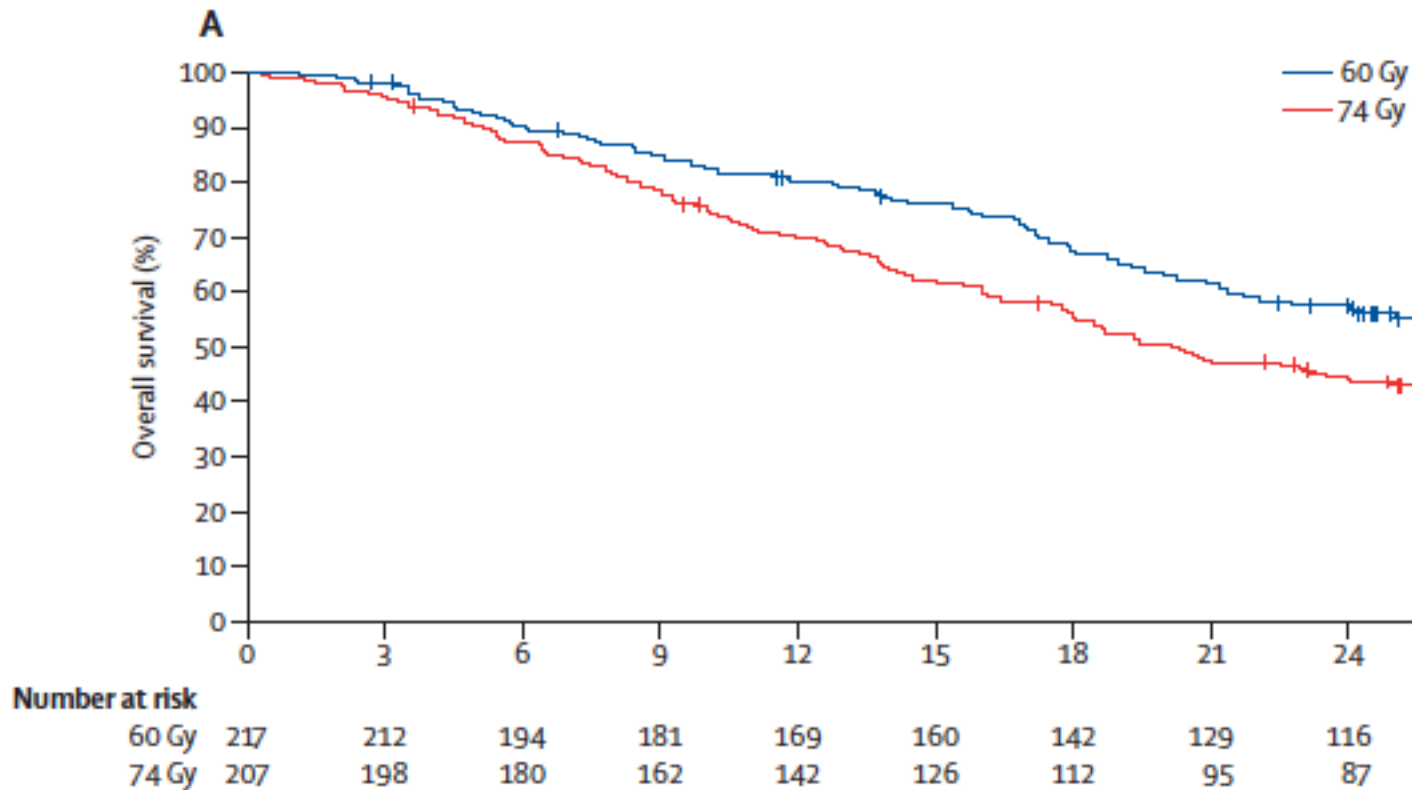




Modifizierte Fraktionierung NSCLC: CHARTWEL



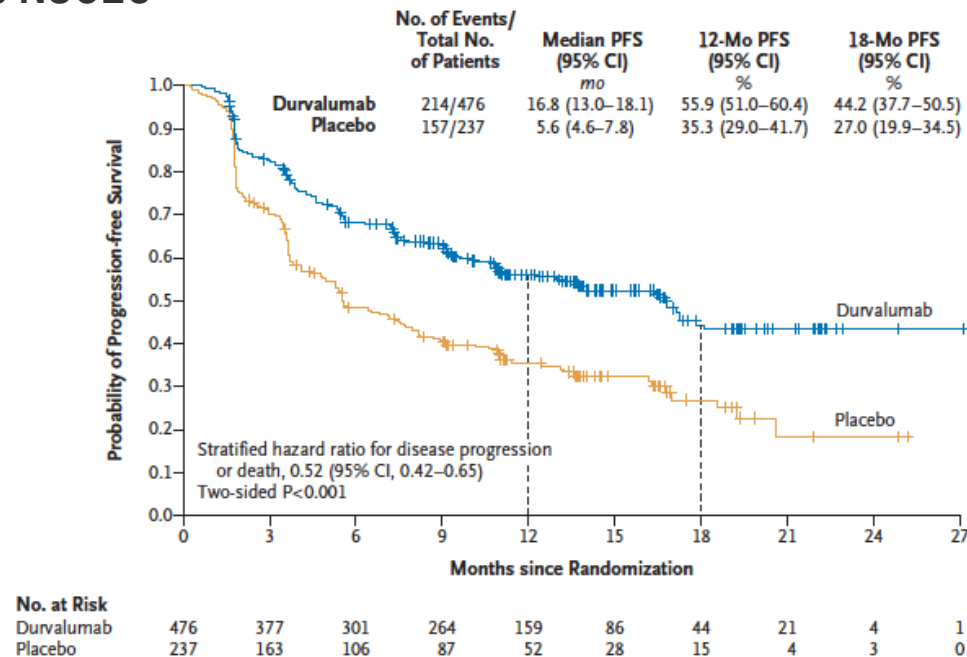
Dosiseffekt NSCLC (RTOG 0617): Erhöhte Toxizität = vermindertes Überleben?



Bradley J et al., Lancet Oncol 2015; 16: 187–99

Strahlentherapie bei Lungenkrebs: Kombination mit Immuntherapie

Durvalumab vs Placebo randomisiert 1-42 Tage nach Radiochemotherapie nicht progrediente NSCLC



Antonia SJ et al., NEJM 2017; 377: 1919-29

Strahlentherapie SCLC: Indikation

kurativ

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

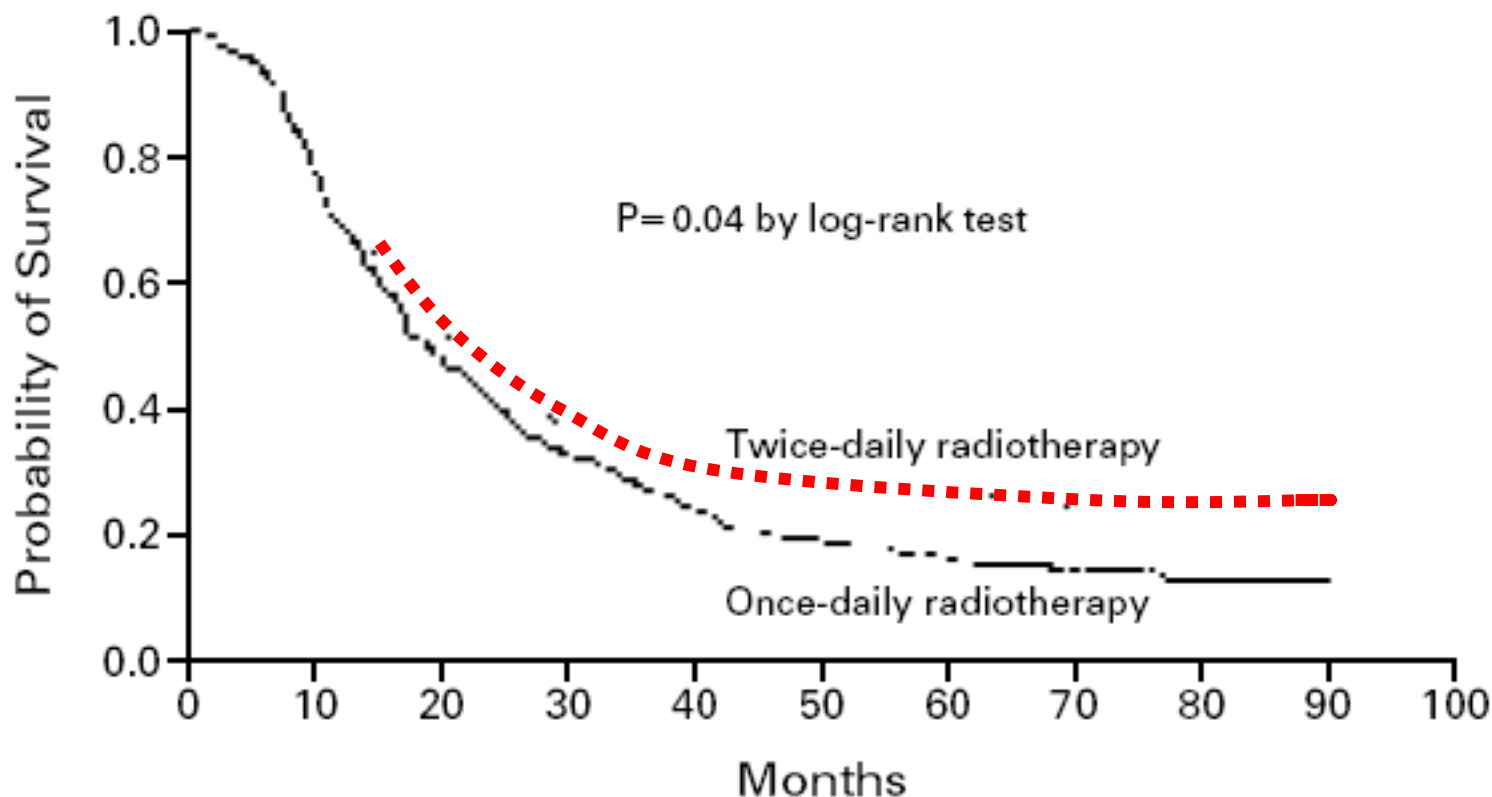
palliativ

- RTx bei Symptomatik

Radiochemotherapie beim SCLC (limited disease)

- Cisplatin/ Etoposid möglichst parallel mit RT beginnen, ev. 1-2 Zyklen vorab
- Dosis 45 Gy
- Dosis/Fraktion 1.5 Gy/ 2x pro Tag
- Therapiedauer 3-6 Wochen
- Planung PET/CT-Planung, 4D-konformal, Tumor und Lymphknotenmetastasen (kein ausgedehnter ENI)
- Hirnbestrahlung prophylaktisch 25-30 Gy/ 2-3W

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)

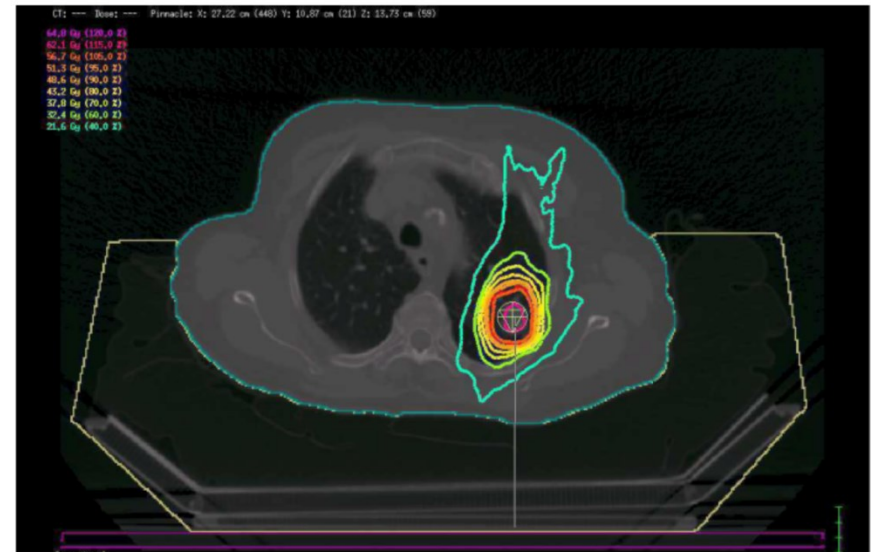
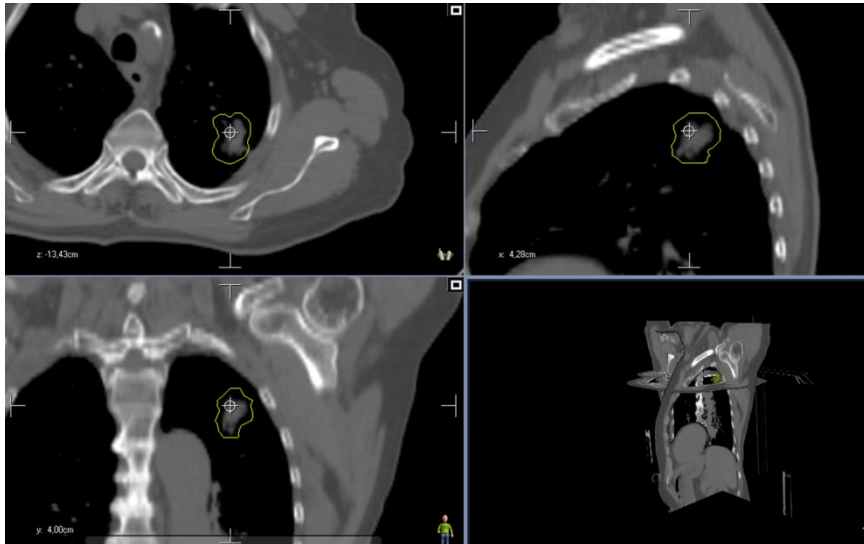
SBRT im Stadium I NSCLC

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, Polyarthritits, Z.n. Vulva-Ca, Z.n. MammaCa Therapie 3 x 18 Gy

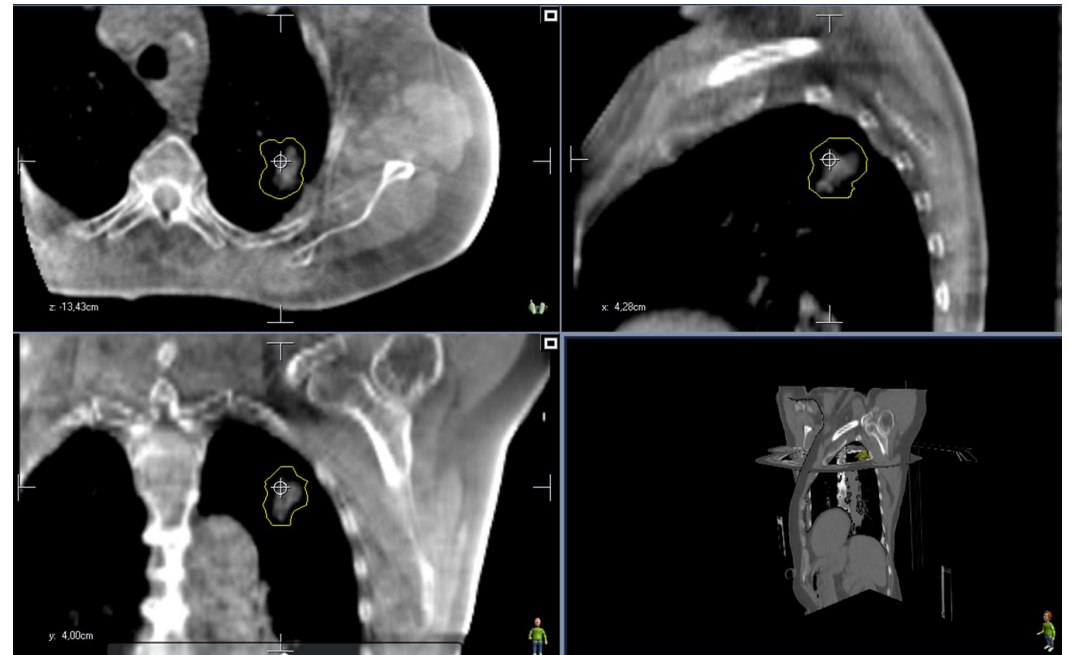


FDG-PET/CT
06/17

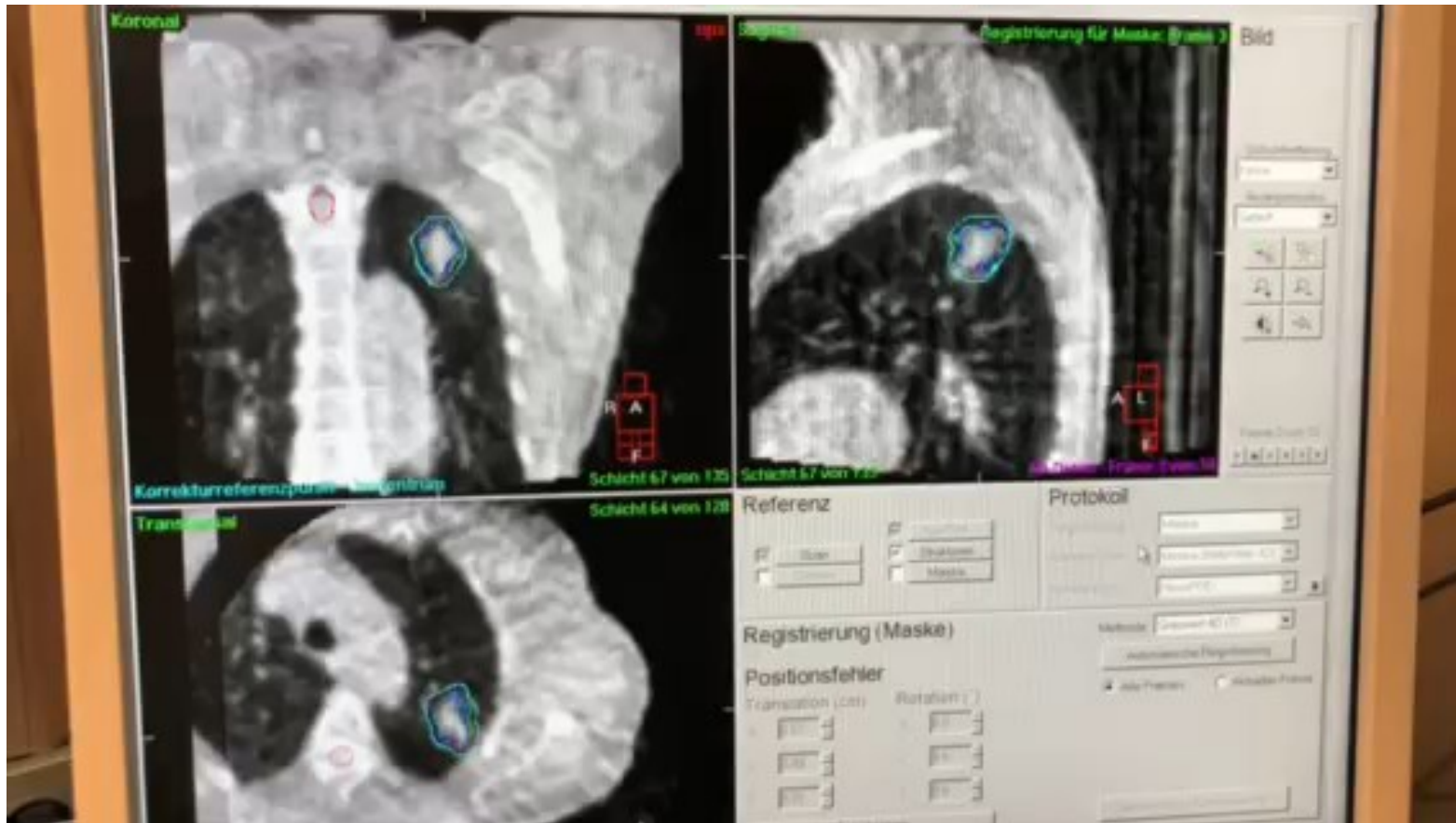
4D Planungs-CT/ VMAT-IMRT



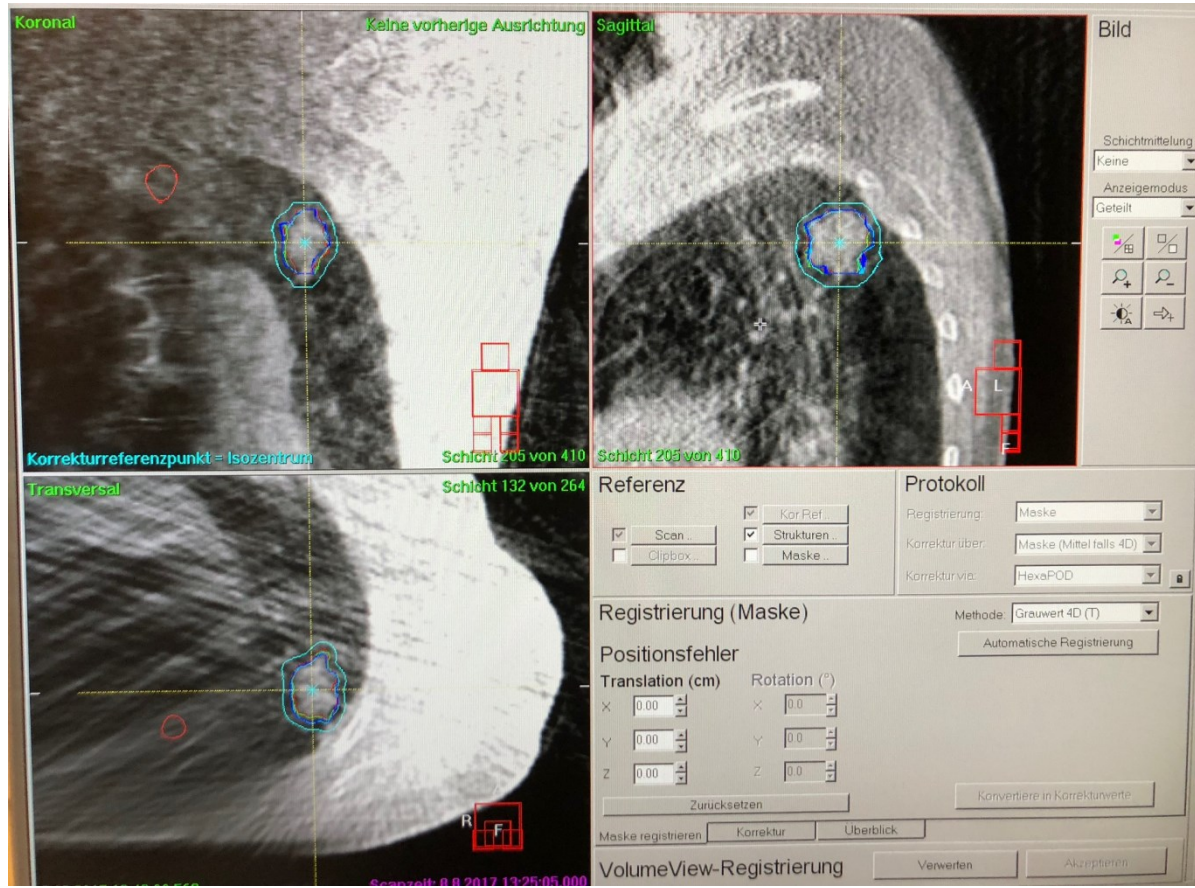
4D Cone-Beam CT (4D-IGRT)



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



4D Intrafraction CBCT





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

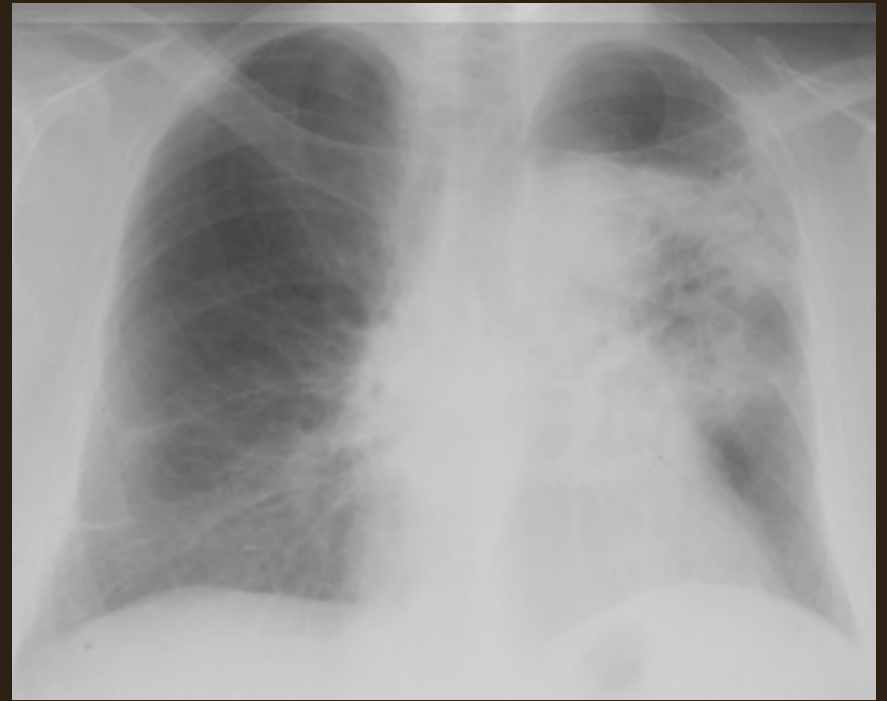


Table 4. Incidence of radiation pneumonitis according to V_{dose} in patients treated with radiotherapy for lung cancer

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 $\leq 20\%$

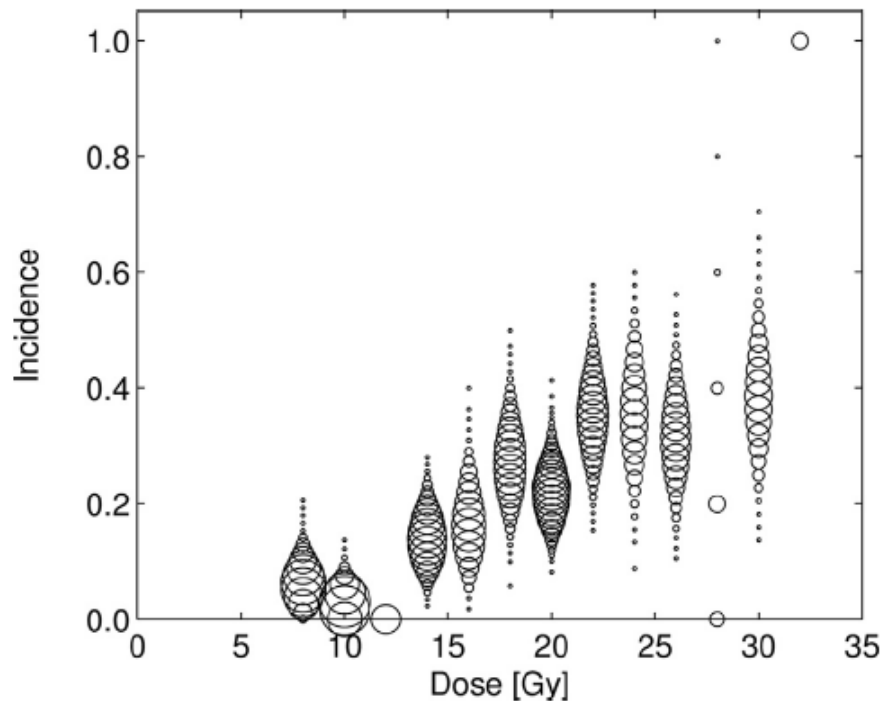


Fig. 2. The incidence rate calculated separately in each of the bootstrap replicates in 2-Gy bins for the pneumonitis data. The data points are weighted by the number of bootstrap occurrences and the number of patients in each dose bin.

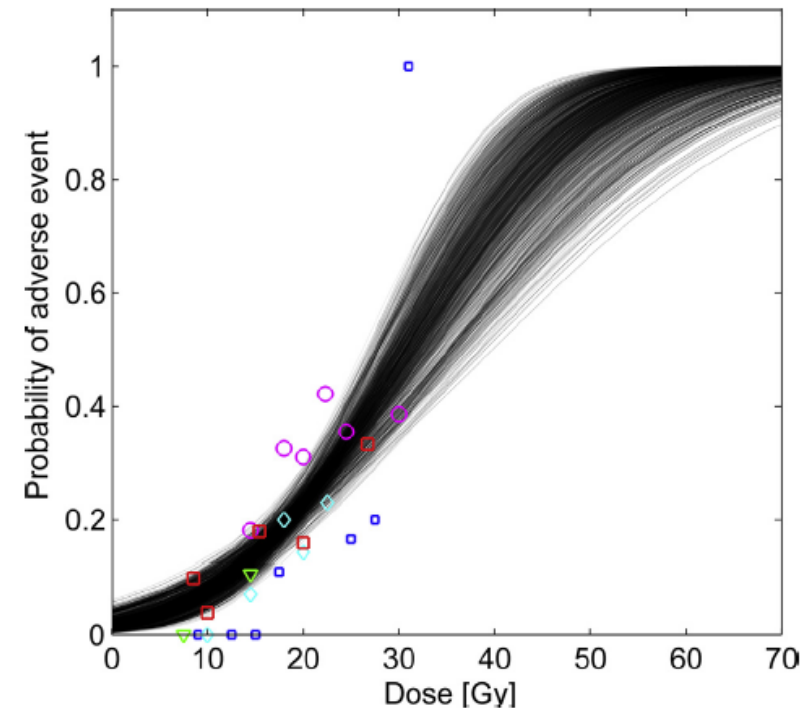
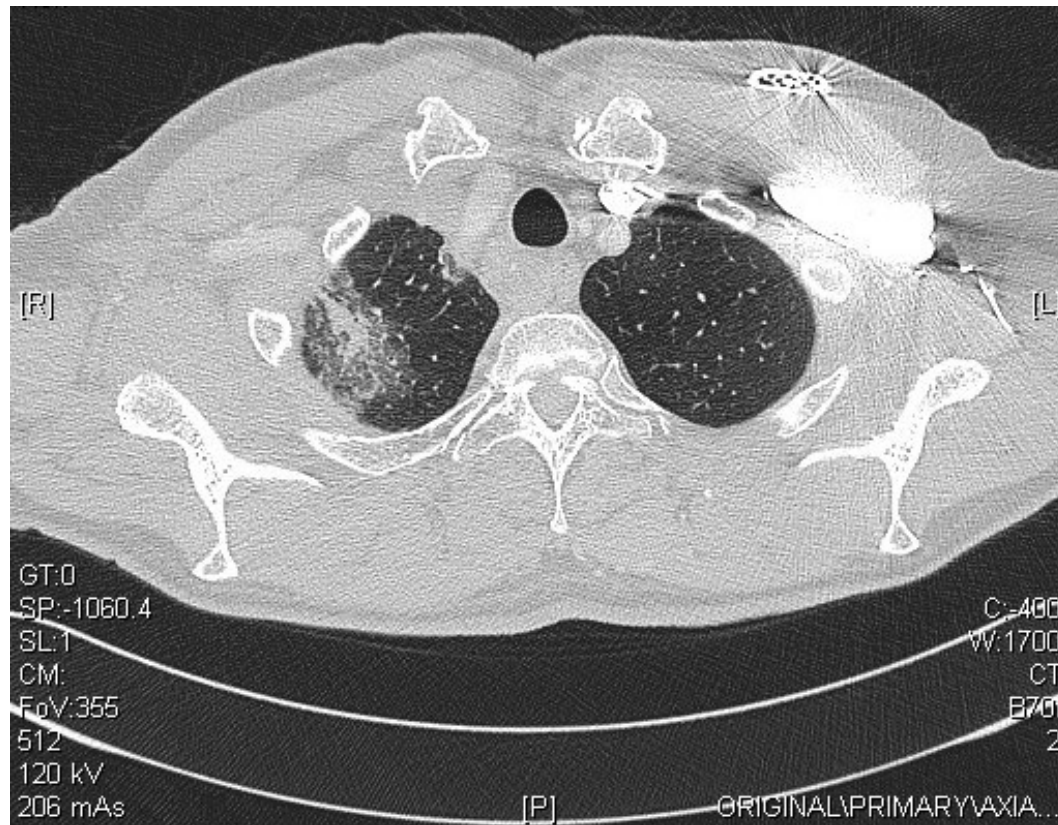


Fig. 3. Dose—response curves shown for $2 \cdot 10^3$ bootstrap replicates of the original pneumonitis incidence data. The Lyman dose—response model was used. The original data points are weighted by the number of patients, N : $N < 10$ blue squares, $10 \leq N < 20$ cyan diamonds, $20 \leq N < 30$ green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