OTTO VON GUERICKE UNIVERSITÄT MAGDEBURG

Deutsche Akademie für Mikrotherapie
DAfMT

CT-gesteuerte Brachytherapie von pulmonalen und mediastinalen Malignomen

Jens Ricke

SAINT 2016

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

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oligometastatic disease

OMD is characterised by the localisation of the disease to a few sites and lesions and is associated with the option to use LAT approaches in patient treatment strategies with a view to improving disease control and therefore clinical outcome in these patients.

Generally, OMD may be characterised by the existence of metastases at up to 2 or occasionally 3 sites and 5 or sometimes more lesions, predominantly visceral and occasionally lymphonodal. Typically, these are the primary, and other involved sites such as the liver, lung, peritoneum, nodes and ovary. Patients with

Van Cutsem E, Cervantes A, Arnold D et al, ESMO Consensus 2016 Online Ann Oncol, July 2016

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Thus, treatment strategies for patients with OMD should be based on the possibility of achieving complete ablation of all tumour masses, using surgical R0 resection (complete resection with clear resection margins and no evidence of microscopic residual tumour) and/or LAT, either initially or possibly after induction treatment with systemic therapy, for both the primary tumour and metastases.

Van Cutsem E, Cervantes A, Arnold D et al, ESMO Consensus 2016 Online Ann Oncol, July 2016

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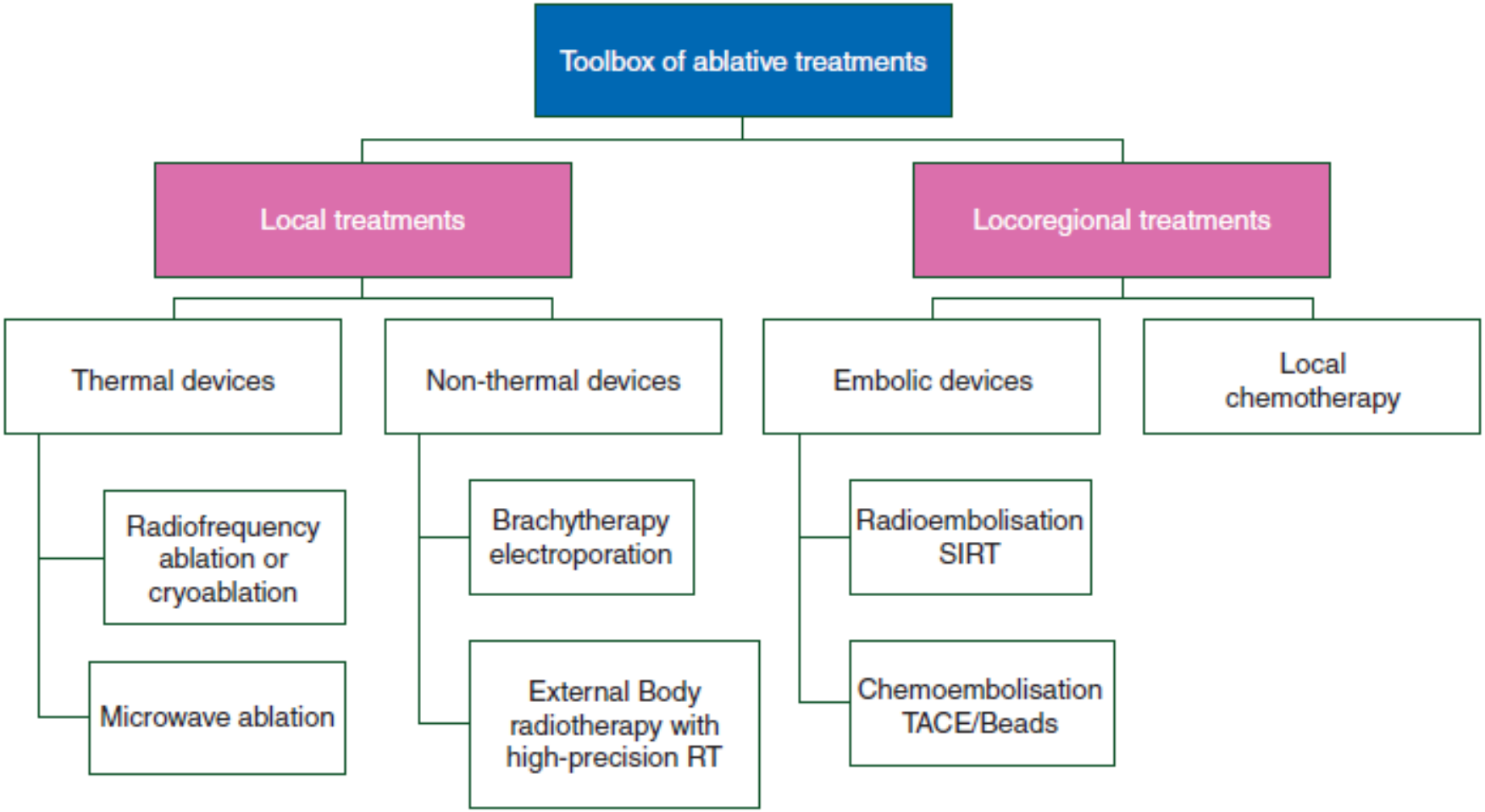
Figure 1: toolbox of ablative treatments



Van Cutsem E, Cervantes A, Arnold D et al, ESMO Consensus 2016 Online Ann Oncol, July 2016

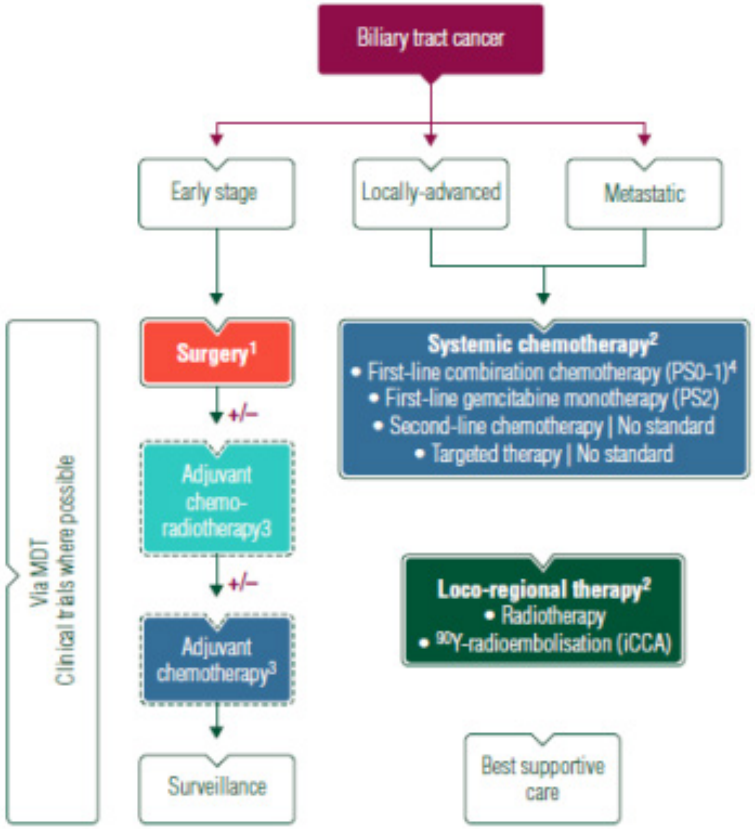
Local and ablative treatment (including surgery)

recommendation 15: local ablation techniques.

- In patients with unresectable liver metastases only, or OMD, local ablation techniques such as thermal ablation or high conformal radiation techniques (e.g. SBRT, HDR-brachytherapy) can be considered. The decision should be taken by an MDT based on local experience, tumour characteristics and patient preference [IV, B].
- In patients with lung only or OMD of the lung, ablative high conformal radiation or thermal ablation may be considered if resection is limited by comorbidity, the extent of lung parenchyma resection, or other factors [IV, B].
- SBRT is a safe and feasible alternative treatment for oligometastatic colorectal liver and lung metastases in patients not amenable to surgery or other ablative treatments [IV, B].
- RFA can be used in addition to surgery with the goal of eradicating all visible metastatic sites [II, B].

Van Cutsem E, Cervantes A, Arnold D et al, ESMO Consensus 2016 Online Ann Oncol, July 2016

Intrahepatic cholangiocellular carcinoma



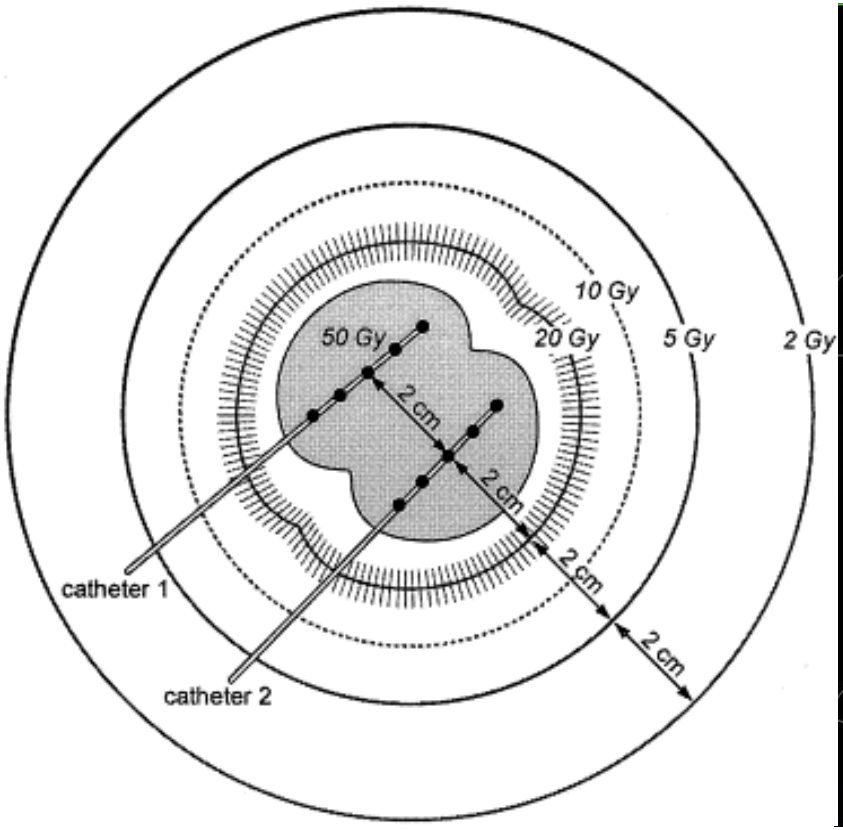
[1] Special considerations:
- Need for pre-operative biliary drainage
- Avoid percutaneous biopsy in resectable disease
- Assess Future Liver Remnant
- Assess need for Portal Vein Embolisation
- Neoadjuvant approach (selected cases)
- Completion surgery for incidental gallbladder cancer of T-stage T1b and above

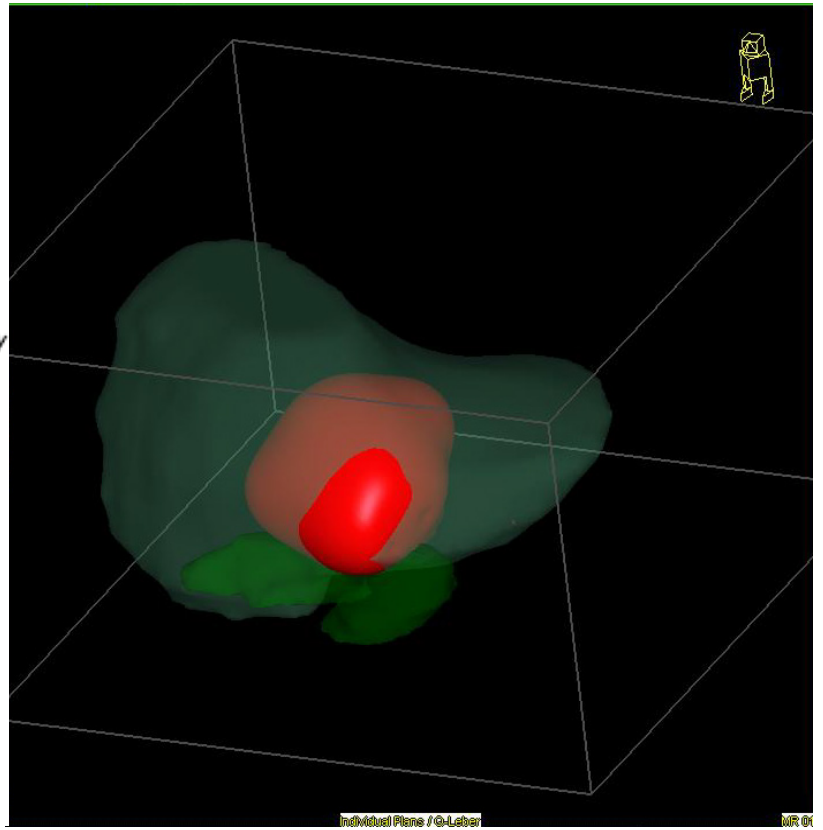
[2] Option of salvage surgery should be considered in responding patients with initially inoperable disease
[3] Level of recommendation IV,C
[4] Cisplatin and gemcitabine [category IA], other gemcitabine-based combination [category IIB]

Valle J Annals Oncol 2016

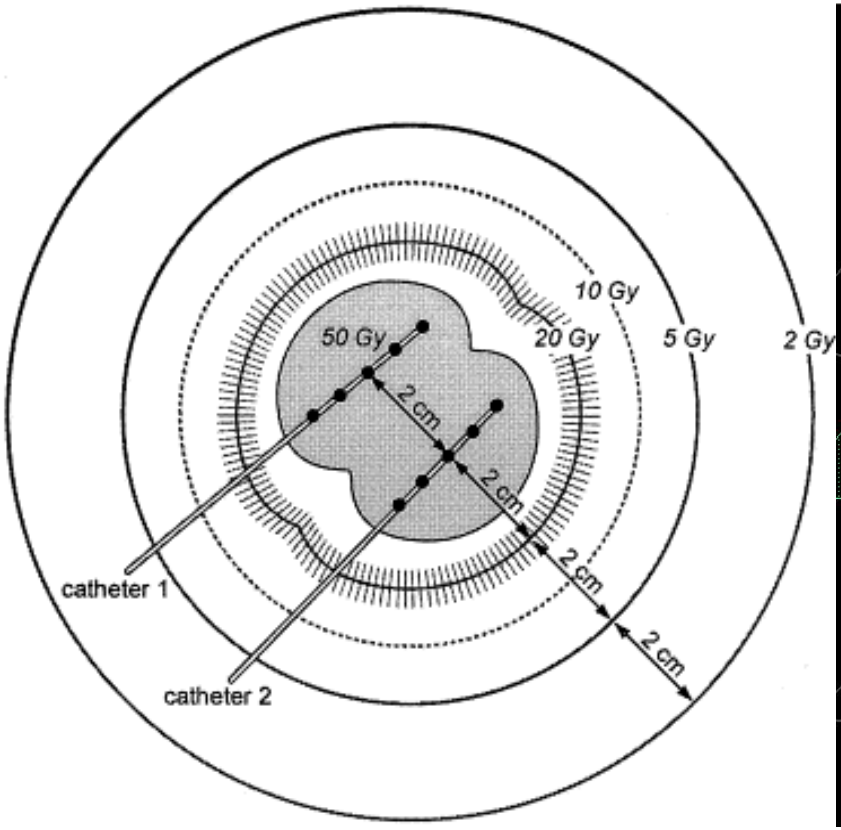
CT-Brachytherapie:

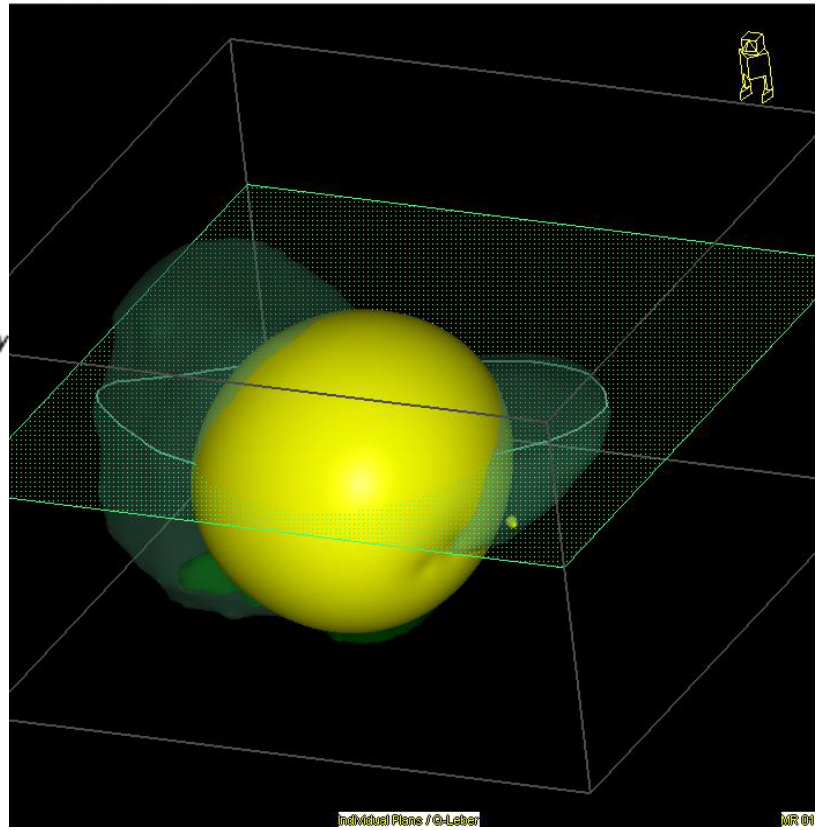
Leber, Lunge, retroperitoneal, mesenterial, …



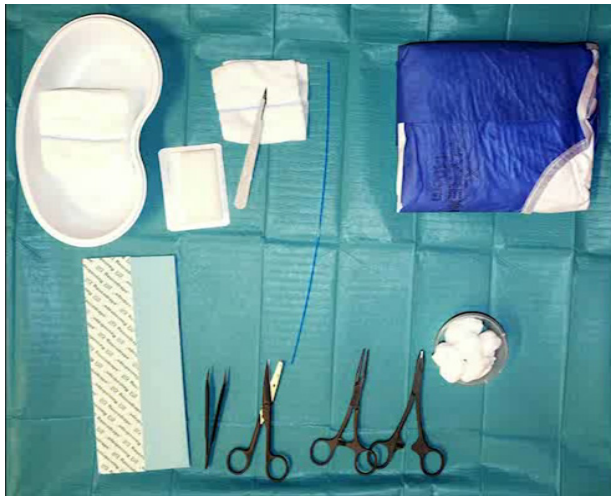


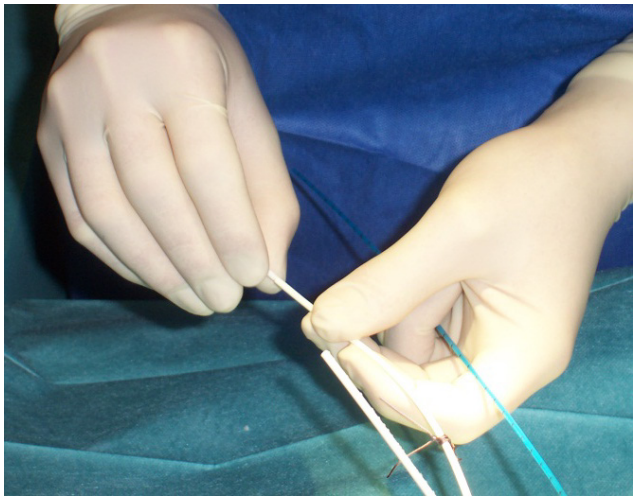
Radiation: CT-Brachytherapy



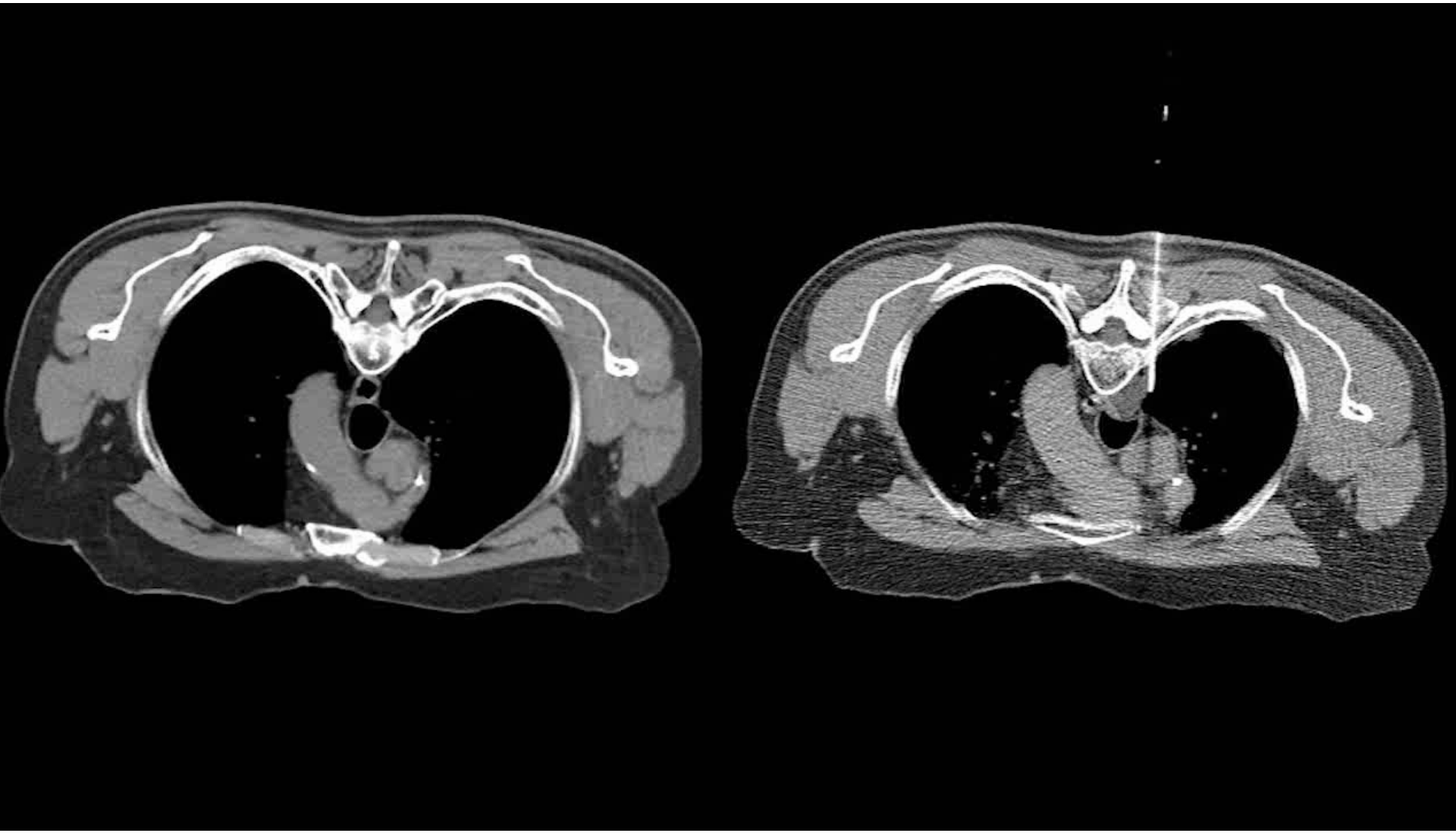


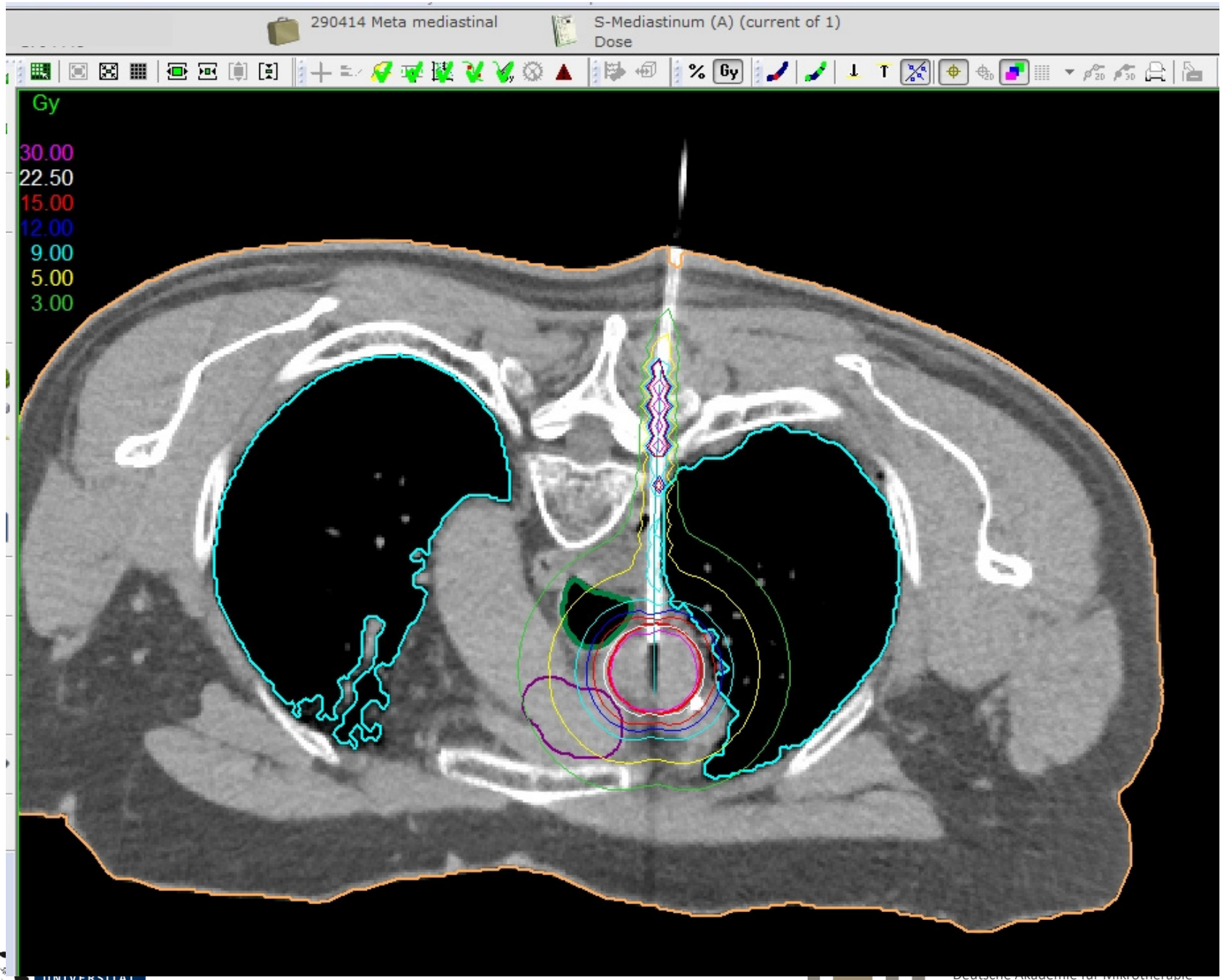
Brachytherapy Workflow





Images: Ricke




290414 Meta mediastinal
S-Mediastinum (A) (current of 1)
Dose
Gy
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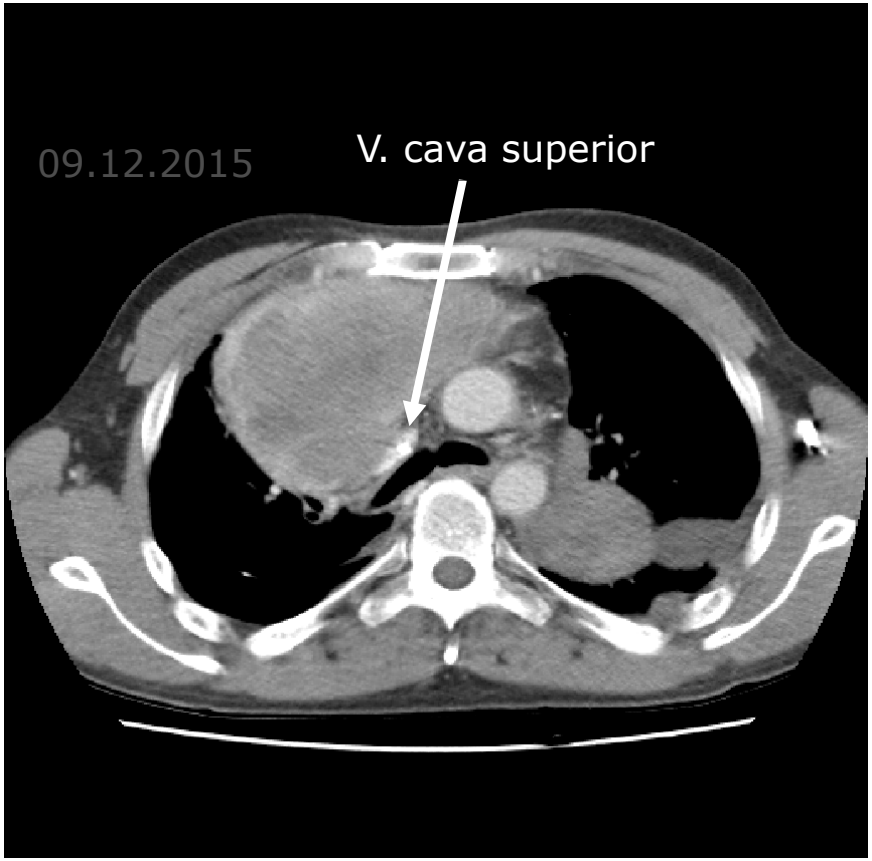
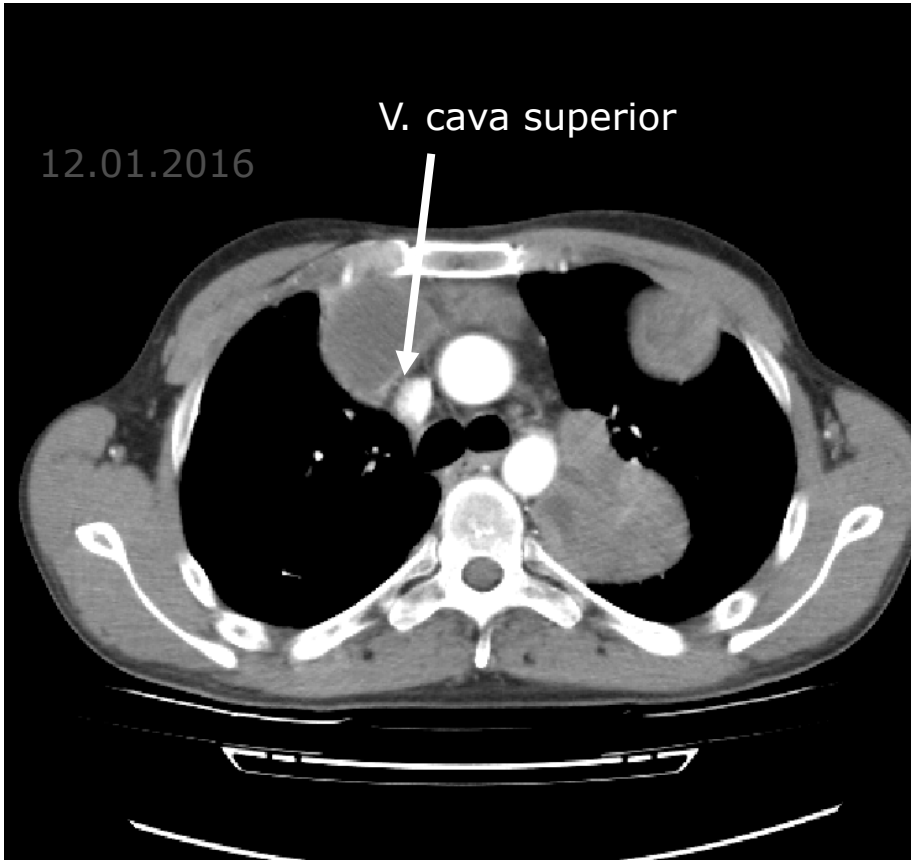
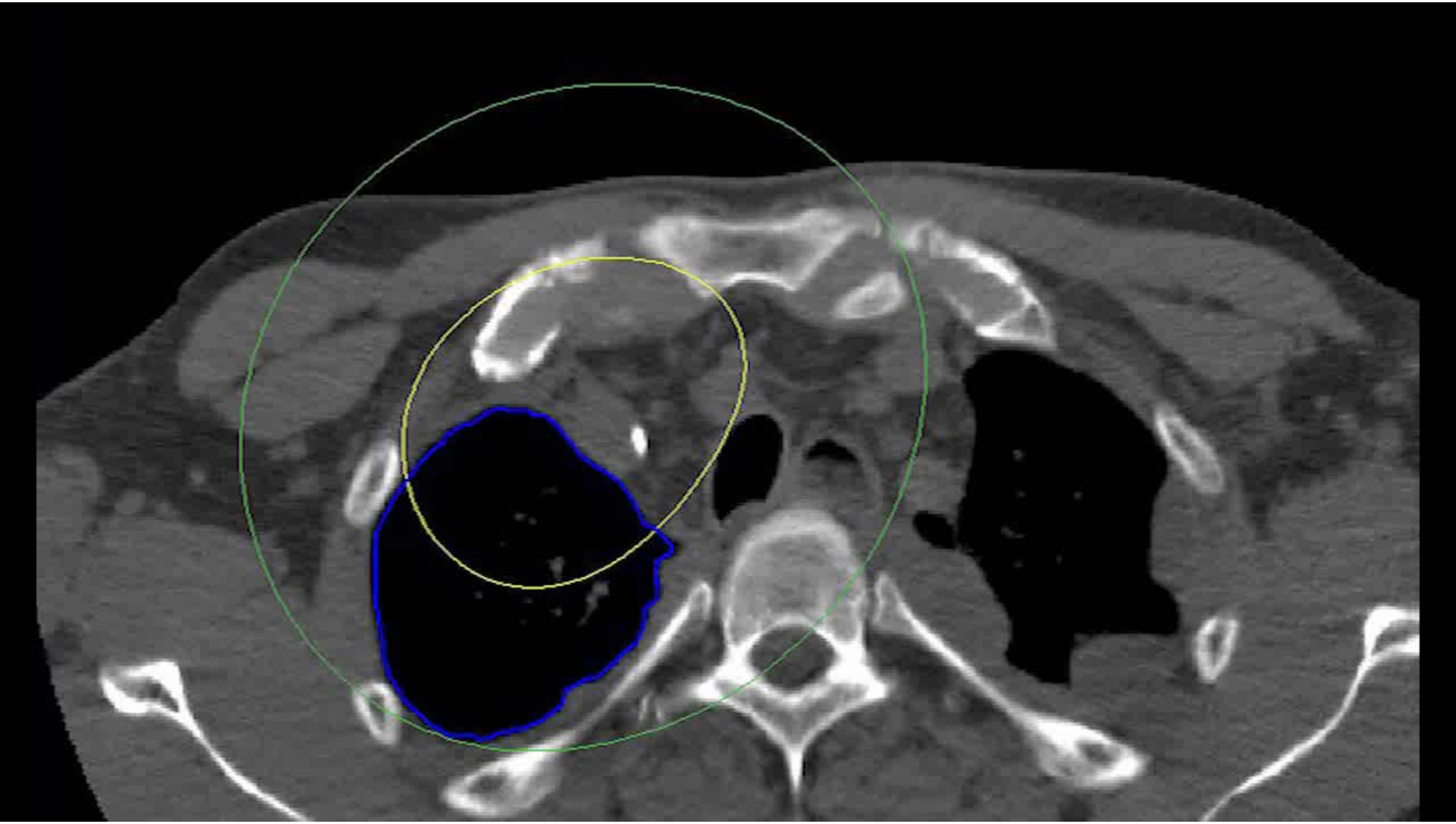
22.50
15.00
12.00
9.00
5.00
3.00

Synovialsarkom, 34y male

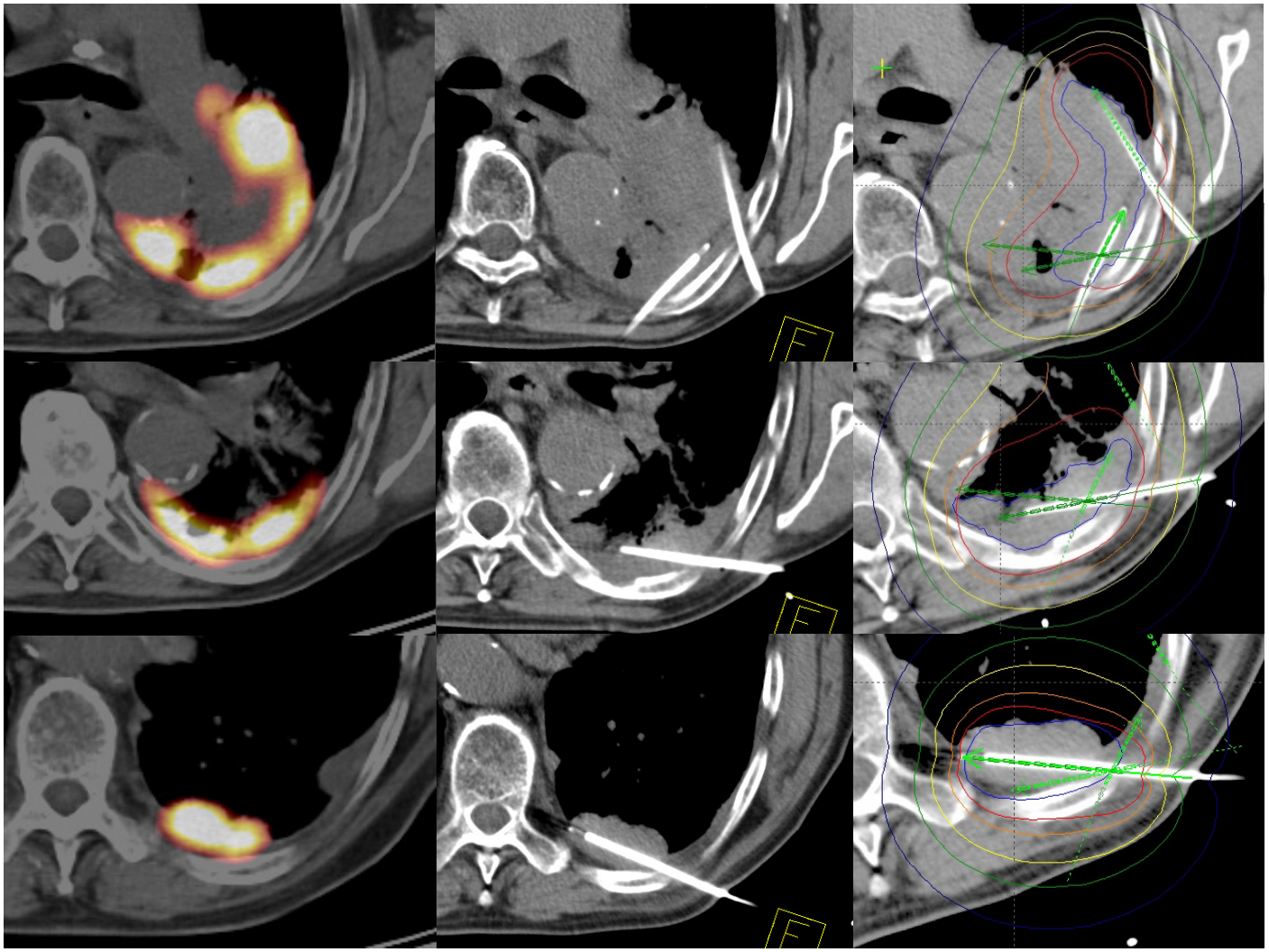




Synovialsarkom, 34y male



Synovialsarkom, 34y male



Lokale Kontrolle nach CT-Brachytherapie

- mCRC: 80 - 90% (12 months, 2-15cm) [1,2]
- Mammaca: >95% (12 months, 3-12cm) [3,4]
- Cholangiozellulär/Adenoca: >80% [5,6]
- HCC: >90% (12 months, 5-15) [7, 8]
- GIST/Sarkome: 80% [9]
- Melanom: >80% [10]

[1,2] Collettini 2014, *Ricke* 2010
[3,4] Collettini 2014, *Wieners, Ricke* 2011
[5,6] Kamphues 2012, Schnapauff 2012
[7,8] Collettini 2012, *Mohnike, Ricke* 2010
[9] *Bretschneider, Ricke* 2016 (submitted)
[10] *Bretschneider, Ricke* 2015

preliminary reports

CT-Guided Interstitial Single-Fraction Brachytherapy of Lung Tumors*

Phase I Results of a Novel Technique

Jens Ricke, MD; Peter Wust, MD, PhD; Gero Wieners, MD; Susanne Hengst, MD; Maciej Pech, MD; Enrique Lopez Hänninen, MD; and Roland Felix, MD

(CHEST 2005; 127:2237–2242)

Results

- 30 lung tumors in 15 patients
- mean diameter 2 cm (range, 0.6 to 12 cm; median diameter, 1.5 cm)
- No major complication
  - no pneumothoraces, hemoptyses, or abscesses
- No changes of VC or FEV1 3 months after the intervention
- Local tumor control was 97% with one tumor recurrence detected after 9 months

Ricke et al. Chest 2005

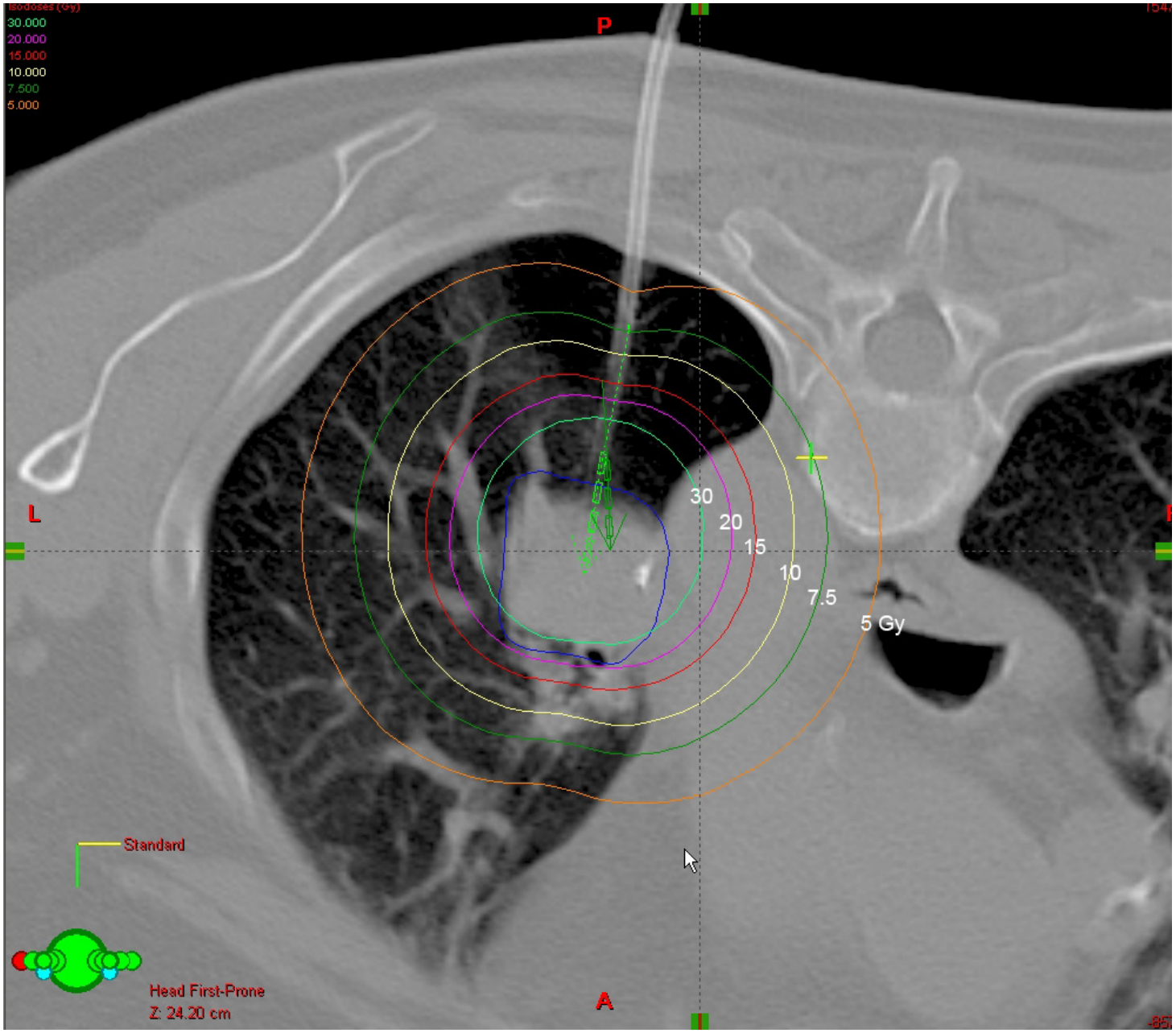
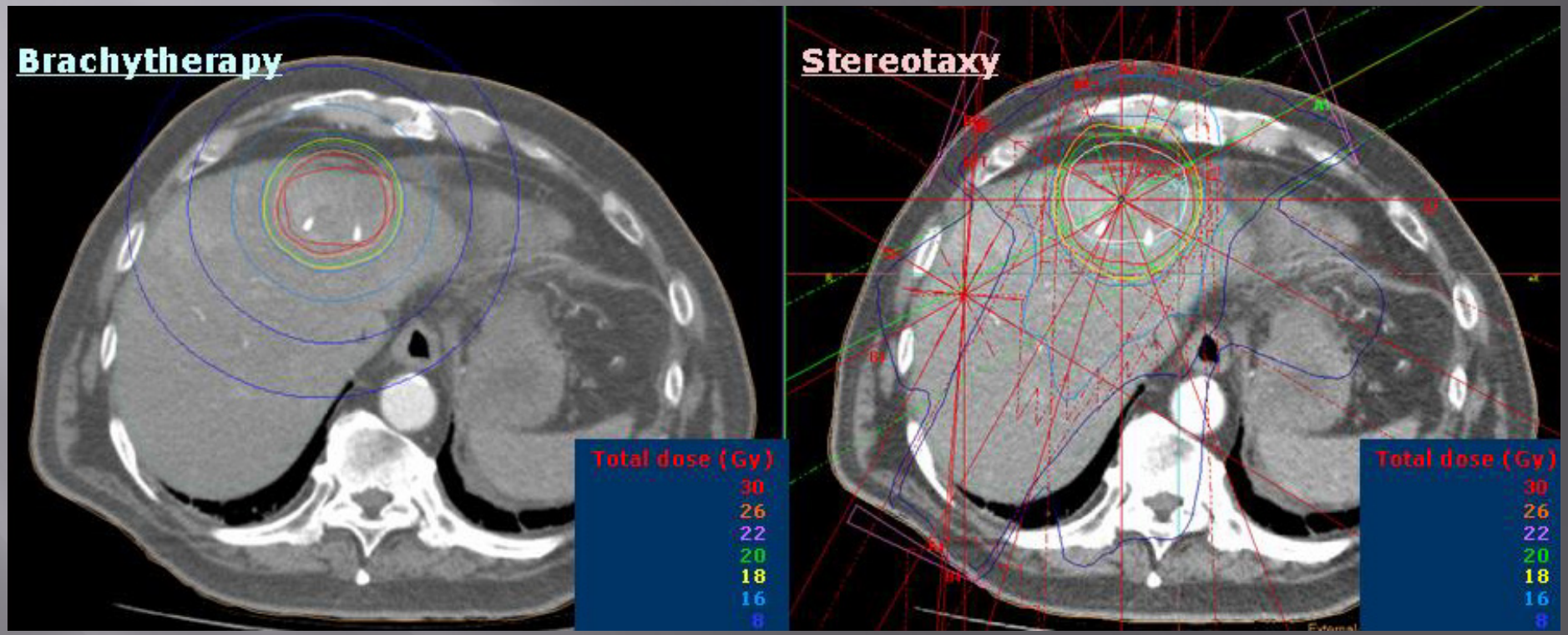

Isodoses (Gy)
30.000
20.000
15.000
10.000
7.500
5.000
P
L
A
30
20
15
10
7.5
5 Gy
Standard
Head First-Prone
Z: 24.20 cm

Table 1—*Estimation of Lung Tissue Exposed Above the Single Tolerance Dose for Various Lesions and Techniques of Brachytherapy*

Tumor	Technique	Volume > 10 Gy, mL	Lung Lobe, %
Sphere with 2-cm diameter	1 central catheter	35	2
	1 excentric catheter	50	3
Lesion of 5 × 3 × 3 cm size	2 catheters	170	9

Ricke et al. Chest 2005

Comparison IBT - SBRT



Hass P, DEGRO 1015

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MAGDEBURG

Results (n=30)

		HDR-BT	SBRT		
CTV: (mean)	D100	19,03 Gy	16,79 Gy	0,000	significant
	D 90	27,86 Gy	19,51 Gy	0,000	significant
Liver-dose: (mean)	5Gy-Vol.	592,60 ml	670,70 ml	0,000	significant

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Strahlentherapie
und Onkologie

Original Article

CT-Guided Interstitial Brachytherapy of Primary and Secondary Lung Malignancies

Results of a Prospective Phase II Trial

Nils Peters[1,2], Gero Wieners[1], Maciej Pech[1], Susanne Hengst[3], Ricarda Rühl[1], Florian Streitparth[3], Enrique Lopez Hänninen[3], Roland Felix[3], Peter Wust[3], Jens Ricke[1]

Background and Purpose: CT-guided interstitial brachytherapy of primary lung malignancies and pulmonary metastases represents a novel interventional technique, combining conventional high-dose-rate (HDR) iridium-192 (^{192}Ir) brachytherapy with modern CT guidance for applicator positioning and computer-aided 3-D radiation treatment planning. The purpose of this study was to assess safety and efficacy of this technique.

Patients and Methods: 30 patients with 83 primary or secondary lung malignancies were recruited in a prospective nonrandomized trial (Table 1). After catheter positioning under CT fluoroscopy, a spiral CT was acquired for treatment planning (Figure 1). All but two patients received a defined single dose (coverage > 99%) of at least 20 Gy from a ^{192}Ir source in HDR technique.

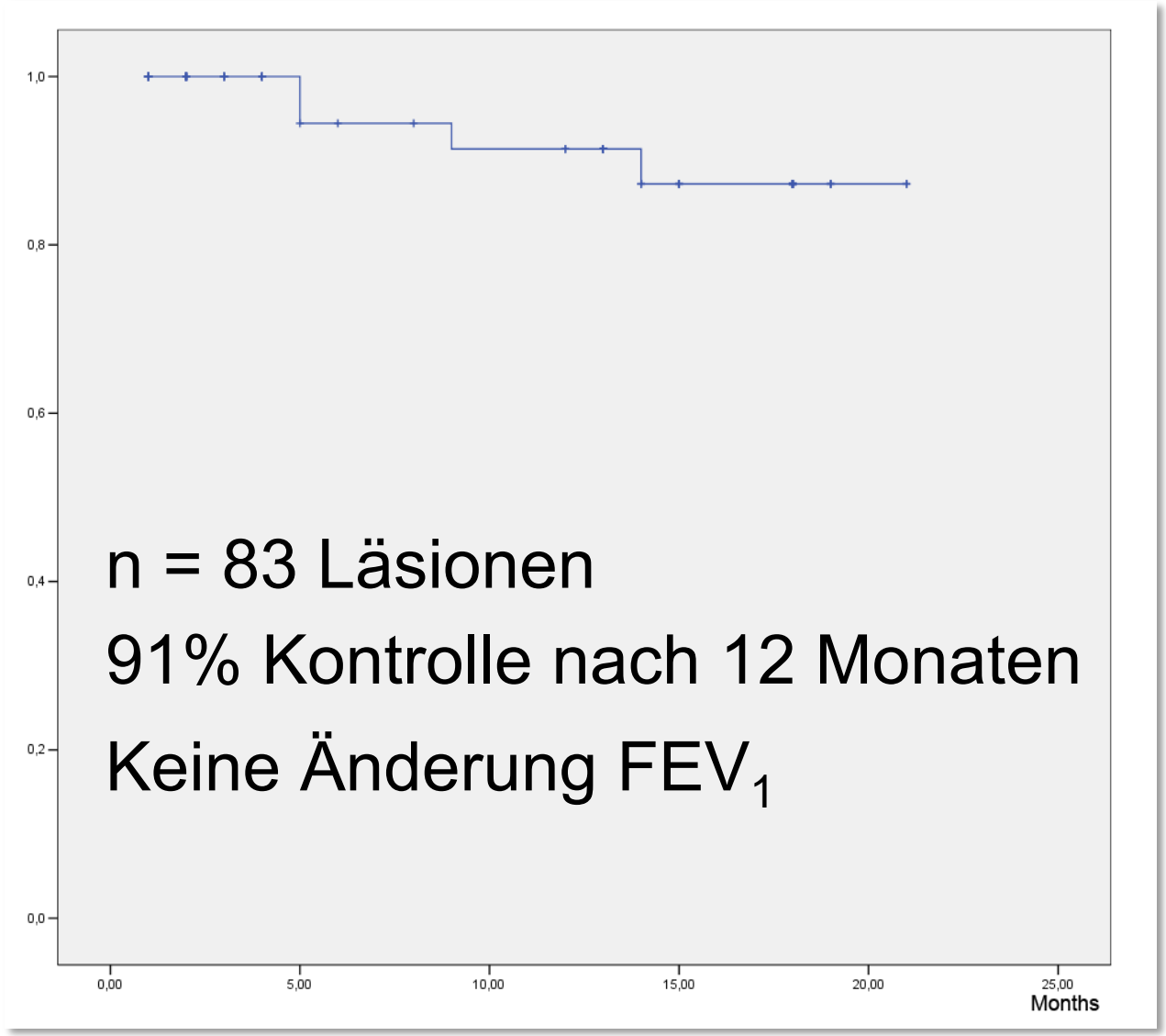
Results: Adverse effects were nausea (n = 3, 6%), minor (n = 6, 12%) and one major pneumothorax (2%). Post intervention, no changes of vital capacity and forced expiratory volume could be detected. The median follow-up period was 9 months (1–21 months) with a local tumor control of 91% at 12 months (Figure 2).

Conclusion: CT-guided interstitial brachytherapy proved to be safe and effective for the treatment of primary and secondary lung malignancies.

CT-Brachy von Lungenmalignomen

Tumor entity	Patients (n)	Patients with singular lesions (n)	Treated lesions (n)	Interventions (n)
Colorectal carcinoma	13	5	35	21
Primary NSCLC	4	4	4	4
Metastases of NSCLC	2	0	4	4
Breast cancer	4	2	8	6
Soft-tissue sarcoma	3	1	10	7
Hypernephroid renal carcinoma	3	2	21	7
Laryngeal cancer	1	1	1	1

- Mean tumor diameter 2.5 cm (0.6–11 cm)
- Minor complications:
  - nausea (n = 3, 6%)
  - discrete pneumothorax (n = 6, 12%) treated conservatively
- One major pneumothorax (n = 1, 2%)
  - 12-F chest tube and constant suction for 24 h



n = 83 Läsionen

91% Kontrolle nach 12 Monaten

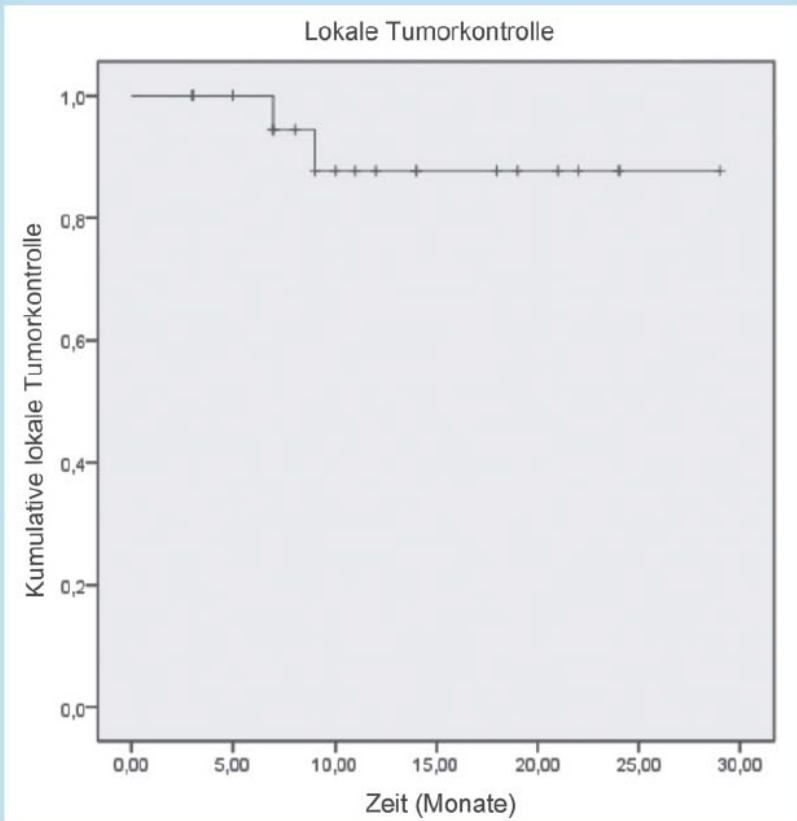
Keine Änderung FEV_1

Perkutane CT-gesteuerte Hochdosis-Brachytherapie (CT-HDRBT) von primären und metastatischen Lungentumoren in nicht chirurgischen Kandidaten

Percutaneous CT-Guided High-Dose Brachytherapy (CT-HDRBT) Ablation of Primary and Metastatic Lung Tumors in Nonsurgical Candidates

Autoren F. Collettini[1], D. Schnapauff[1], A. Poellinger[1], T. Denecke[1], J. Banzer[1], M. J. Golenia[1], P. Wust[2], B. Gebauer[1]

Institute
[1] Radiologie, Charité – Universitätsmedizin Berlin
[2] Strahlentherapie, Charité – Universitätsmedizin Berlin



Collettini et al. 2012

Tab. 1 Charakteristika der Patientenpopulation und der Tumore (Range in Klammern).

Patientenkollektiv	no.	%
Patientenzahl	22	
Durchschnittsalter	65,4 Jahre (45 – 82)	
Geschlechtsverteilung		
weiblich	10	45,4
männlich	12	54,5
Anzahl der Tumoren	33	
Primarius		
Bronchialkarzinom	1	4,5
kolorektales Karzinom	4	18,1
HNO-Tumor (Parotis, Larynx)	2	9
Mammakarzinom	1	4,5
Ovarialkarzinom	1	4,5
Ösophaguskarzinom	2	9
Pankreaskarzinom	3	13,6
Weichteilsarkom	8	36,3

Tab. 2 Überblick über die Ergebnisse der eigenen Untersuchung zur CT-HDRBT von primären und metastatischen Lungentumoren (Range in Klammern).

Interventionen/Hochdosis-Brachytherapie	no.	%
Interventionen	34	
mittleres Zielvolumen (CTV) (ml)	29,2 (1,2 – 91,7)	
mittlerer Durchmesser (mm)	33,3 (10 – 85)	
mit 20 Gy behandelte Läsionen	25	75,7
mit 15 Gy behandelte Läsionen	8	24,2
periinterventionelle Komplikationen	3	8,8
Lokalrezidive	2	6,25
Nachbeobachtungszeit		
mittlere Verlaufskontrollzeit	13,7 (3 – 29)	
mittlere lokale Tumorkontrolle	12,3 (3 – 29)	
mittlere progressionsfreie Zeit	7,8 (2 – 29)	
mittlere Überlebenszeit	17,7 (3 – 29)	

Mittlerer Durchmesser der 33 Lungenherde betrug 33,3mm (Range: 10 – 86)

Collettini et al. 2012

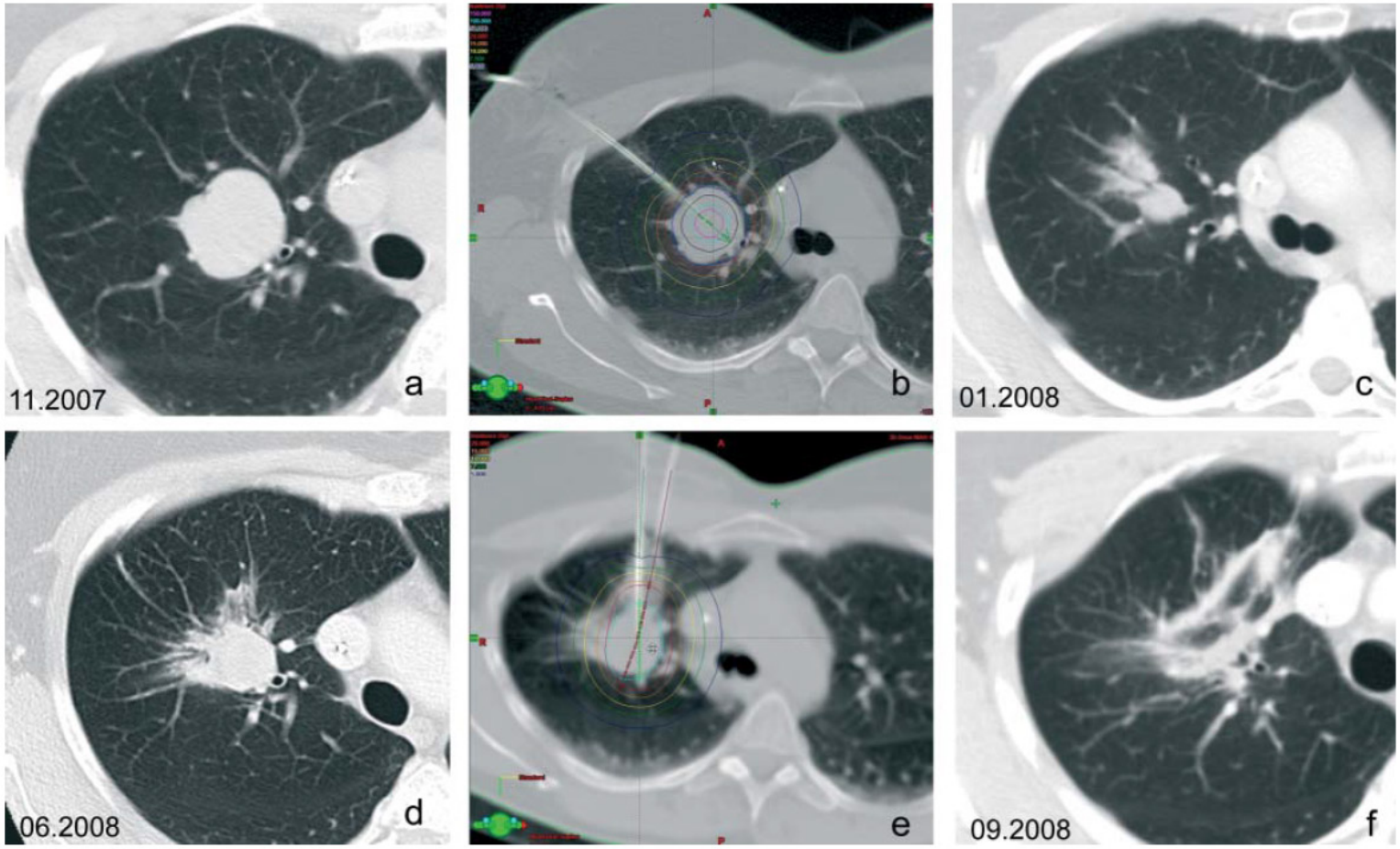


Abb. 3 46 Jahre alte Frau mit einer Lungenmetastase eines myxoiden Lipsarkoms. **a** zeigt den Ausgangsbefund der 4,2 cm großen Metastase. Nach Therapie mittels Afterloading (20 Gy tumorumschließend) zeigt sich eine deutliche Größenregredienz **b**. 7 Monate später trat ein lokaler Progress der Metastase auf **c**, welcher durch erneute Ablation mit CT-HDRBT erfolgreich behandelt wurde [23].

Collettini et al. 2012

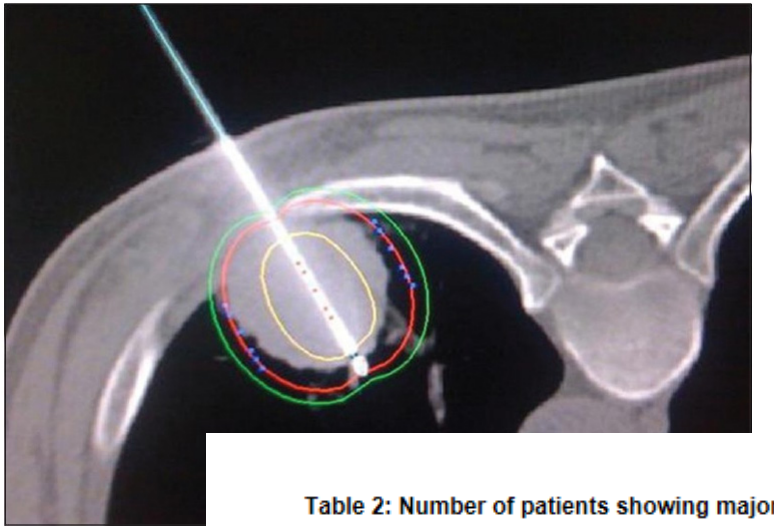


Table 2: Number of patients showing major and minor complications (N = 8 patients)

	Major	Minor
Pneumothorax	0	0
Hemothorax	0	1
Hemoptysis	0	1
Thrombo-embolism	0	-
Total	0 (0%)	2 (25%)

Table 3: Number of patients showing tumor control

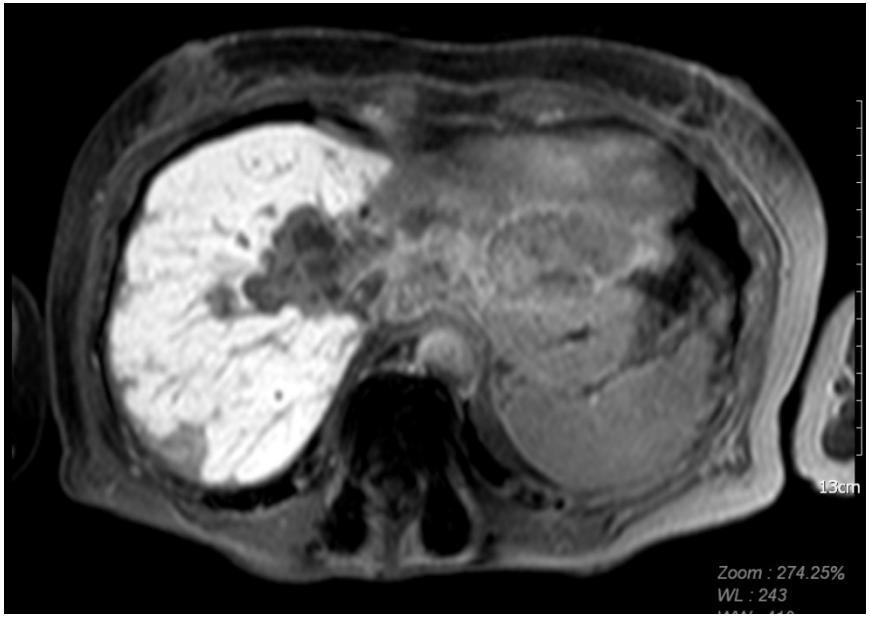
	At 1 month	At 3 months	At 6 months
CR	0	2	3
PR	4	3	3
NR / PD	4	2	2
CR + PR	4 (50%)	5 (62%)	6 (75%)

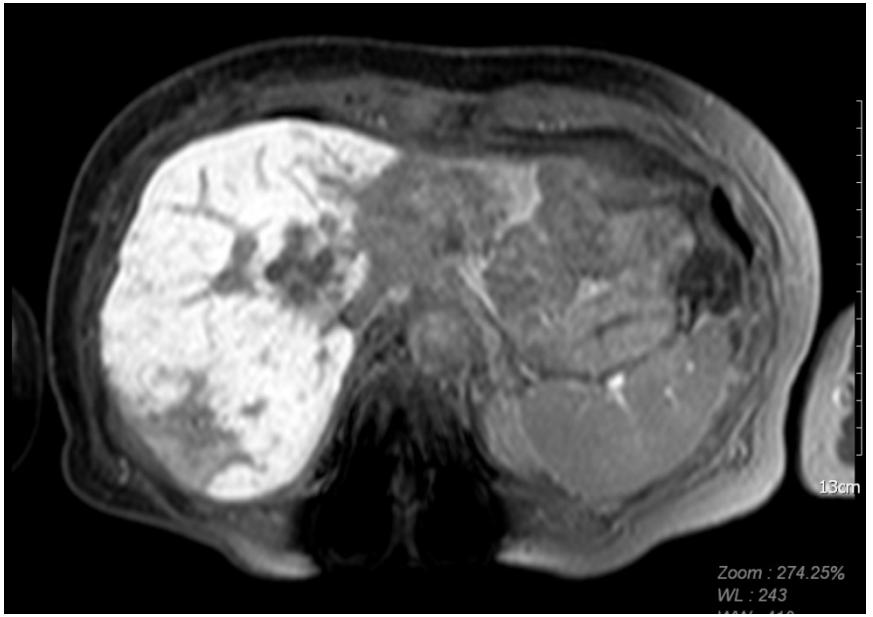
CR: Complete response, PR: Partial response, NR: No response, PD: Progressive disease

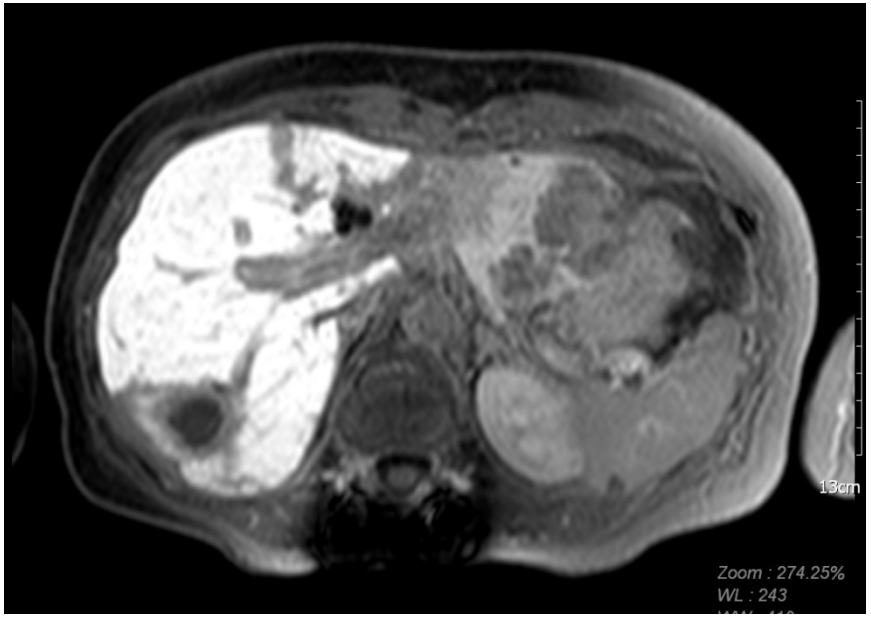
Sharma DN et al. J Cancer Res Ther. 2011

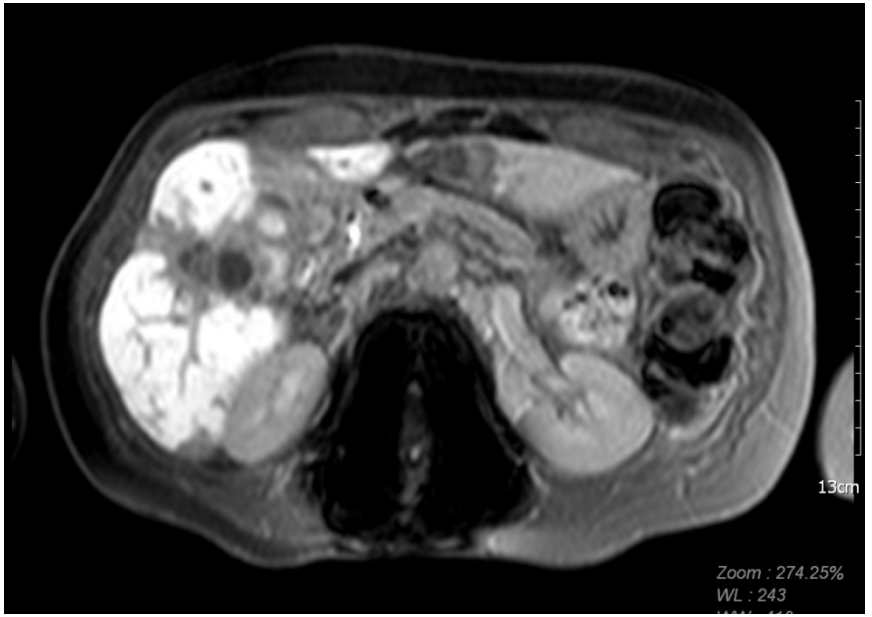
Take home

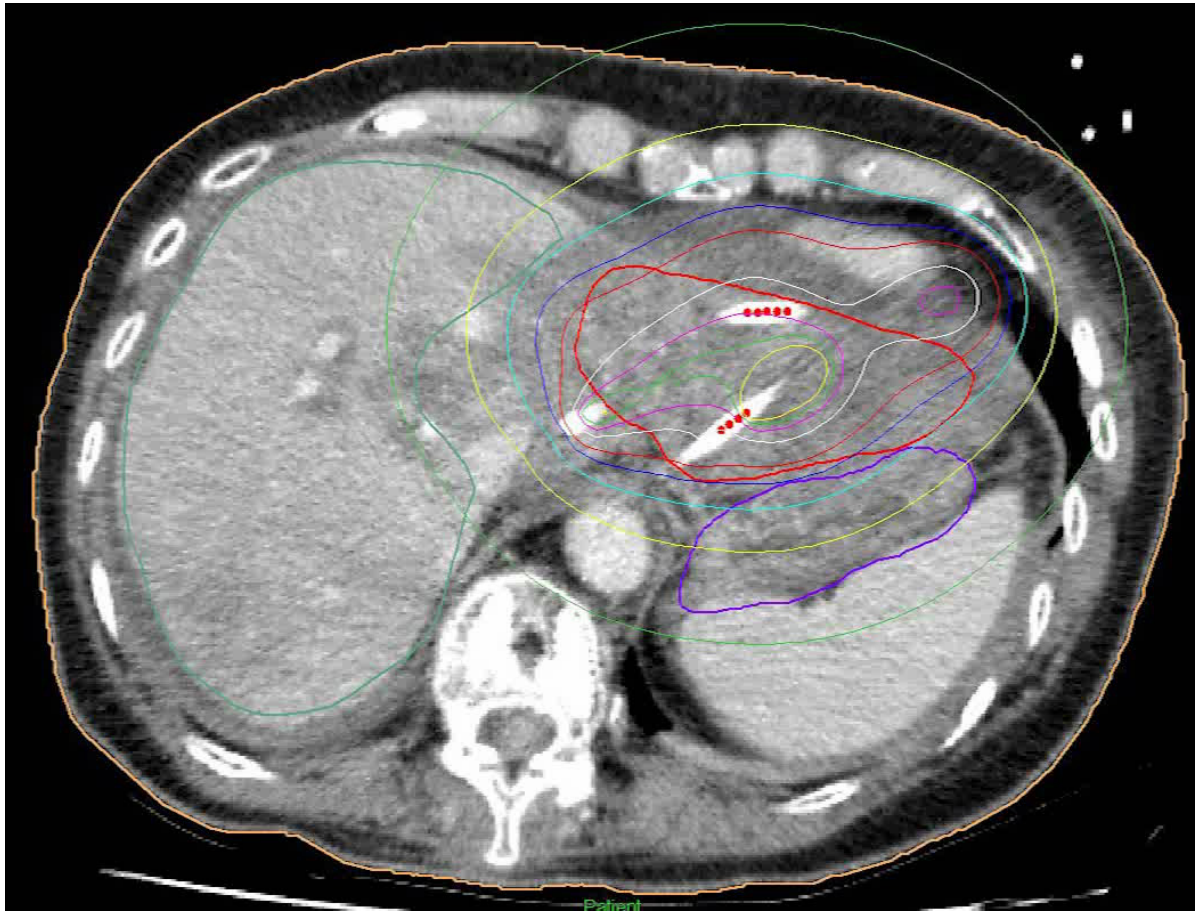
- CT-gesteuerte Brachytherapie auch in der Lunge sicher und effektiv für „alle“ Tumorbiologien
- Teil der ESMO Leitlinien mCRC und ICC 2016
- Extreme „technische“ Indikationsbreite
  - (fast) unlimitierte Tumorgrößen
- Überlegene physikalische Eigenschaften gegen SBRT
  - Dosisexposition von Risikoorganen, Tumorgröße
  - …aber invasiv
- Ideal für multiple oder große Herde

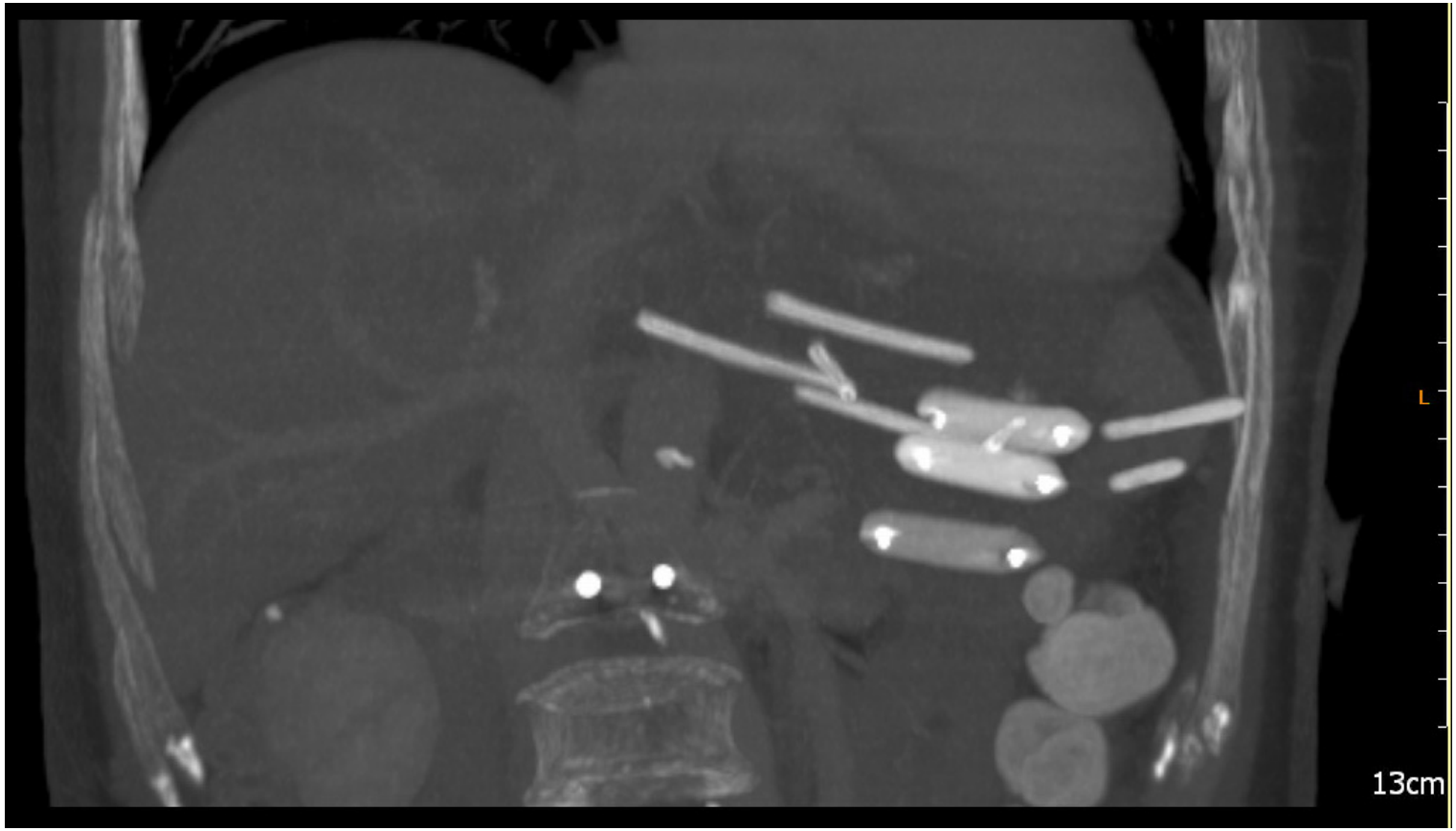

13cm
Zoom : 274.25%
WL : 243


13cm
Zoom : 274.25%
WL : 243

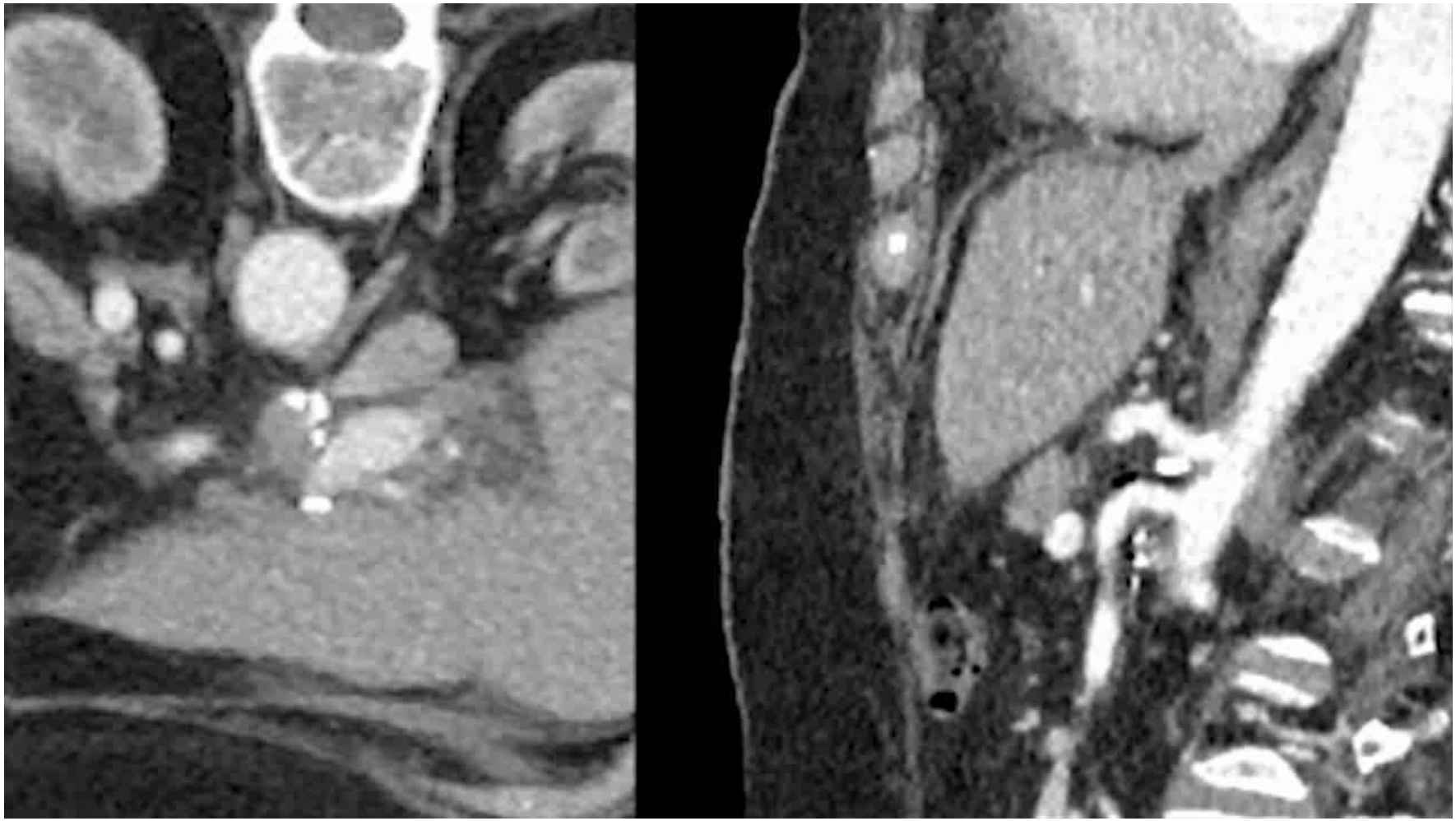

13cm
Zoom : 274.25%
WL : 243


13cm
Zoom : 274.25%
WL : 243


Patient


L
13cm

Images: Ricke



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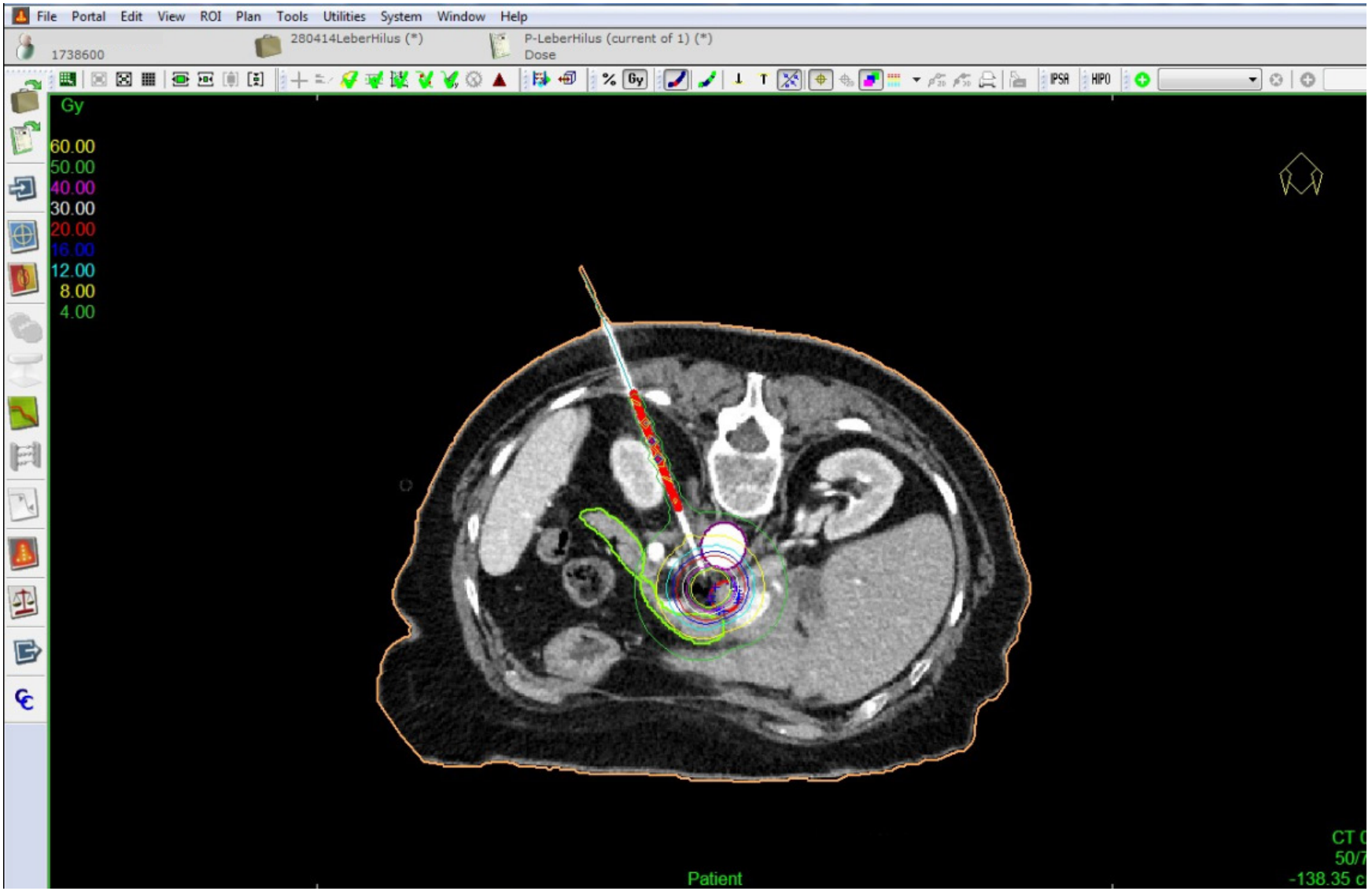
Images: Ricke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1738600
280414LeberHilus (*)
P-LeberHilus (current of 1) (*)
Dose
Gy
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Patient