Lungenmetastasen: Regionale Chemotherapie und Ablation

uct Universitäres Centrum für Tumorerkrankungen Frankfurt
University Cancer Center

Deutsche Krebsgesellschaft
Zertifiziertes Darmzentrum

Gewinner des
KLINIK AWARD 2010

Thomas J. Vogl, N. Nour-Eldin
I D I R: Institut für Diagnostische und Interventionelle Radiologie
Goethe-Universität, Frankfurt am Main

www.uni-reconstruction.de
Frischer
Wind
an der
Goethe-
Uni
U
uni bis
l 2009

Interventionelle Onkologie: Thermoablation und Regionale Chemotherapie von Lungenmetastasen

- Onkologische Konzepte
- Intervention: - Technik
  - Patientenmanagement
- Ergebnisse Thermoablation
- Neue Entwicklungen // Schlussfolgerung

Institut für Diagnostische und Interventionelle Radiologie, Goethe-Universität, Frankfurt

Interventionelle Onkologie

Thermische Ablation

- RFA
- MWA
- LITT
- Kryotherapie
- Elektroporation
- Nanoknife

Vaskuläre Therapien

- TACE
  - transarteriell
- TAE
- TPCE
- SIRT
- Chemo-saturation

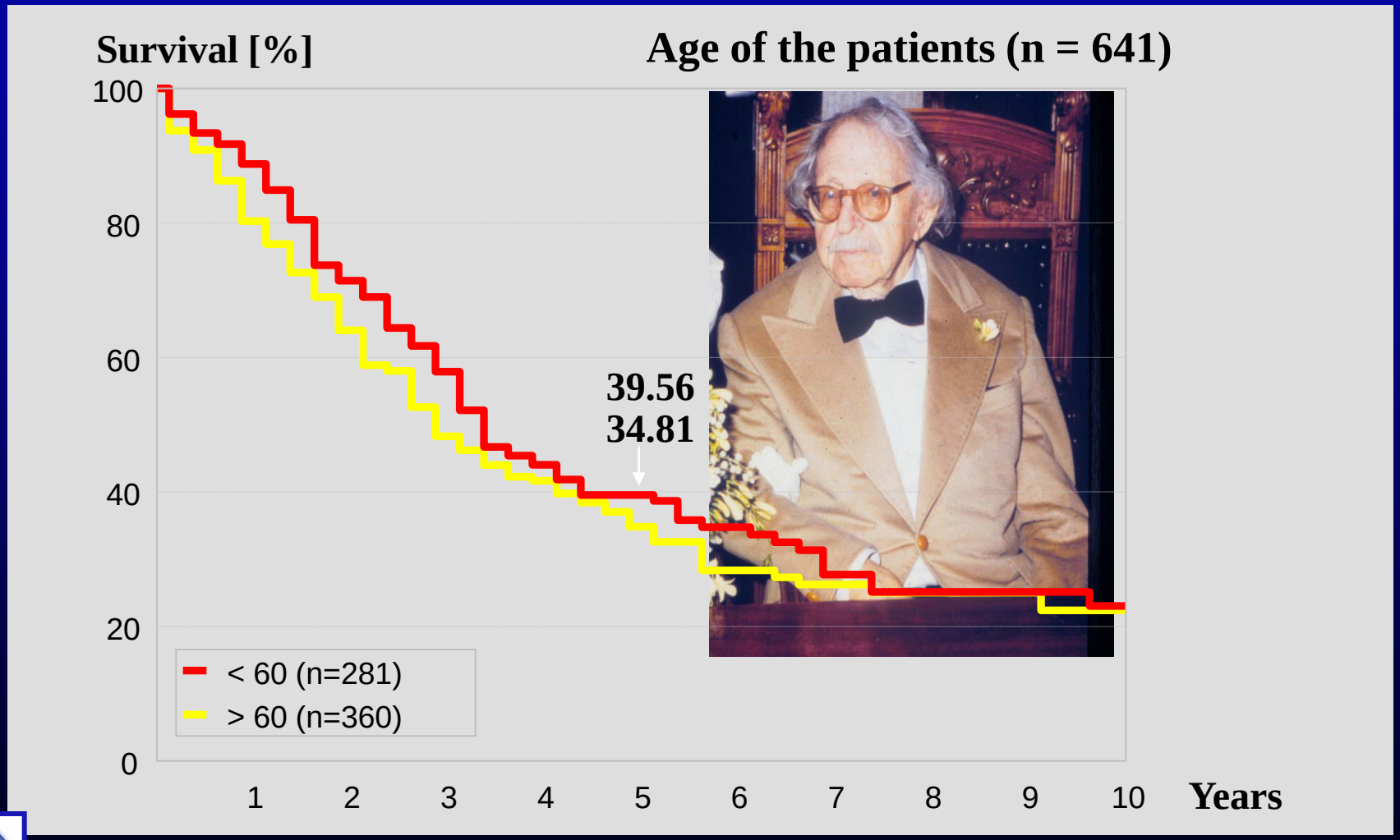
Palliative Therapien

- Schmerztherapie
- Stents
- Biopsien
- Vaskuläre Rekanalisation
- Port, Stent

Interventionelle Onkologie

- **Klinische Patientenversorgung**
- **Ambulante, teilstationäre, stationäre Versorgung**
- **Management: Nebenwirkungen, Komplikationen**
- **Nachsorge**

Interventionelle Onkologie ohne Altersbeschränkung



Entscheidungsfindung: Lungenmetastasen

CT
MRT
Sono
PET-CT

→ Multidisziplinäres Tumorboard

→ Primäre OP

→ Radiofrequenzablation (RFA)
Mikrowellenablation (MWA)
Laserinduzierte Thermotherapie (LITT)
Transpulmonale Chemoembolisation (TPCE)
Regionale Chemotherapieverfahren

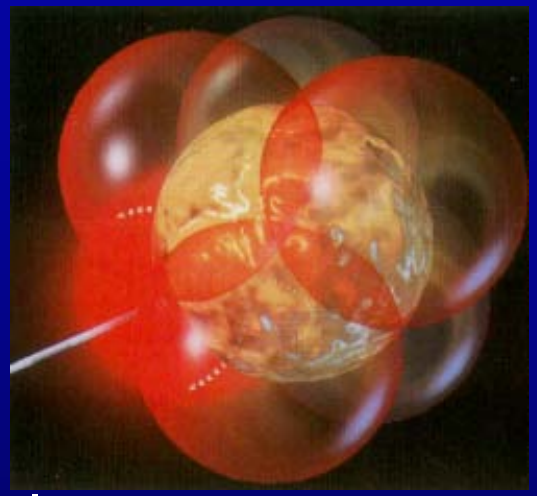
→ Primäre Radiatio → Sekundäre OP ?

→ Palliative Chemotherapie

Tumorablation Lunge: Therapieziel

1. Cytoreduktion, supportiv
2. Downstaging, perioperativ
3. Technisch tumorfrei („cA0“)

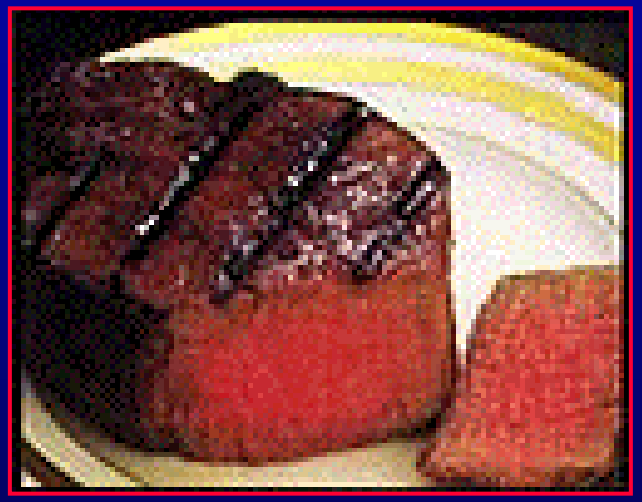
Tumorablation: Fragen

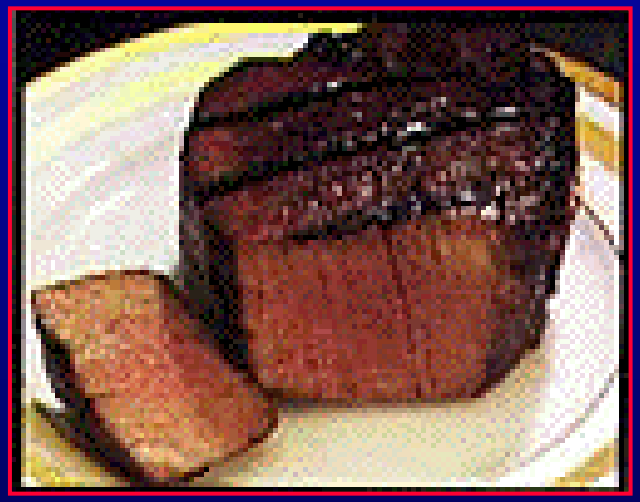


- Was ist die beste Methode?
  ⇒ LITT, RFA, MWA oder Cryo?
- Was ist die geeignetste Steuerung?
  ⇒ Sono, CT, Echtzeit-MRT?
- Welches Monitoring des Therapieerfolgs?
- Welche Rolle spielt die Kombinationstherapie?
  ⇒ Chemo, TPCE
- Welche Tumoren zeigen das beste Ansprechen?

Thermotherapie

rare **medium** **well**



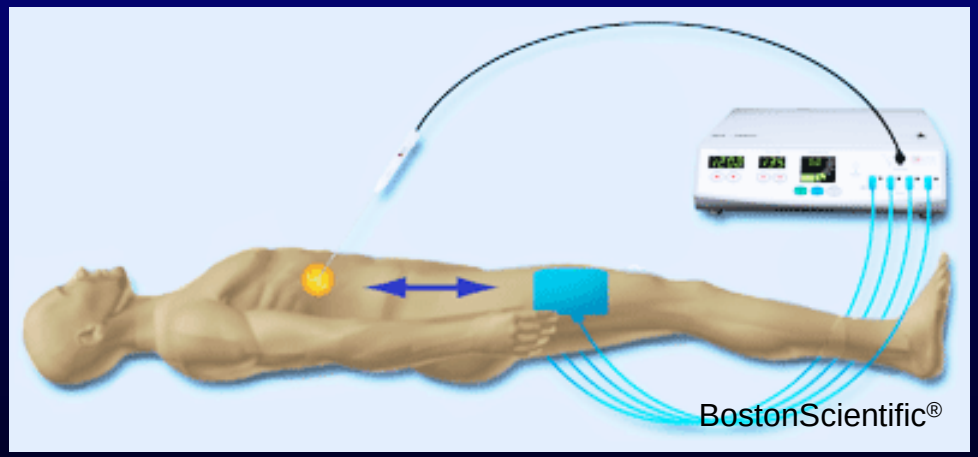


Tumorablation von Lungenmetastasen: Technik

Dupuy DE, Am J Roentgenol 2000; 147:57-59
Steinke K, CVIR 2002; 25(6):543-6
Simon CJ, Radiology 2007; 243:268-75
Chua TC, Ann Oncol 2010; 21(10):2017-22

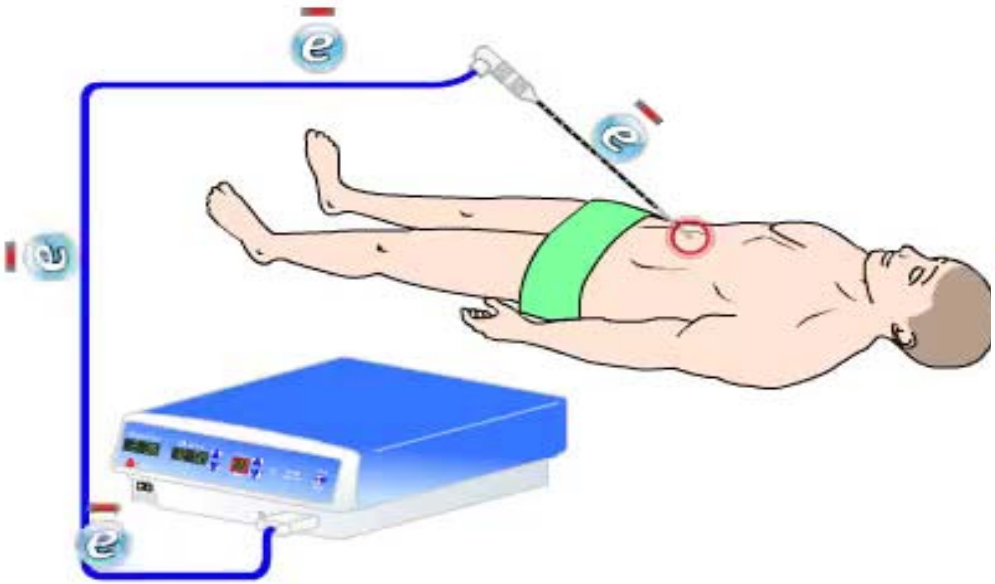
Radiofrequenzablation (RFA)

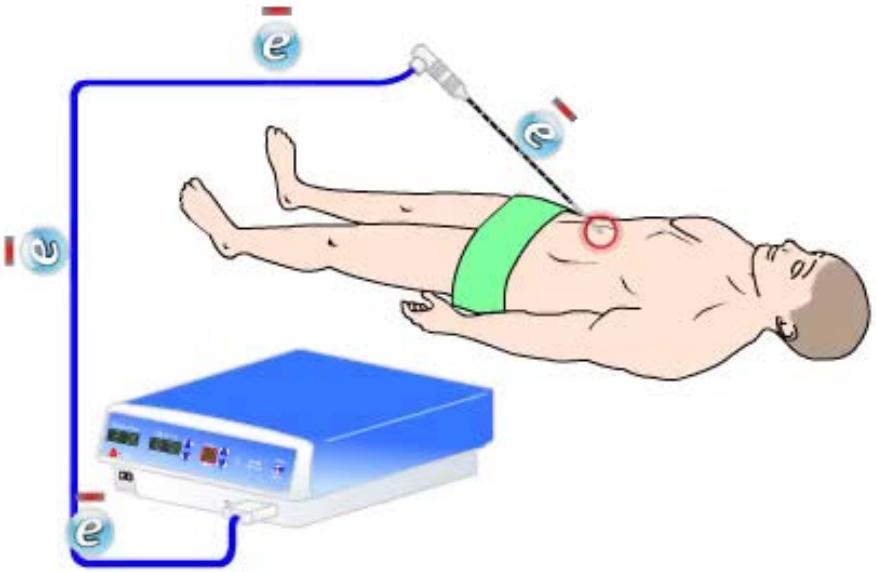
- Strom 450-500 kHz

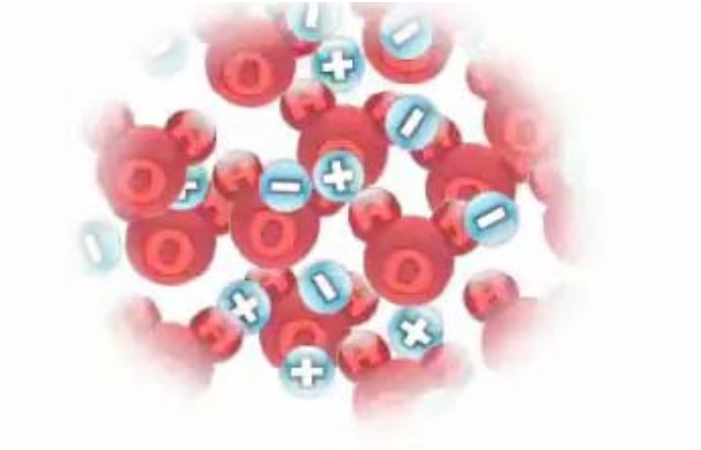


Mikrowellenablation

RF-Ablation







Radiofrequenzablation

Berchtold

Radiotherapeutics

Bipolar

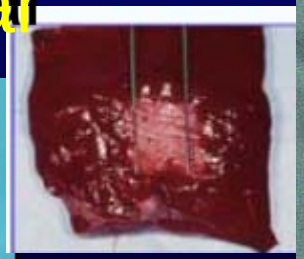
„Track ablation“

RITA Medical

Multifokal

Celon

Monopolar



Radionics

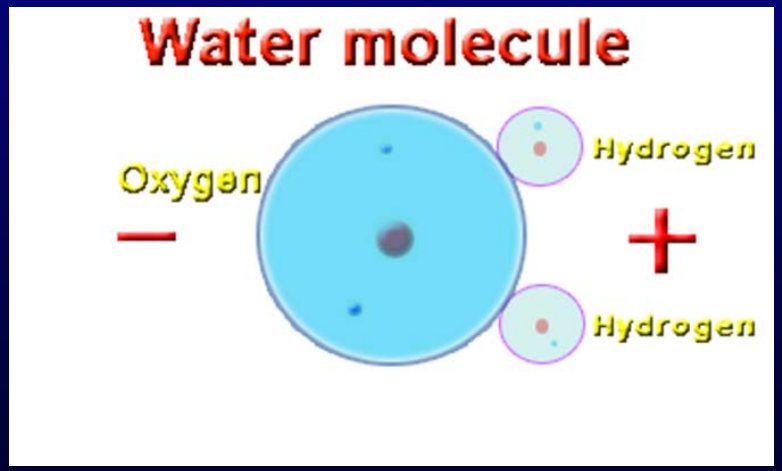
Impedanz

Tumorablation von Lungenmetastasen: Technik

Wolf FJ, Radiology 2008 247: 871-79
Vogl TJ, Radiology 2011 261 (2): 643-51

Mikrowellenablation (MWA)

- Elektromagnetische Wellen 915 mHz - 2,4 GHz



Mikrowellenablation

I. Schneller ↑

II. Homogener ↑

III. Schärfere Demarkation ↑

> RFA

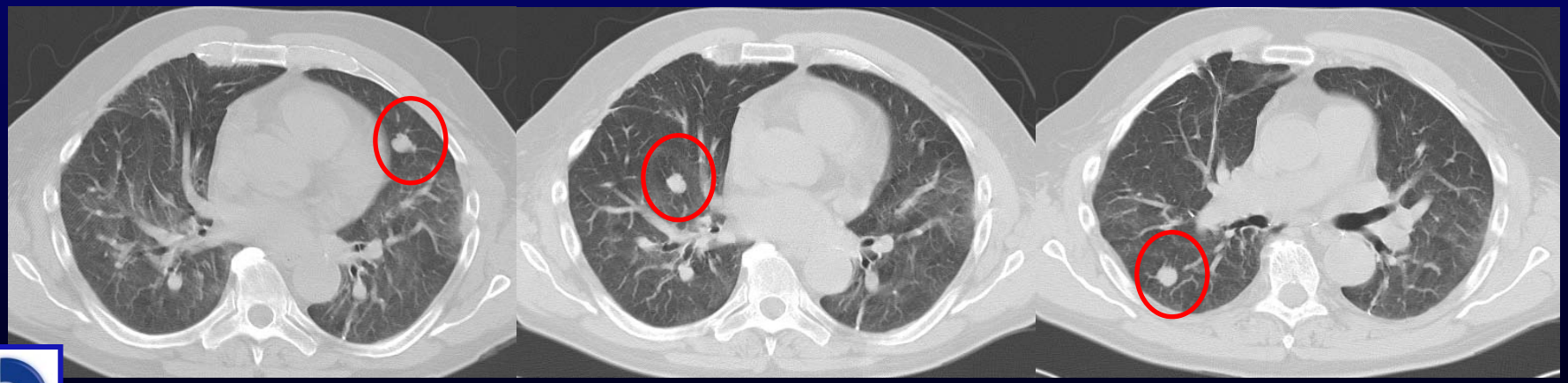
IV. Schmerzen ↓

V. Umpositionierung möglich,
da schnelle Ablation

Fall 1

62-jähriger Patient mit einem Sigmakarzinom (T2N2M0):

- Sigmoidektomie mit nachfolgender adjuvanter Chemotherapie
- Auftreten von Metastasen im li Leberlappen 18 Monate nach Op
- Hemihepatektomie li mit nachfolgender Chemotherapie (FOLFOX)
- Ein Jahr später Entwicklung von 3 Lungenmetastasen:
  2 Metastasen im rechten Unterlappen (subpleural und parahilär) und
  1 Metastase im linken Unterlappen (parakardial)
- Diabetes und Hypertonus



Fall 1

A) Eine Thermoablation in diesem Fall ist:

1) Durchführbar mit kurativer Intention

2) Nicht durchführbar wegen multipler Metastasen

3) Nicht durchführbar: zu hohes Risiko

Fall 1

B) Die schwerwiegendste Komplikation nach pulmonaler Thermoablation ist:

1) Pneumothorax

2) Pulmonale Blutung

3) Infektion und Kavitation

4) Bronchopleurale Fistel

5) Pleuraerguss

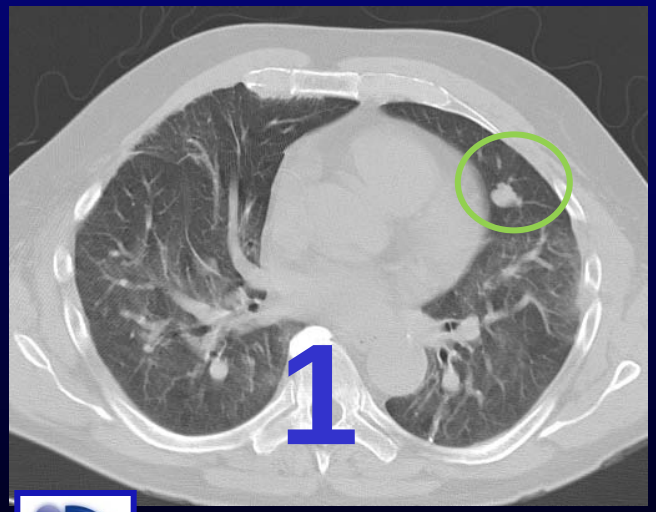
Fall 1

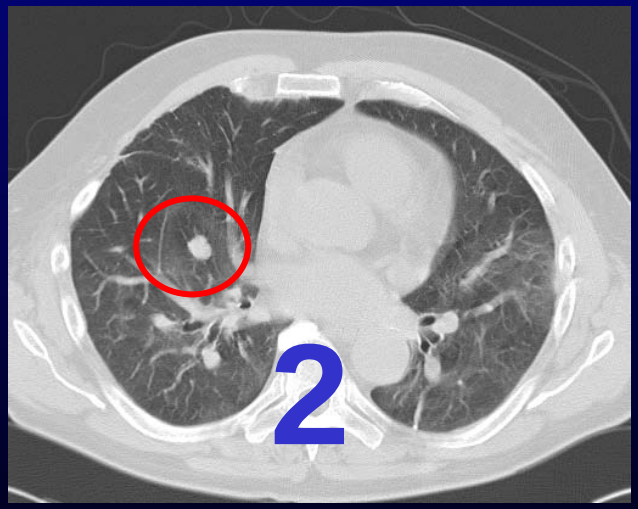
C) Bei welcher Läsion besteht das höchste Risiko für Komplikationen?

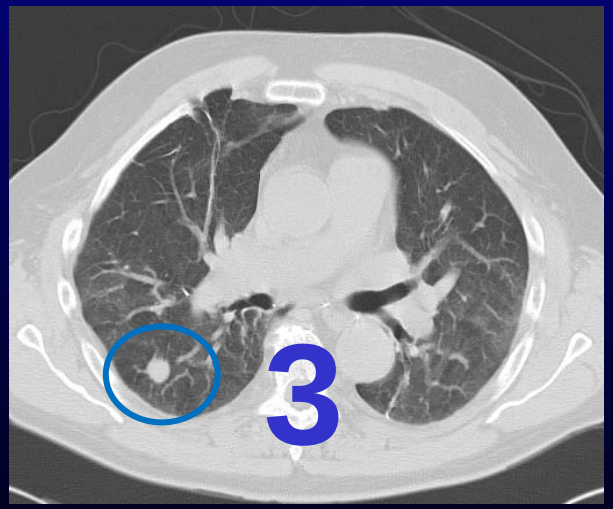
1)

2) ✓

3)

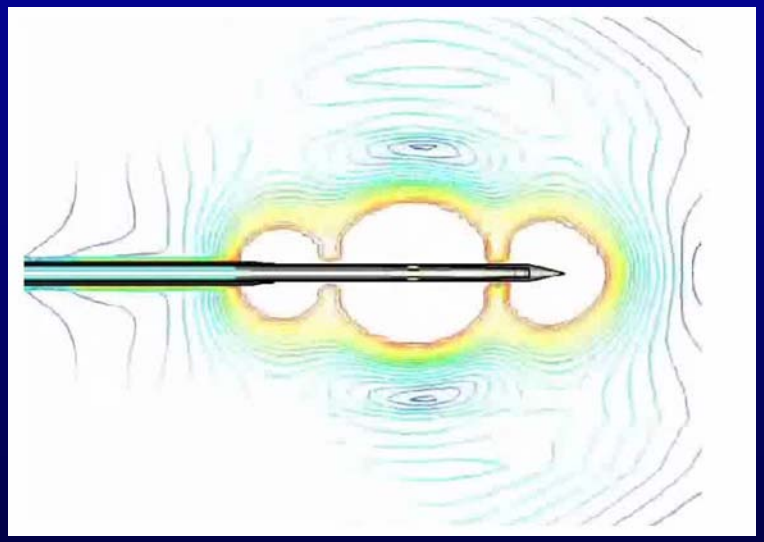


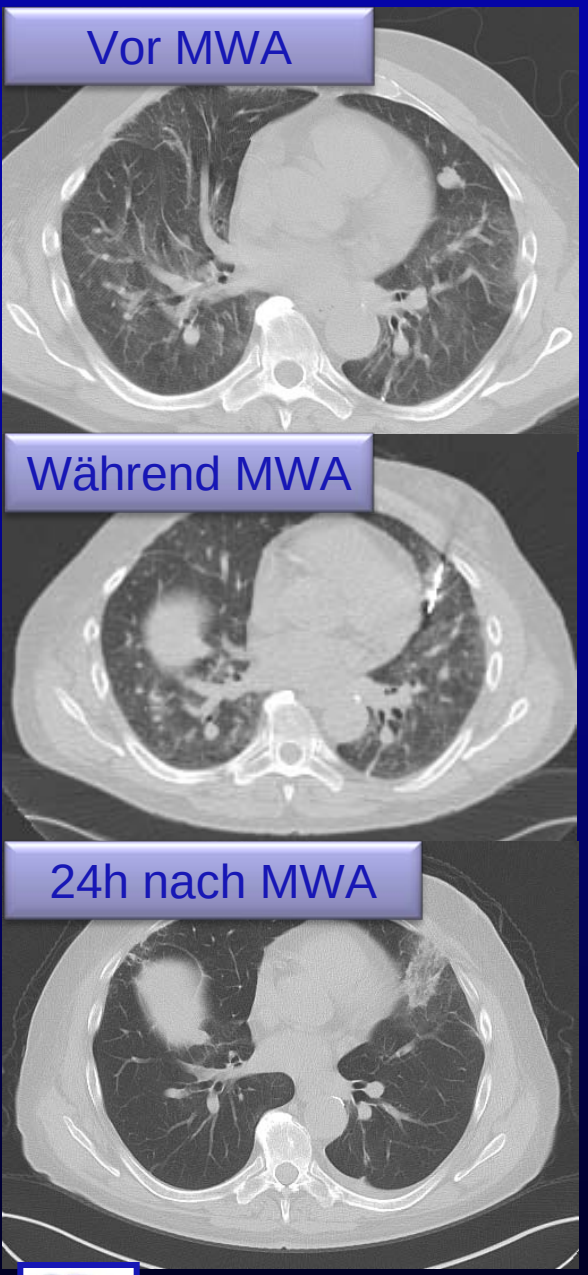


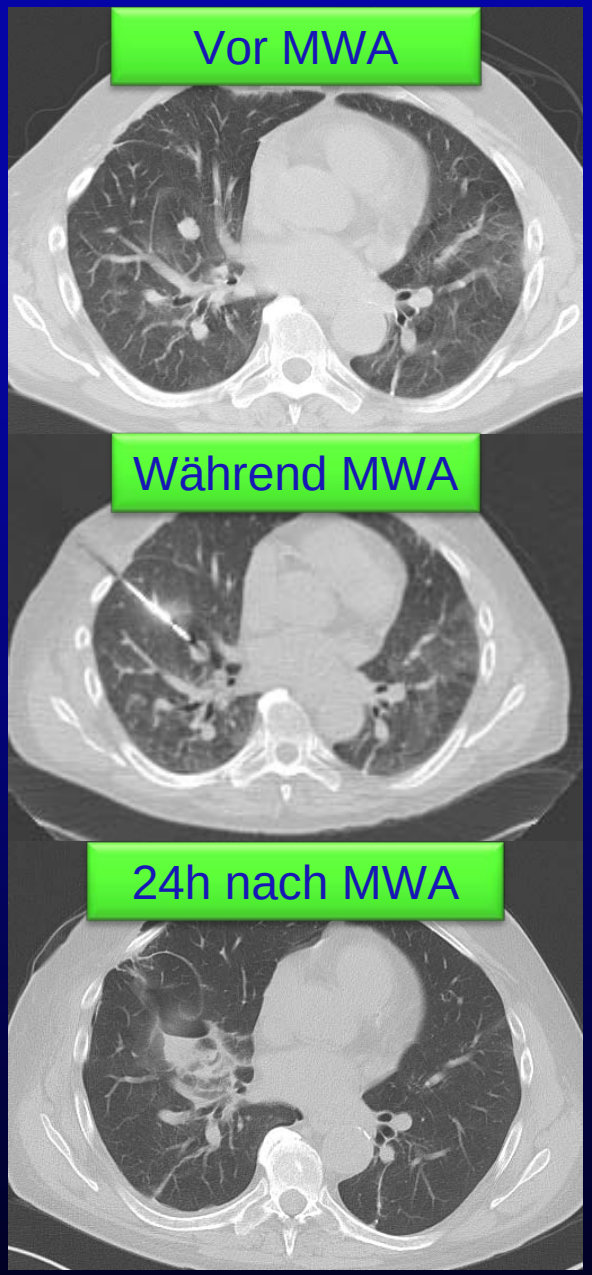


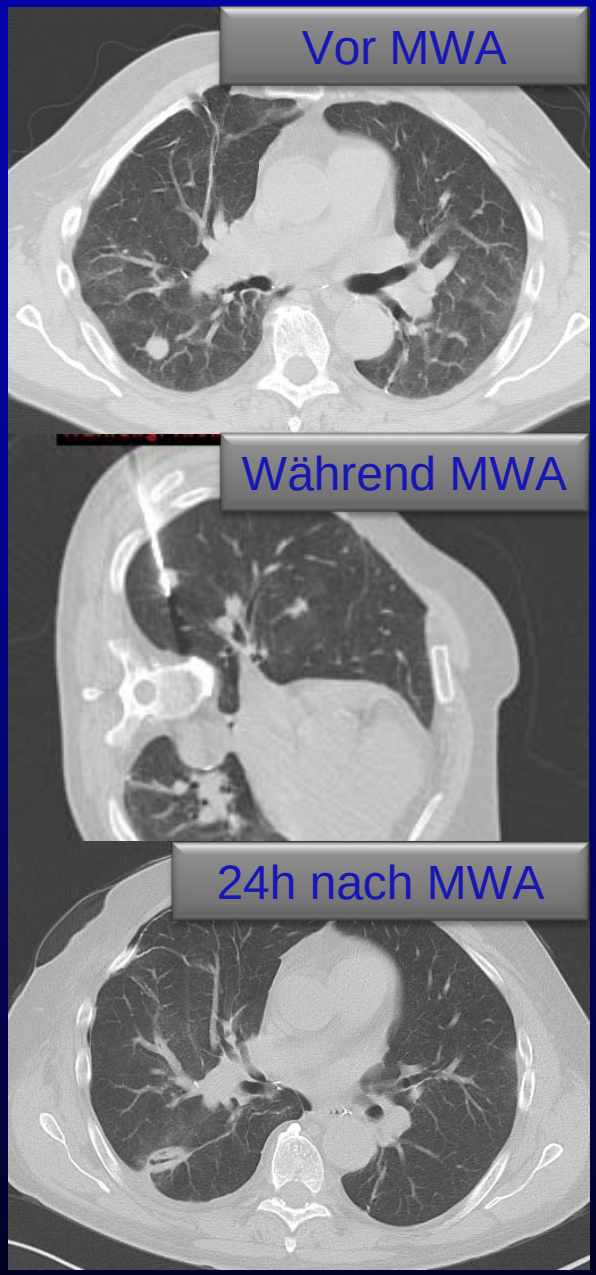
Fall 1

1) Therapieentscheidung: Mikrowellenablation mit kurativer Intention
2) Die MW-Ablation wurde mit einem System von Covidien Valleylab® durchgeführt.
3) Es erfolgten 3 separate Sitzungen in 1- oder 2-Wochen-Intervallen.
4) Ablation: 10-20 Minuten @ 45 Watt.




Vor MWA
Während MWA
24h nach MWA


Vor MWA
Während MWA
24h nach MWA

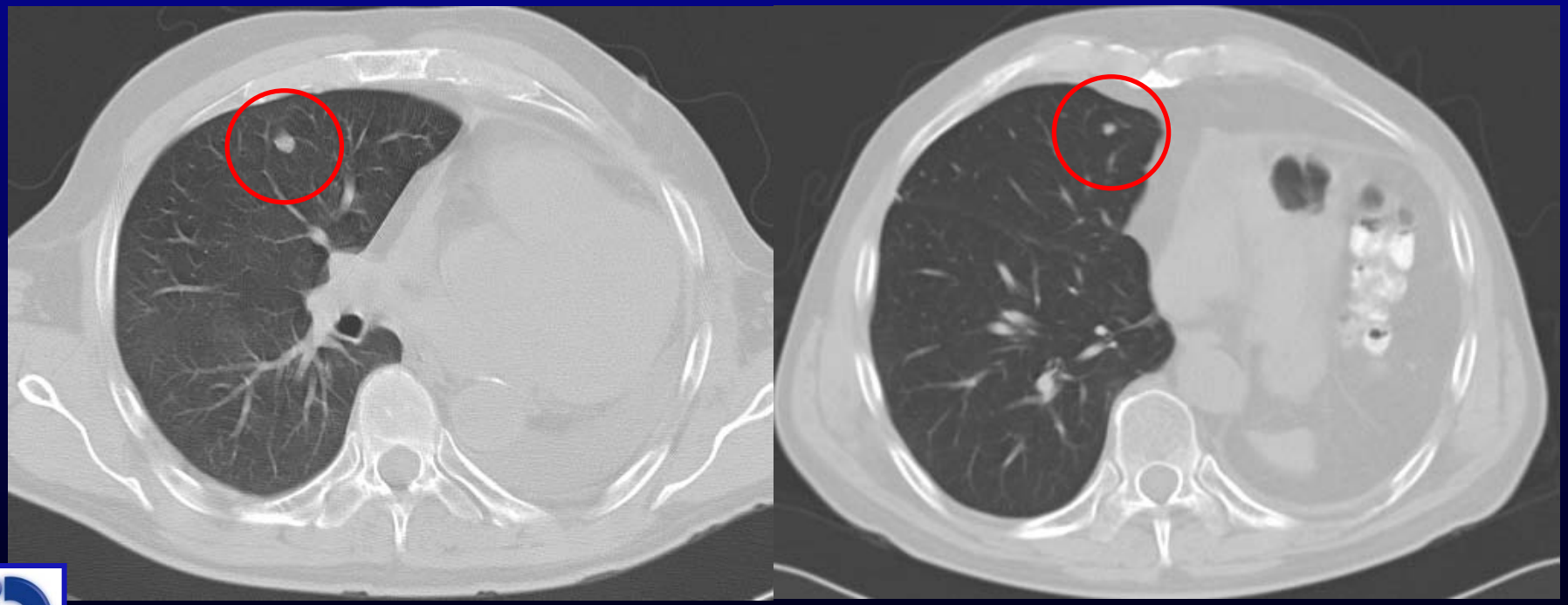

Vor MWA
Während MWA
24h nach MWA

Fall 1

Fall 2

58-jähriger Patient mit einem Bronchialkarzinom im linken Lungenflügel - NSCLC (T2N2M0):

- Pneumonektomie links und Lymphadenektomie
- Auftreten von 2 Metastasen im rechten Lungenmittellappen nach einem Jahr



Fall 2

A) Für eine Thermoablation in diesem Fall besteht:

1) Ein niedriges Risiko

2) Ein hohes Risiko

3) Eine Kontraindikation

Radiology

Radiology is a monthly journal devoted to clinical radiology and allied sciences, owned and published by the Radiological Society of North America, Inc.

Pulmonary Radiofrequency Ablation in Patients with a Single Lung: Feasibility, Efficacy, and Tolerance

Expand

Agathe Hess, MD, Jean Palussière, MD, Jean-François Goyers, MD, Axel Guth, MD, Anne Aupérin, MD, PhD and Thierry de Baère, MD

+ Author Affiliations

Address correspondence to
A.H. (e-mail: agathehess@aol.com).

Author contributions: Guarantors of integrity of entire study, A.H., T.d.B.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, A.H., J.P., T.d.B.; clinical studies, A.H., J.P., J.F.G., A.G., T.d.B.; experimental studies, J.P.; statistical analysis, J.P., A.A.; and manuscript editing, A.H., J.P., T.d.B.

Abstract

Purpose: To evaluate the feasibility, efficacy, and tolerance of pulmonary radiofrequency (RF) ablation for the treatment of lung tumors in patients with a single lung.

This Article

doi: 10.1148/radiol.10100771
February 2011 Radiology, 258, 635-642.

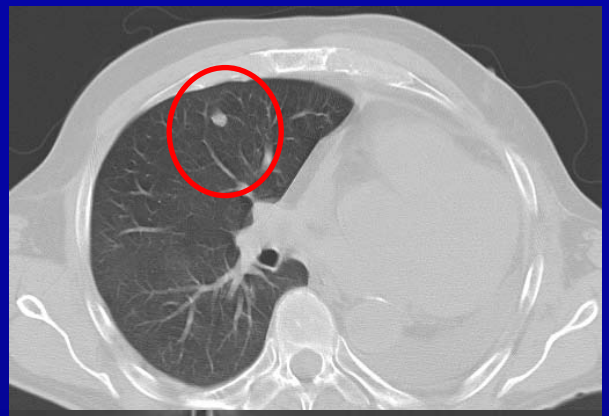
Abstract Free
Figures Only
» Full Text
Full Text (PDF)

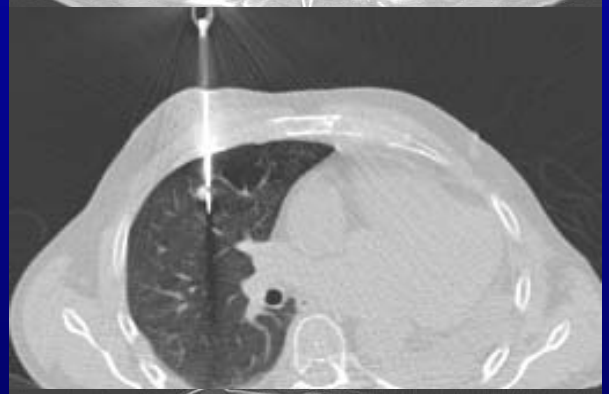
Classifications

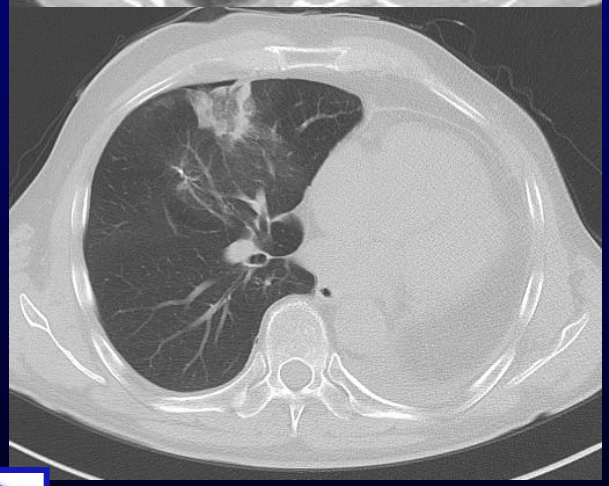
Original Research
Vascular and Interventional Radiology

Services

- Email this article to a friend
- Alert me when this article is cited
- Alert me if a correction is posted
- Alert me when eletters are published
- Similar articles in this journal
- Similar articles in PubMed



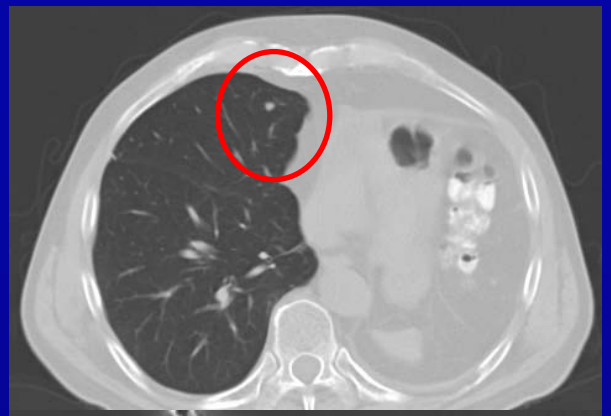


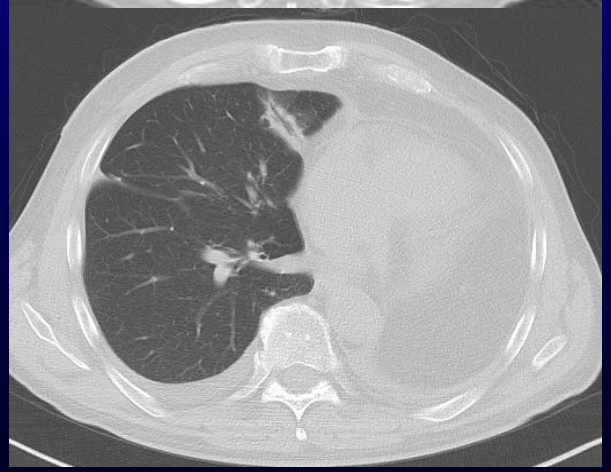


Metastasen eines Bronchialkarzinoms

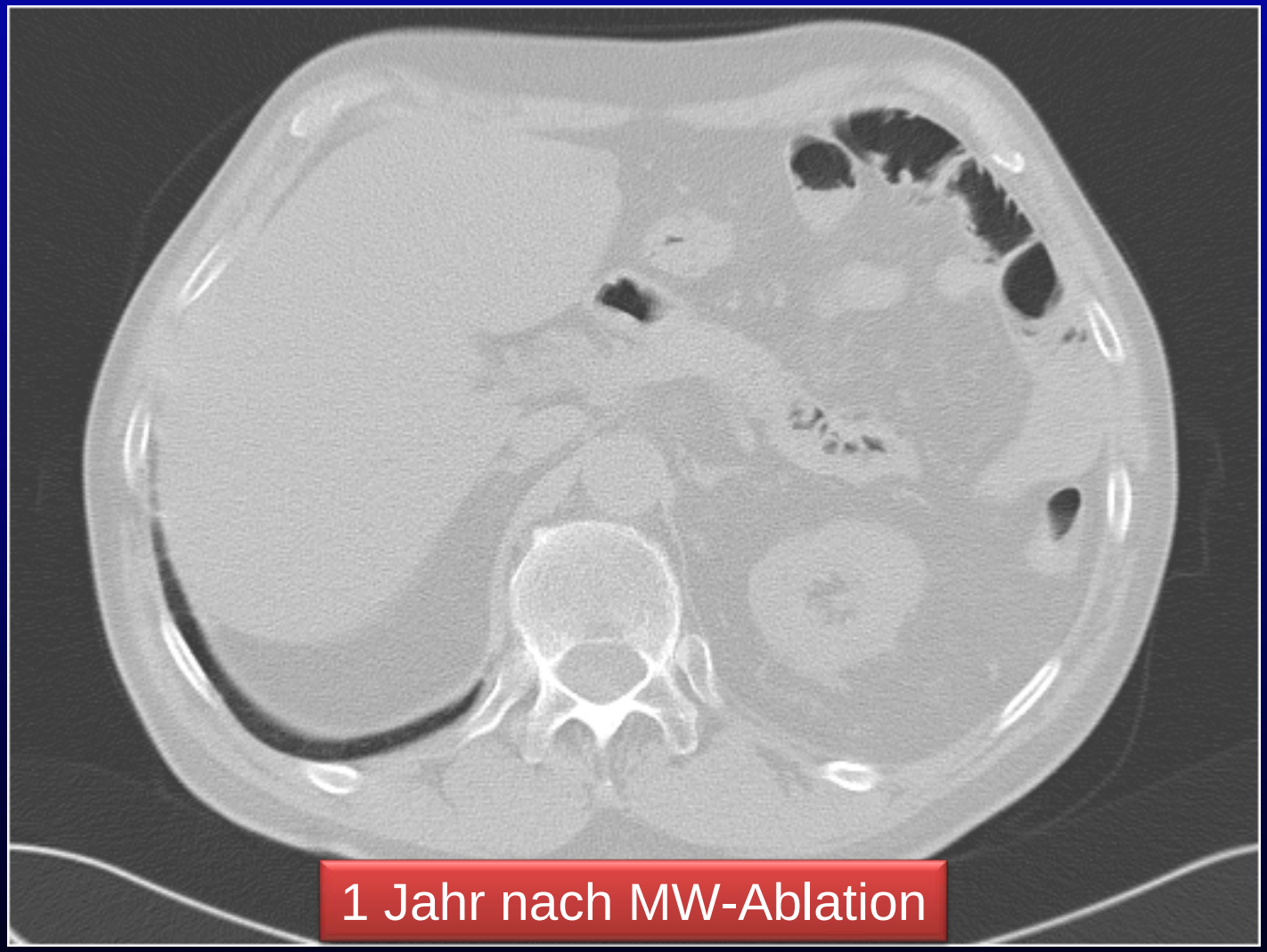
MW-Ablation

24h nach MW-Ablation





Fall 2



Fall 2

B) Auf den Erfolg einer pulmonalen Ablation könnte sich signifikant auswirken:

1) Tumorlokalisation: Ober- vs. Unterlappen

2) Histopathologie des Primärtumors

3) Periphere vs. hiläre Lokalisation der Läsion

4) Ovale vs. runde Form der Läsion

5) Begleitender Pleuraerguss

Radiology

Radiology is a monthly journal devoted to clinical radiology and allied sciences, owned and published by the Radiological Society of North America, Inc.

Microwave Ablation Therapy: Clinical Utility in Treatment of Pulmonary Metastases

Expand

Thomas J. Vogl, MD, Nagy N. N. Naguib, MSc, Tatjana Gruber-Rouh, MD, Karen Koitka, MBBCh, Thomas Lehnert, MD and Nour-Eldin A. Nour-Eldin, MD, MSc

+ Author Affiliations

Address correspondence to
T.J.V. (e-mail: t.vogl@em.uni-frankfurt.de).

Author contributions: Guarantors of integrity of entire study, T.J.V., K.K., T.L., N.A.N.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, T.J.V., N.N.N.N., T.G., N.A.N.; clinical studies, T.J.V., N.N.N.N., T.L., N.A.N.; statistical analysis, T.J.V., N.N.N.N., T.L., N.A.N.; and manuscript editing, all authors

Abstract

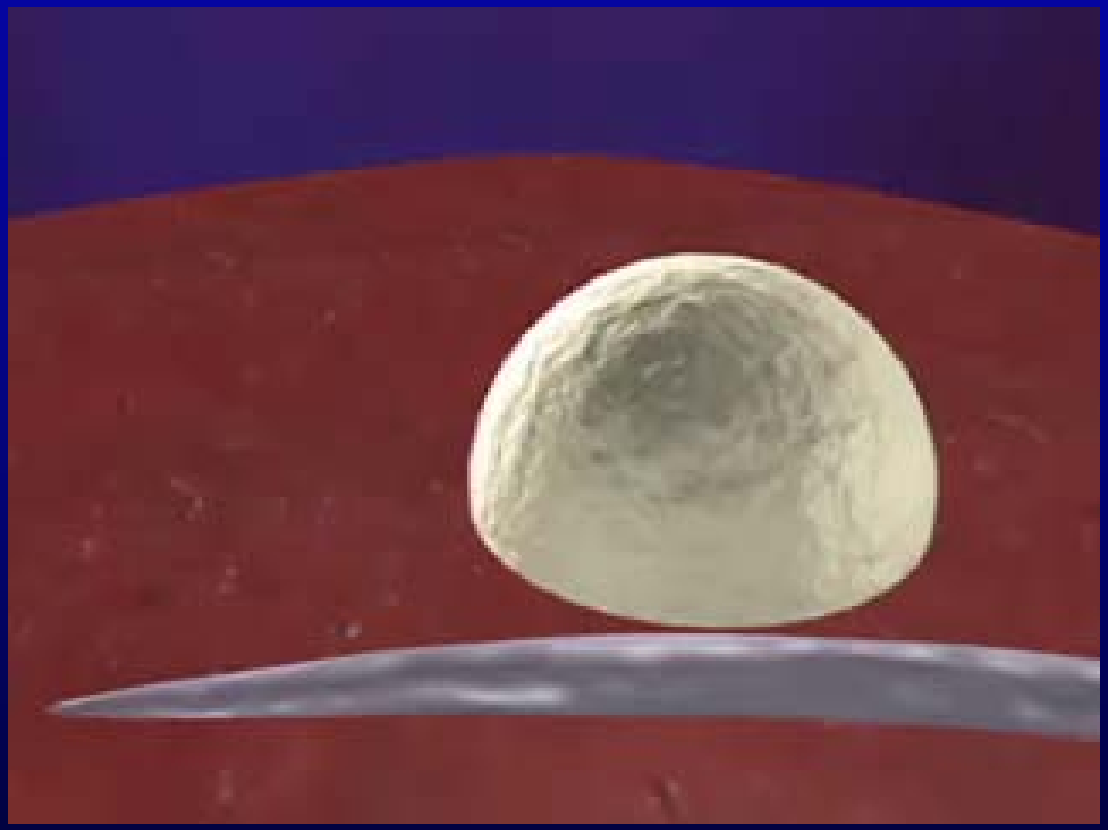
Purpose: To prospectively evaluate the safety and efficacy of microwave ablation therapy of unresectable pulmonary metastases.

Materials and Methods: All patients provided informed consent for this prospective institutional review board–approved study. Eighty patients (30

This Article

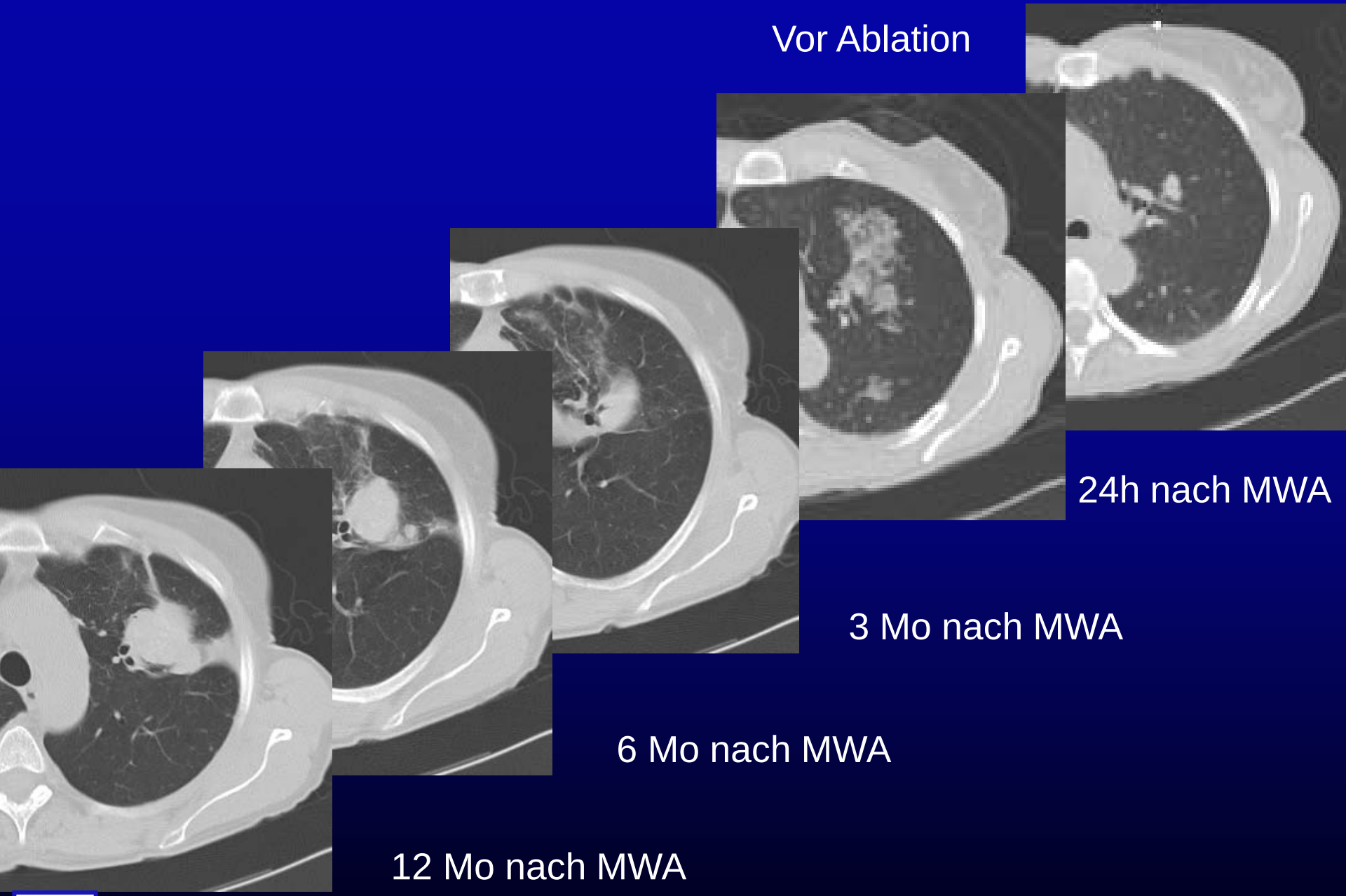
doi: 10.1148/radiol.11101643
November 2011 Radiology, 261, 643-651.

Tumorablation Lunge



Peripher gelegene Läsionen sind signifikant besser therapierbar als zentral gelegene - $p < 0.05$.

Institut für Diagnostische und Interventionelle Radiologie, Goethe-Universität, Frankfurt



Institut für Diagnostische und Interventionelle Radiologie, Goethe-Universität, Frankfurt

Tumorablation Lunge: Komplikationen

Year	Author	Pneumothorax	Chest tube	Hemorrhage	Infection
2004	Steinke (RFA)	43%	7%	9%	n.a.
2004	Yamakado (RFA)	37%	20%	n.a.	1%
2006	Weigel (LA)	40%	7%	9%	1%
2007	Simon (RFA)	28%	10%	3%	2%
2010	Wolf (MWA)	39%	12%	n.a.	1%
2011	Vogl (MWA)	9%	1%	6%	n.a.

„LUFU nach RFA nicht beinträchtigt“ Lanuti M, J Thorac Cardiovasc Surg 2009

Lungenmetastasen: Outcome

Author, year		Technique	Primary tumor	# of patients	Survival 1 y	2 y	3 y
McCormack	1992	Thoracotomy	CRM	144	-	-	40
Friedel	1999	Thoracotomy	DivM	5206	84	46	33-45
Inoue	2000	Thoracotomy	CRM	25	-	-	39
Landreneau	2000	VATS	CRM	80	-	-	31
Pfannschmidt	2003	Thoracotomy	CRM	167	-	-	32
Yan	2007	RFA	CRM	55	85	46	-
Yamakado	2007	RFA	CRM	71	84	46	-
Lencioni	2008	RFA	CRM	53	89	-	-
Wolf	2008	MWA	LC+DivM	50	73	61	-
Rosenberg	2009	LA	DivM	64	81	44	27
Chua	2009	RFA	DivM	148	-	60	45
Vogl	2011	MWA	DivM 3cm	80	91	75	-

Lungenmetastasen: Outcome

Prognosefaktoren:

1. Entität Primärtumor
2. Einzelgröße
3. Metastasenzahl

De Baere T, Cardiovasc Int 2010

Rosenberg C, AJR 2009

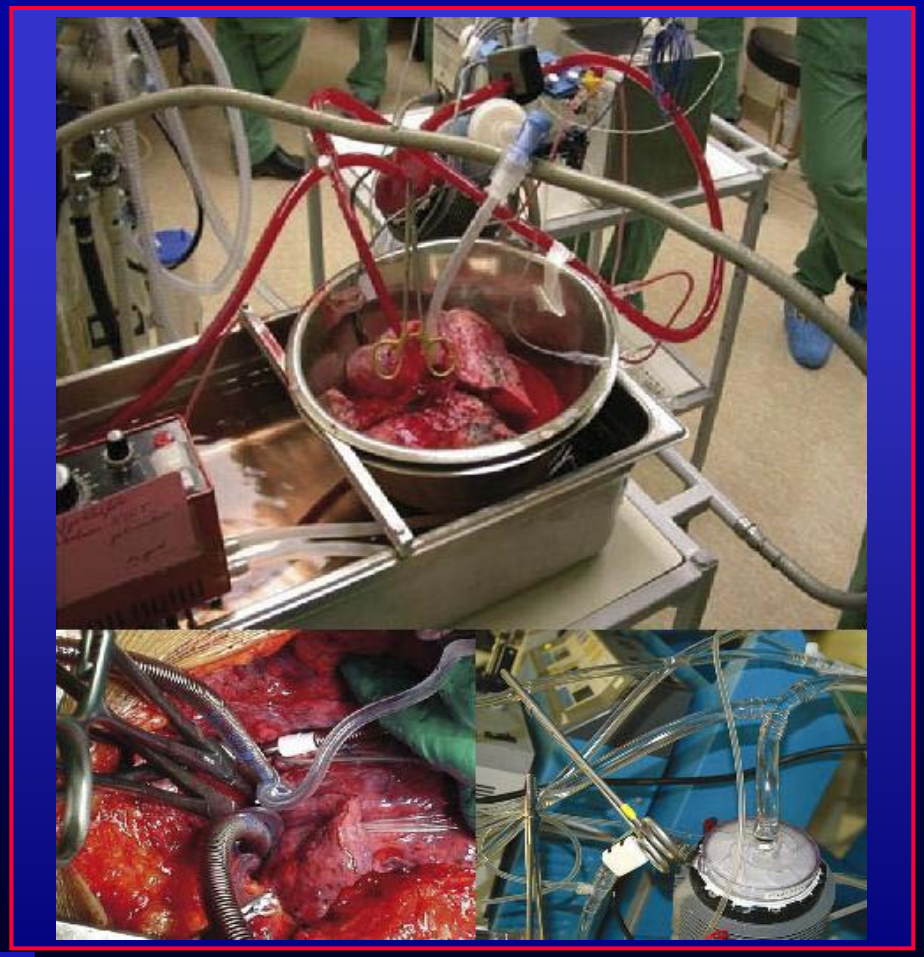
Yan TD, Ann Surg Oncol 2006

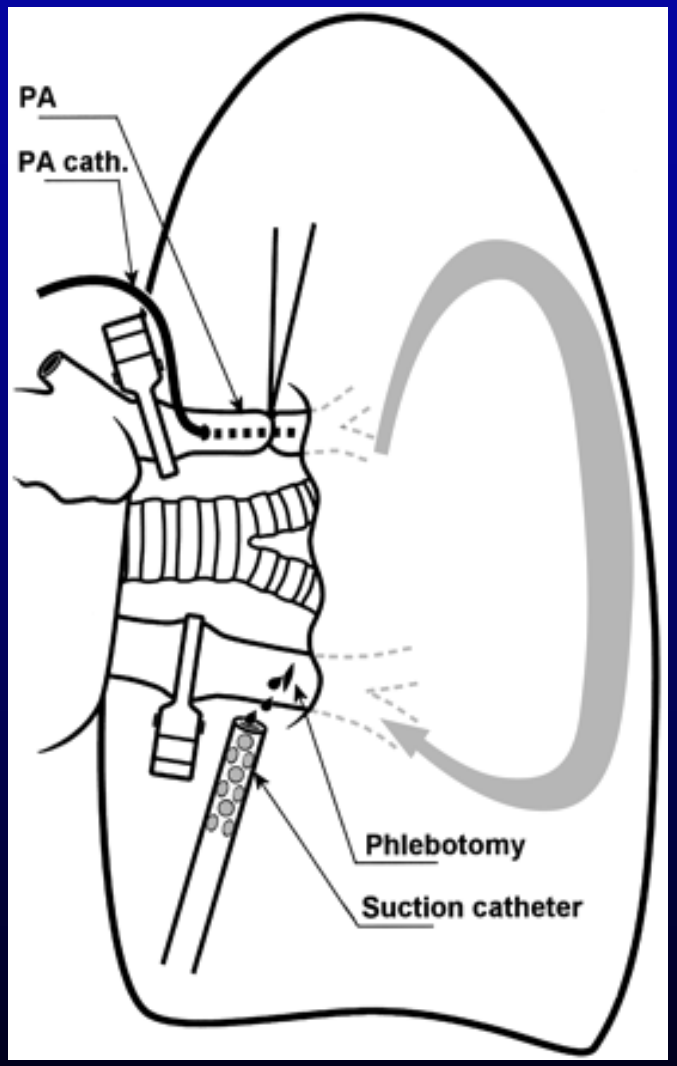
Tumorablation Lunge: Primary Success

Tumorgröße (limitierend):

Lee et al 2004 (RFA)	3 cm
Simon et al 2007 (RFA)	3 cm
Rosenberg et al 2009 (LA)	4 cm
Vogl et al 2011 (MWA)	3 cm

Isolierte Lungenperfusion





Isolated Lung Perfusion: Review

Perfusion 2006; **21**: 267–276

Isolated lung perfusion for pulmonary metastases, a review and work in progress

This procedure is technically safe and feasible; however, clinical value and efficacy remain unclear. The aim of this paper is to give a review of literature on ILuP in humans, and to describe the development of the perfusion procedure in our institute. *Perfusion* (2006) **21**, 267–276.

frequent metastatic pulmonary diseases resected originate from soft tissue sarcoma and colorectal carcinoma. Although surgical resection is presently a widely accepted treatment for pulmonary metastases, 5-year survival rates of 20–40% after complete resection of pulmonary metastases remain poor.[2] Many patients develop recurrent disease even if complete resection was achieved. Isolated lung perfusion (ILuP) is an effective method of delivering high-dose local chemotherapy with minimal systemic concentrations, avoiding toxic drug metabolism through the liver and kidneys.[3] Safety and

Isolated lung perfusion

Isolated lung perfusion in humans

Reports of ILuP in humans are relatively scarce, and the study population and its treatment are heterogeneous (Table 1). Most studies are performed in patients with unresectable disease, in contrast to our study that included patients with resectable disease. Furthermore, all investigations were made in patients with metastatic disease of different histopathological origin, eg, colon carcinoma, sarcoma, renal carcinoma, etc. Also, a variety of chemotherapeutics has been used, making pharmacokinetic

Chemoembolization of Lung Metastases – Pharmacokinetic Behaviour of Carboplatin in a Rat Model

NCBI Resources How To

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

Search: PubMed Limits Advanced search Help

Search Clear

Display Settings: Abstract Send to:

Anticancer Res. 2007 Mar-Apr;27(2):809-15.

Chemoembolization of lung metastases--pharmacokinetic behaviour of carboplatin in a rat model.

Pohlen U, Rieger H, Meyer BT, Loddenkemper C, Buhr HJ, Heitland P, Koester HD, Schneider P.

Department of Surgery, Charité Campus Benjamin Franklin Medical Center, Hindenburgdamm 30, D-12200 Berlin, Germany. Uwe.pohlen@charite.de

Abstract

AIM: To improve tumor control in lung metastases using a novel method: unilateral chemoembolization of the lung by instillation of degradable starch microspheres (DSM) and cytotoxic agents via the pulmonal artery. MATERIALS AND METHODS: A rodent model of solitary metastasis (CC531 adenocarcinoma) was studied. The animals were randomized into three groups: the control group receiving carboplatin (45 mg/kg) intravenously, an isolated lung perfusion (ILP) group recieving buffered starch solution and carboplatin (15 mg/kg) and a third group receiving chemoembolization with carboplatin (15 mg/kg) and DSM (2 ml/kg). The total platinum concentration in serum, lung and lung tumor at defined times (15, 30, 60, 120 min) was measured using an inductively coupled plasma mass spectrometer (ICP-MS). RESULTS: The area under concentration (AUC) versus time curves showed a 7.9- to 42.6-fold higher concentration in the tumor tissue comparing the ILP and chemoembolization group to the control group ($p < 0.01$). In the comparison of the AUCs of ILP versus chemoembolization, the tumor tissue of the lung showed a 5.4-fold higher concentration in the chemoembolization group ($p < 0.01$). CONCLUSION: tissue, without histological damage of the surrounding lung parenchyma.

PMID: 17465206 [PubMed - indexed for MEDLINE]

Transbronchiale Chemoembolisation: Probleme

Zugang

Transbronchial

- (Super-) selektive Therapie
  = komplizierter
- Zusätzliches Risiko einer spinalen Ischämie

Transpulmonal

- (Super-) selektiver Zugang
  = einfacher
- Kein Risiko einer spinalen Ischämie

Transbronchiale Chemoembolisation: Probleme

- Brustschmerzen: 24 - 91%
- Dysphagie: 0,7 - 18,2% (2-7 Tage nach Embolisation)
- Dissektion der Intima der Bronchialgefäße
- Lungeninfarkt
- Rückenmarksinfarzierung
- KM-bedingte Neurotoxizität:
  - Bronchoösophageale Fistel
  - Bronchialinfarkt

Material & Methodik

- **Einschlusskriterien:**
  - Guter Allgemein- und Ernährungszustand
  - Karnofsky-Index > 70%
  - Keine Einschränkung der Lungenfunktion
  - Ausreichende Compliance

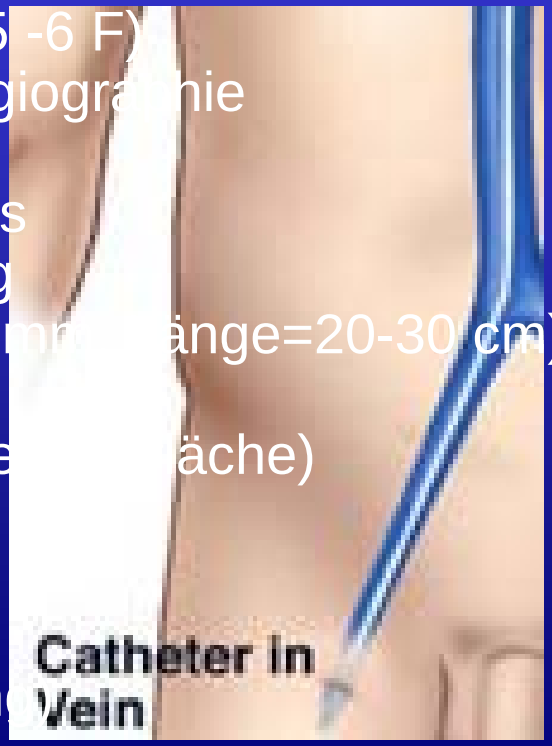
- **Ausschlusskriterien:**
  - Karnofsky-Index < 70%
  - Respiratorische, kardiovaskuläre oder renale Dysfunktion (Serumkreatinin > 2 mg%)
  - Partielle oder komplette Thrombosierung der Pulmonalarterie

Artis Zeego

TPCE: Technik

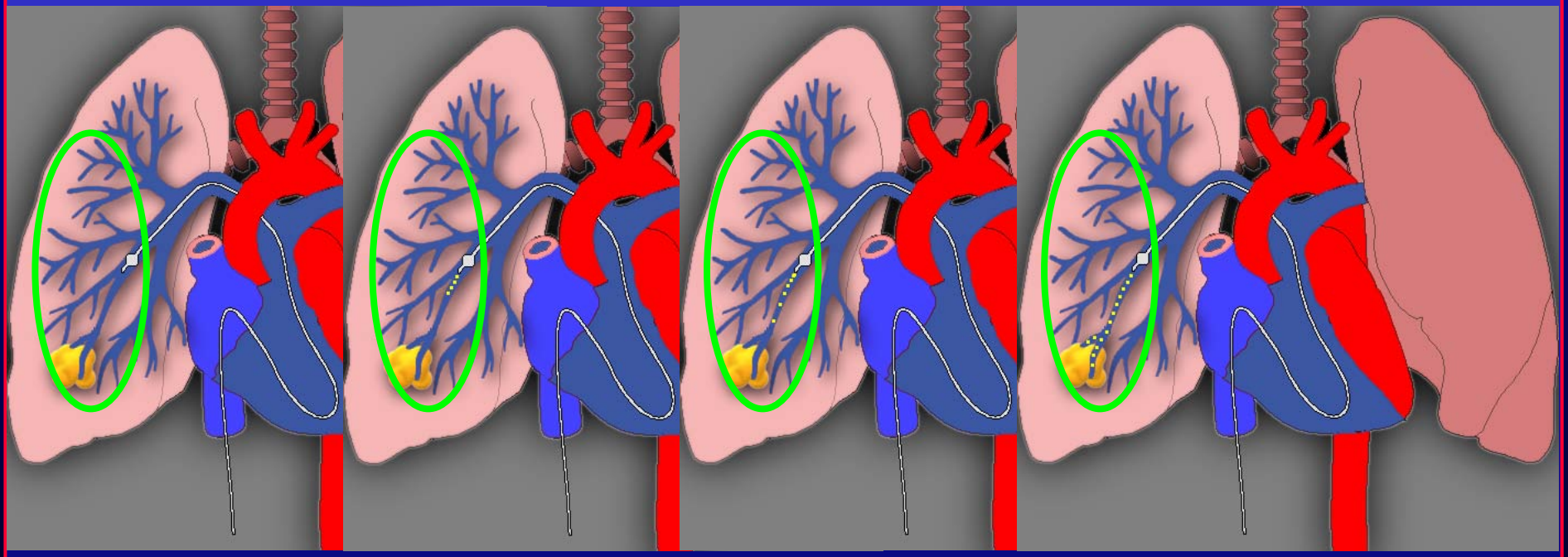
• Behandlung •

1. Venöser femoraler Zugang (5 -6 F)
2. Katheterisierung der Pulmonalarterie (5 -6 F)
3. Selektive/superselektive Pulmonalisangiographie
   → Evaluation: - Feeder
   - pulmonale AV-Shunts
   - biplanare Darstellung
4. Blockung durch Ballonkatheter (∅=7-8 mm; Länge=20-30 cm)
5. Lokoregionale Applikation von:
   - Mitomycin C (5-10 mg; 5 mg/m² Körperoberfläche)
   - Gemcitabine (1000 mg/m²)
   - Cisplatin (30 mg)
   - Lipiodol (5-10 ml)
   - Mikrosphären (EmboCept: 200-450 m

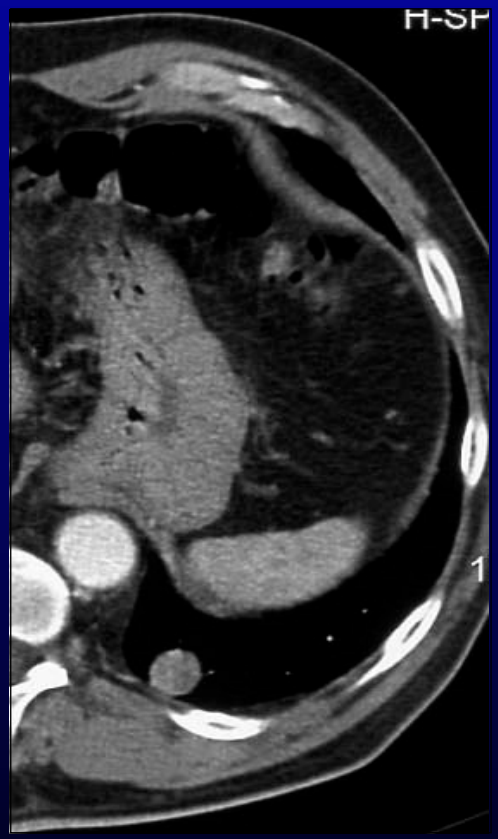


TPCE: Technik

• Behandlung •

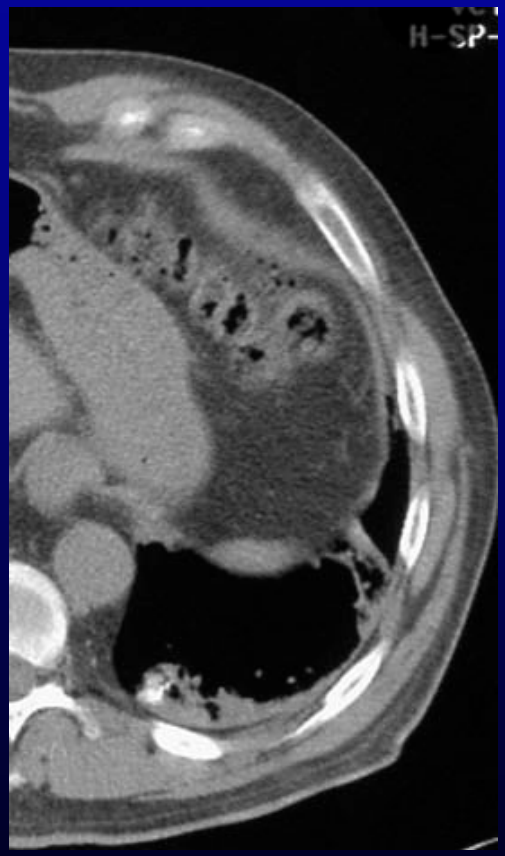


TPCE: Lipiodolaufnahme

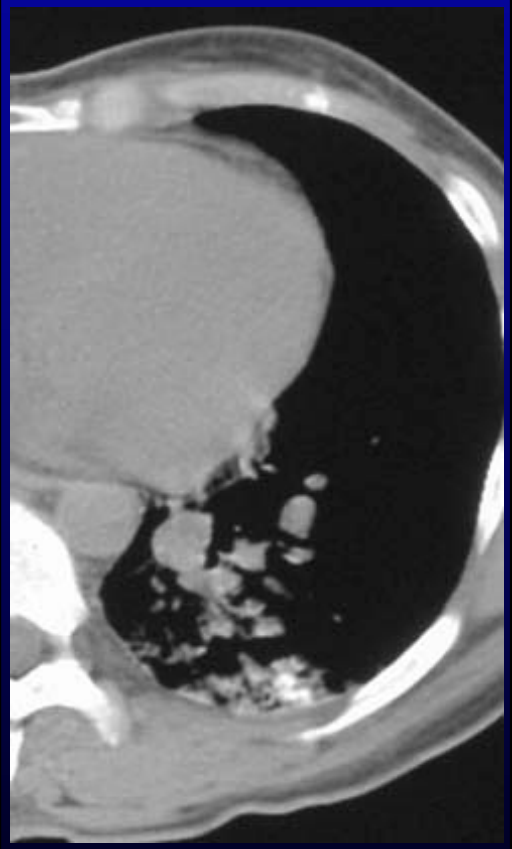
Vor TPCE	Angiographie	Nach TPCE
		

TPCE: Follow-up

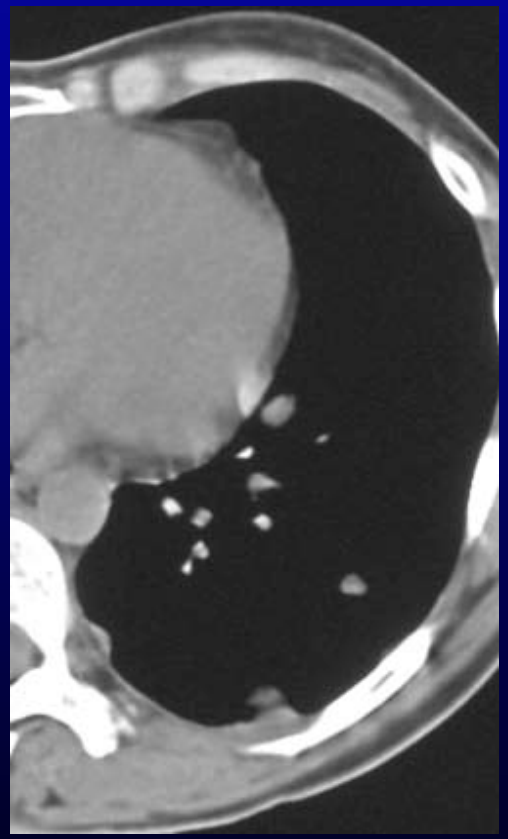
2. TPCE



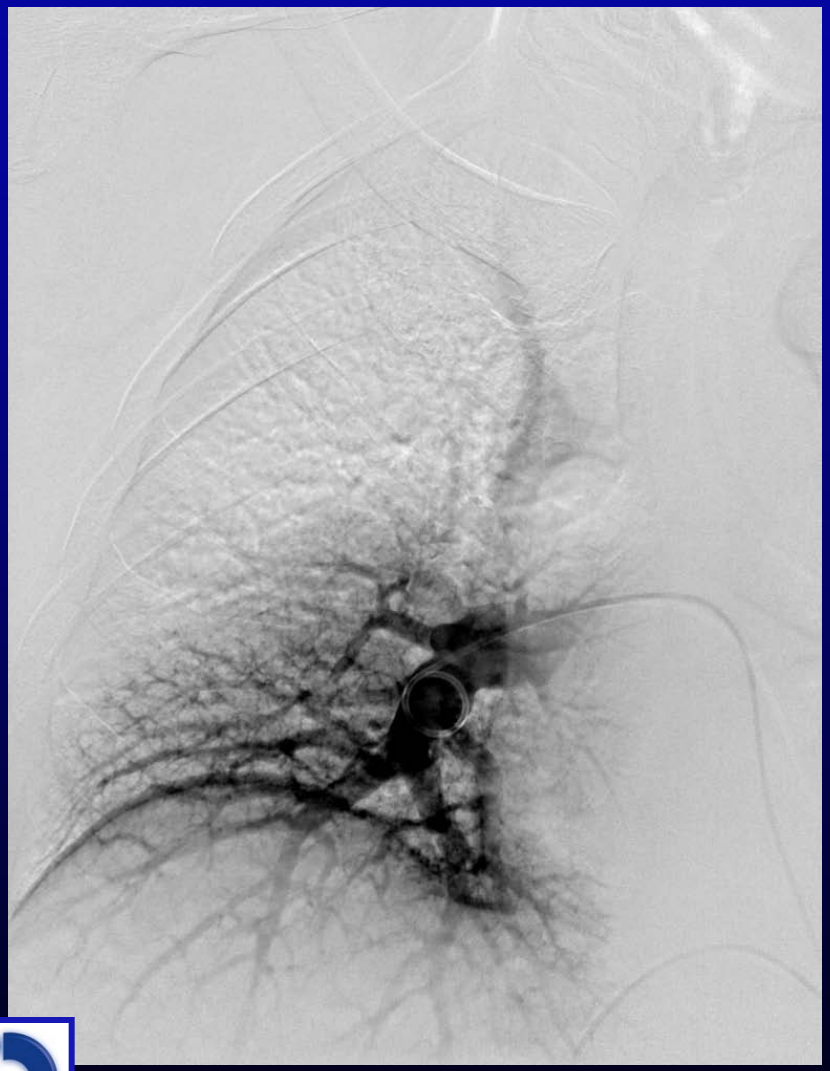
3. TPCE

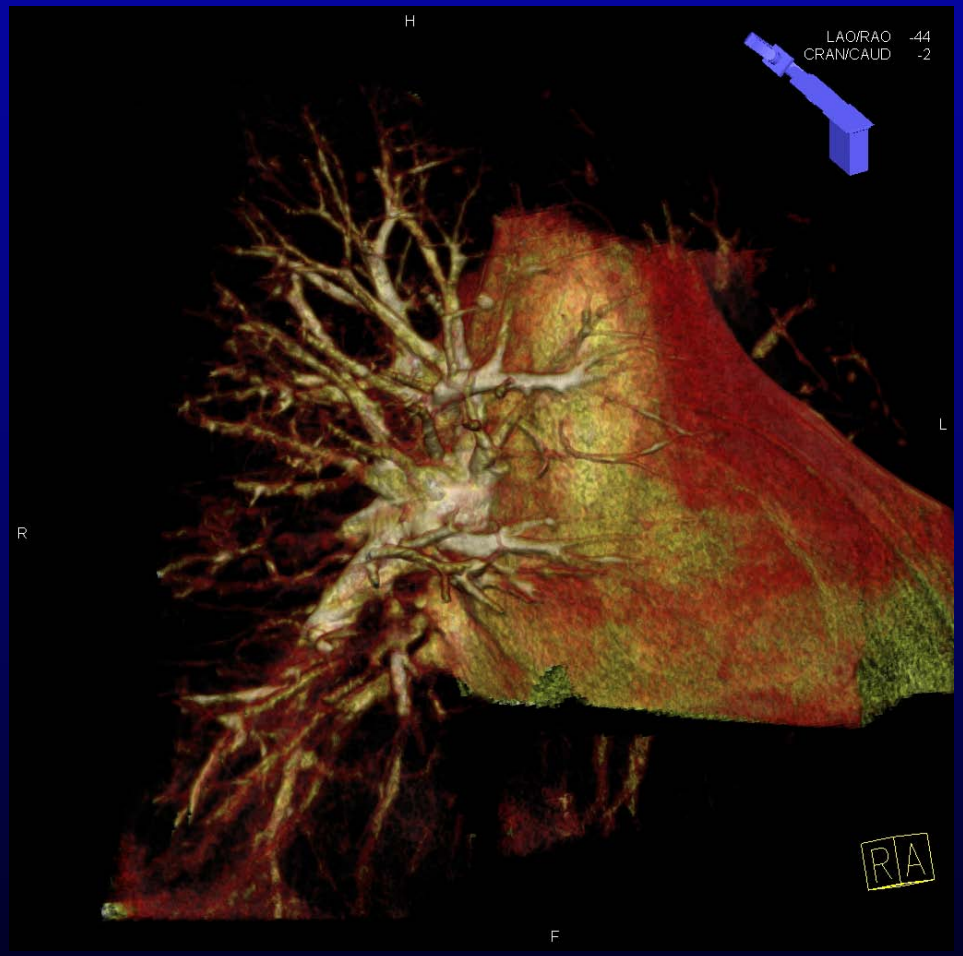


4. TPCE

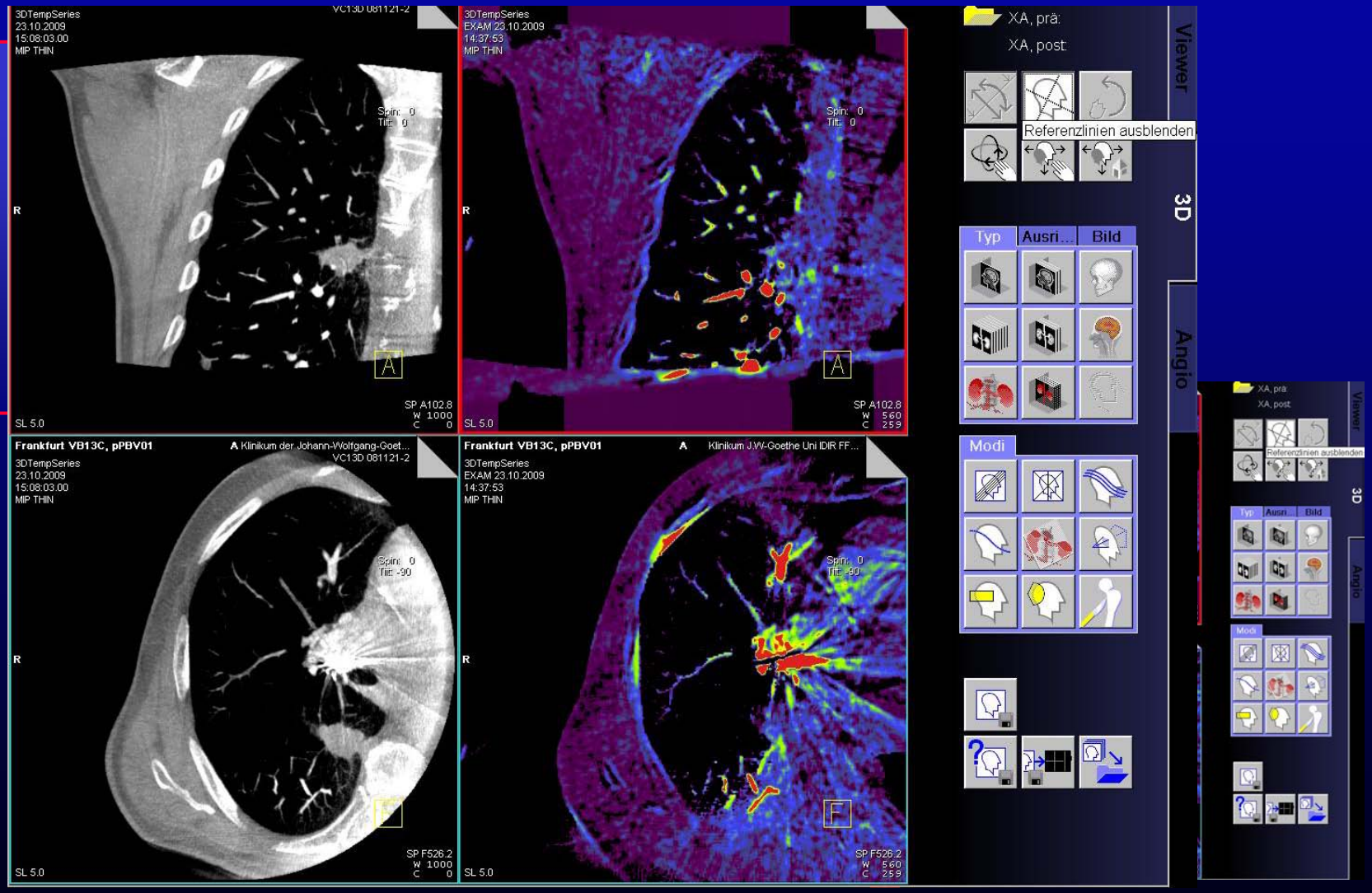


Dyna-CT: „Routenplanung“





Patient PBV 01



TPCE: Patienten (2006-2012)

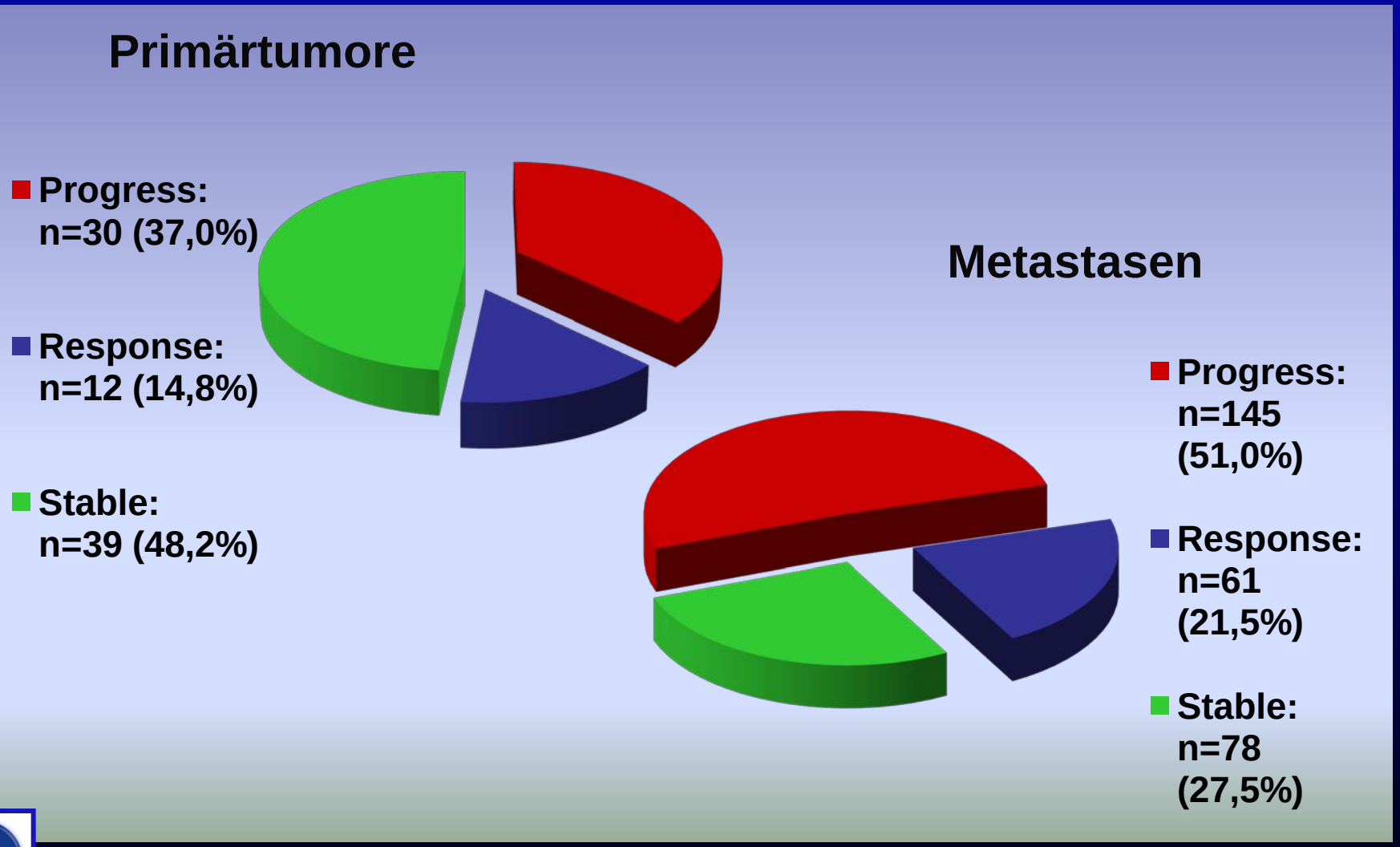
Primärtumore

Anzahl der Patienten [n]	Alter im Mittel [Jahre]	Anzahl der Läsionen [n]	Anzahl der Behandlungen im Mittel [n]	Tumorvolumen vor/nach TPCE [ml]
81 m/w = 40/41	61,2 (38-91)	n=980 ∅ 12,1	3,7 (1-26)	vor: ∅ 246,05 nach: ∅ 326,26

Lungenmetastasen

Anzahl der Patienten [n]	Alter im Mittel [Jahre]	Anzahl der Läsionen [n]	Anzahl der Behandlungen im Mittel [n]	Tumorvolumen vor/nach TPCE [ml]
284 m/w = 132/152	57,7 (12-94)	n=6560 ∅ 23,1	3,2 (1-16)	vor: ∅ 58,34 nach: ∅ 95,46

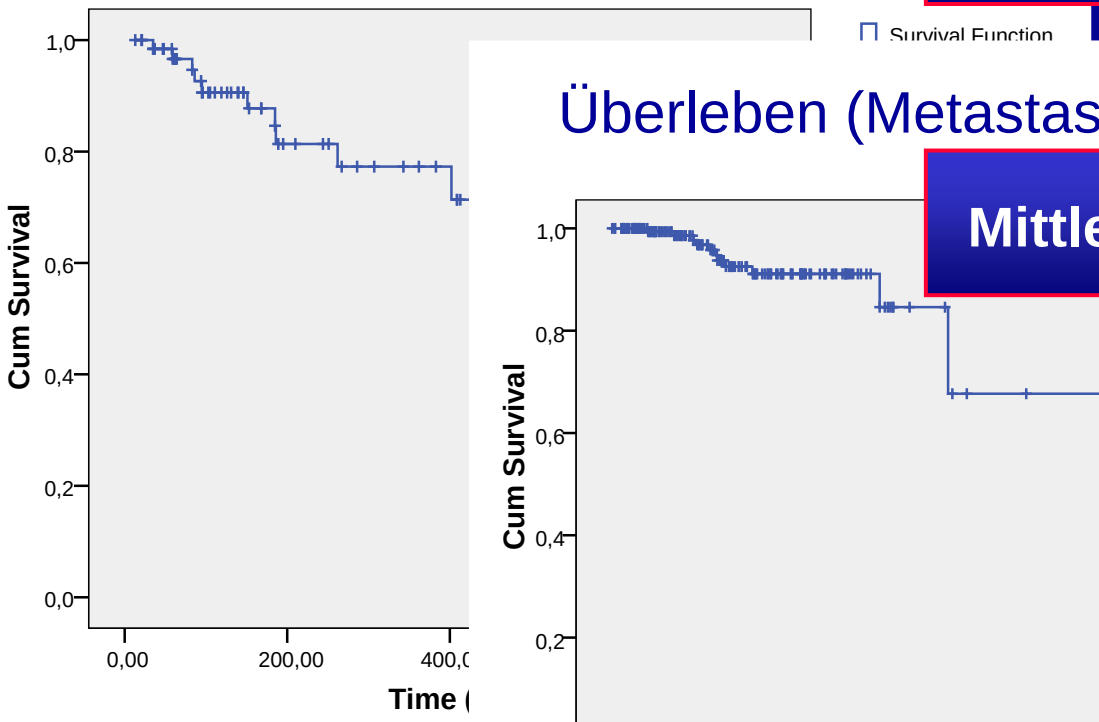
TPCE: Behandlungserfolg



TPCE: Überleben (Kaplan-Meier)

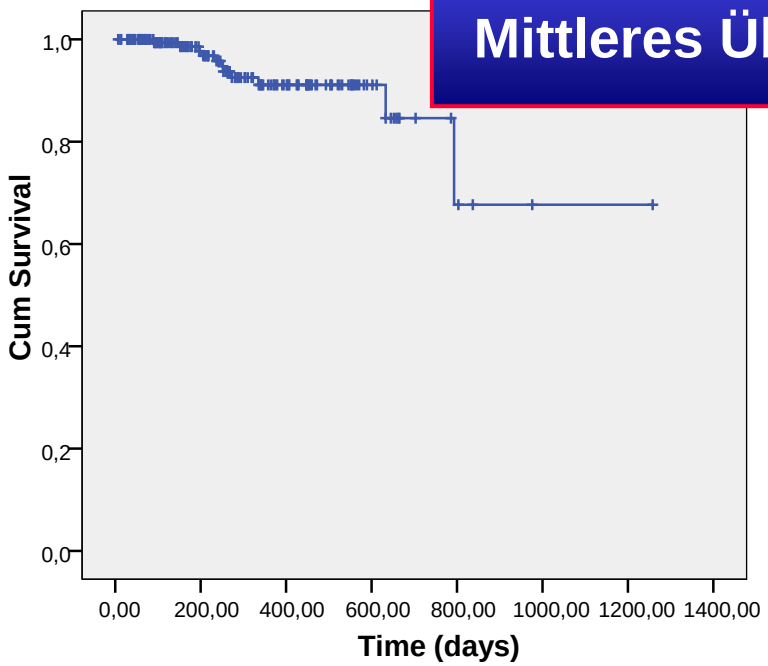
Überleben (Primärtumore)

Mittleres Überleben: 1047,6 Tage



Überleben (Metastasen)

Mittleres Überleben: 556,6 Tage



TPCE: Publikationen

Radiology

Eur Radiol (2008) 18: 2449–2455
DOI 10.1007/s00330-008-1056-0

CHEST

Thomas J. Vogl
Thomas Lehnert
Stephan Zangos
Katrin Eichler
Renate Hammerstingl
Huedayi Korkusuz
Sebastian Lindemayr

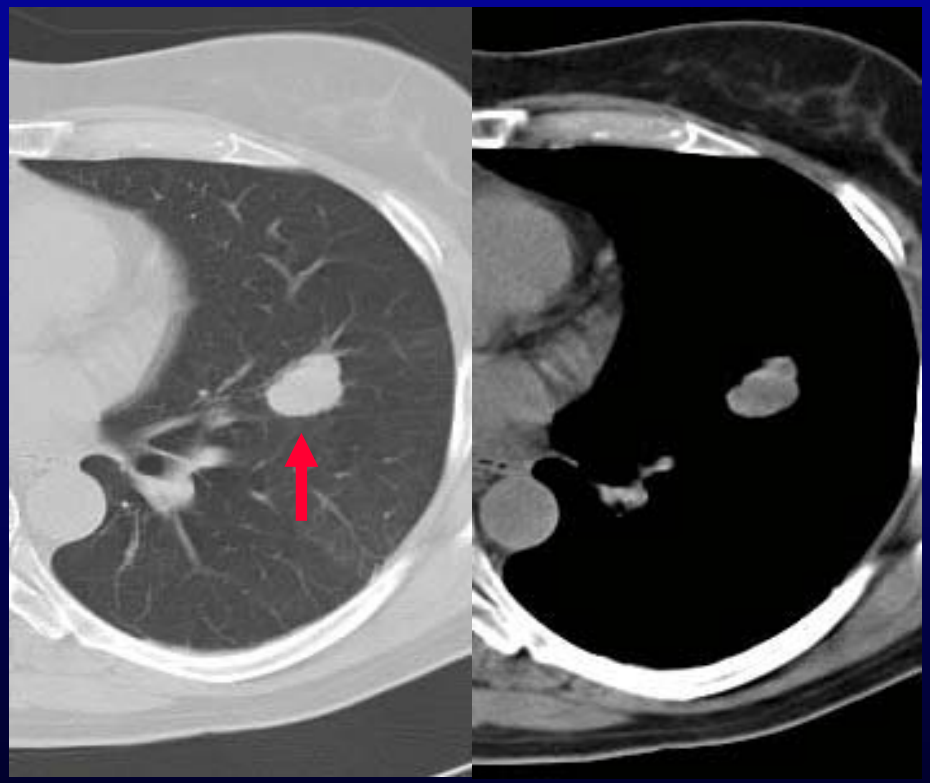
Transpulmonary chemoembolization (TPCE) as a treatment for unresectable lung metastases

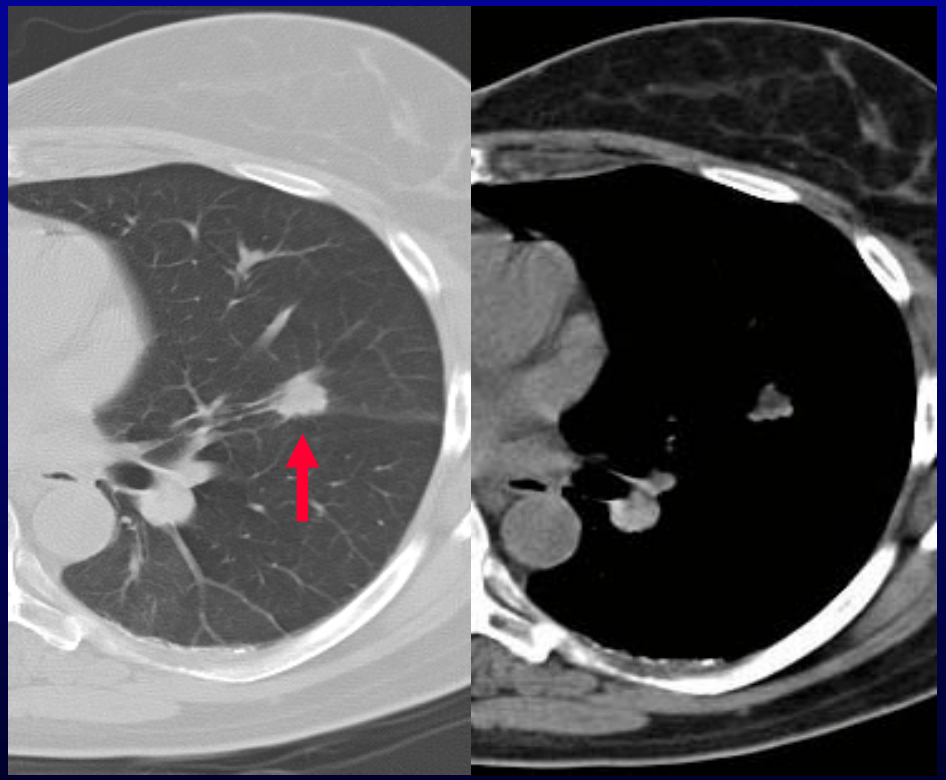
Received: 29 August 2007
Revised: 2 April 2008
Accepted: 7 April 2008
Published online: 14 June 2008
© European Society of Radiology 2008

Abstract To evaluate tumor response after treating unresectable lung metastases with transpulmonary chemoembolization (TPCE) in palliative intention. From 2001 to 2005, 52 follow-up was accomplished at 4-week intervals using unenhanced and contrast-enhanced CT. After sequential therapy, follow-up was performed every 3 months for a period of 6

48-jährige Patientin mit Mamma-Ca

Vor TPCE	Nach 3. TPCE





Neoadjuvante TPCE: Material & Methodik

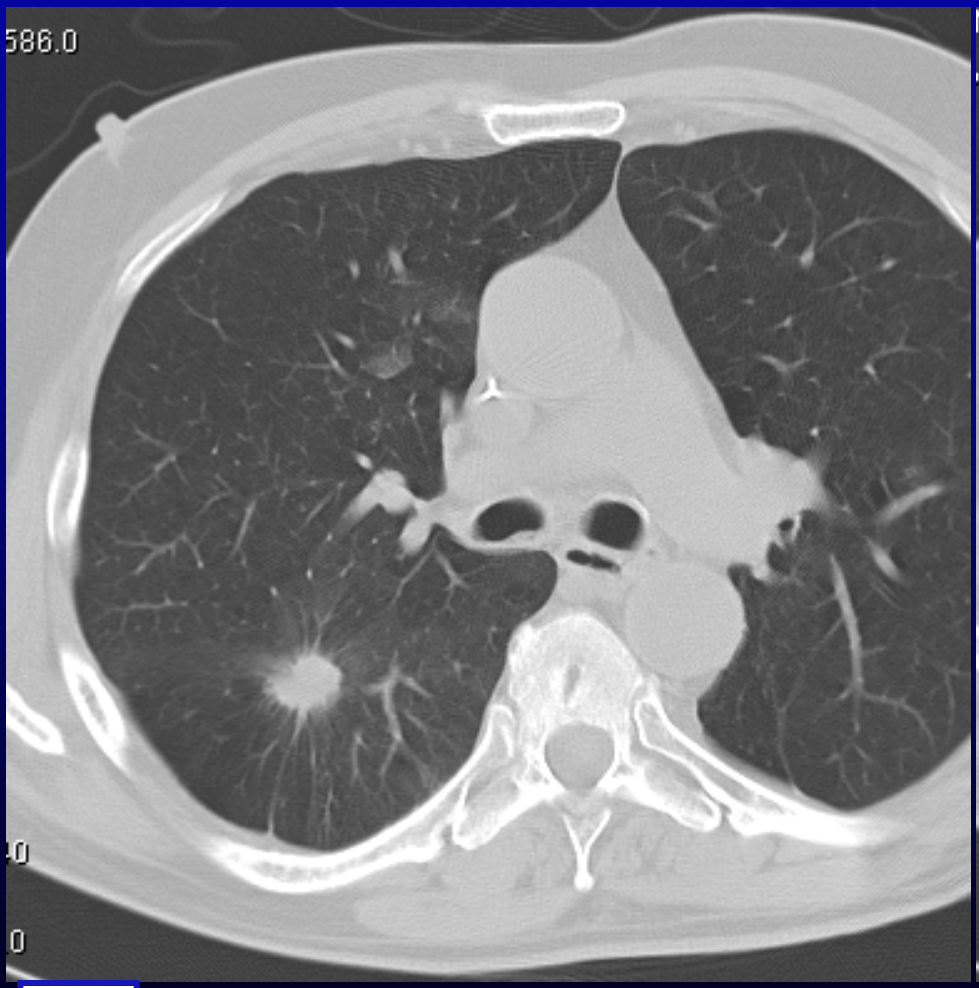
- Zeitraum: 2007 – 2010

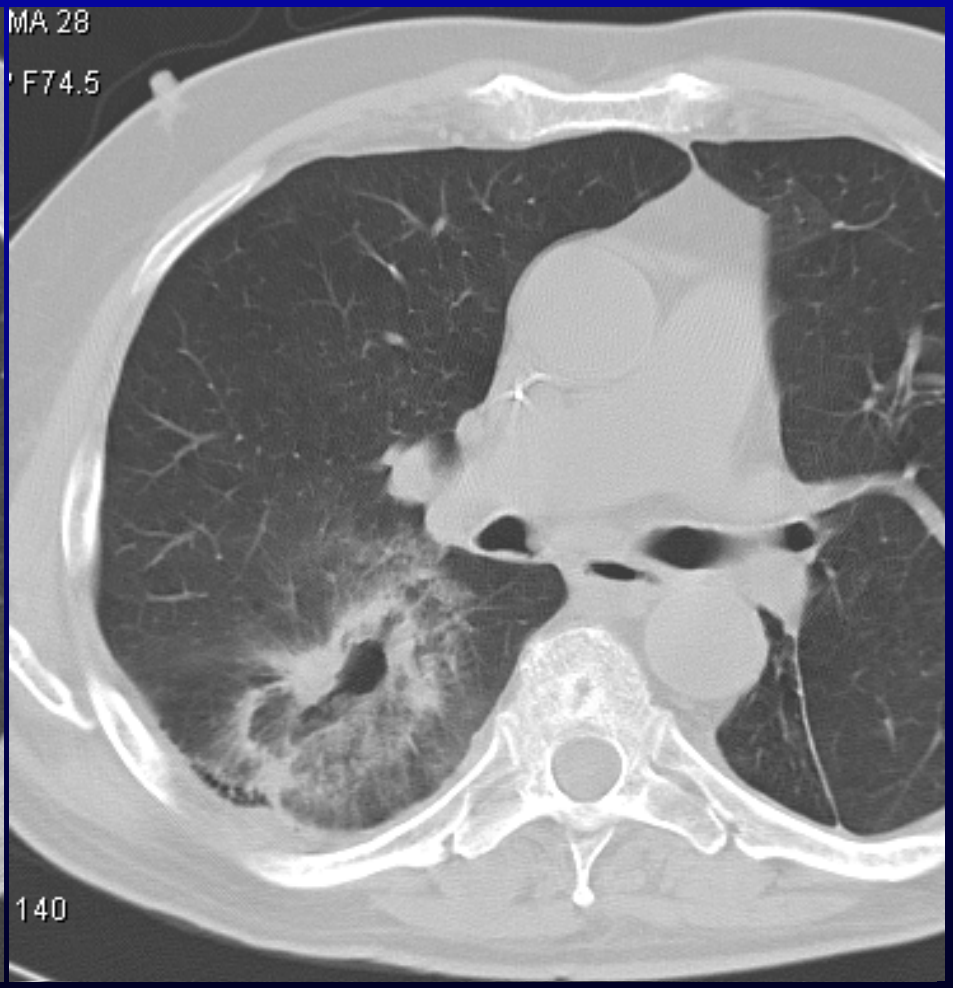
- Patienten:
  - n = 50 mit nicht resektablen Lungenläsionen
    → Primäre Lungentumore: n = 12
    → Lungenmetastasen: n = 38
  - mittleres Alter: 60,0 Jahre (Range: 28-83)
  - männlich/weiblich: 26/24

- Therapie:
  - RFA: n = 10
  - MWA: n = 40

  → TPCE vor der Ablation: n = 30
  $\bar{x}$ = 4,2 Sitzungen (Range: 1-16)

NSCLC: Neoadjuvante Therapie mit TPCE vor MWA





TPCE mit Doxorubicin-beladenen DC-Beads

- Stable disease (n=2)
- Progressive disease (n=2)
- Drop-out: (n=1)

- Tumorvolumen vor der Behandlung: ∅ = 27,62 ml
  [Range: 0,67 ml – 48,50 ml]

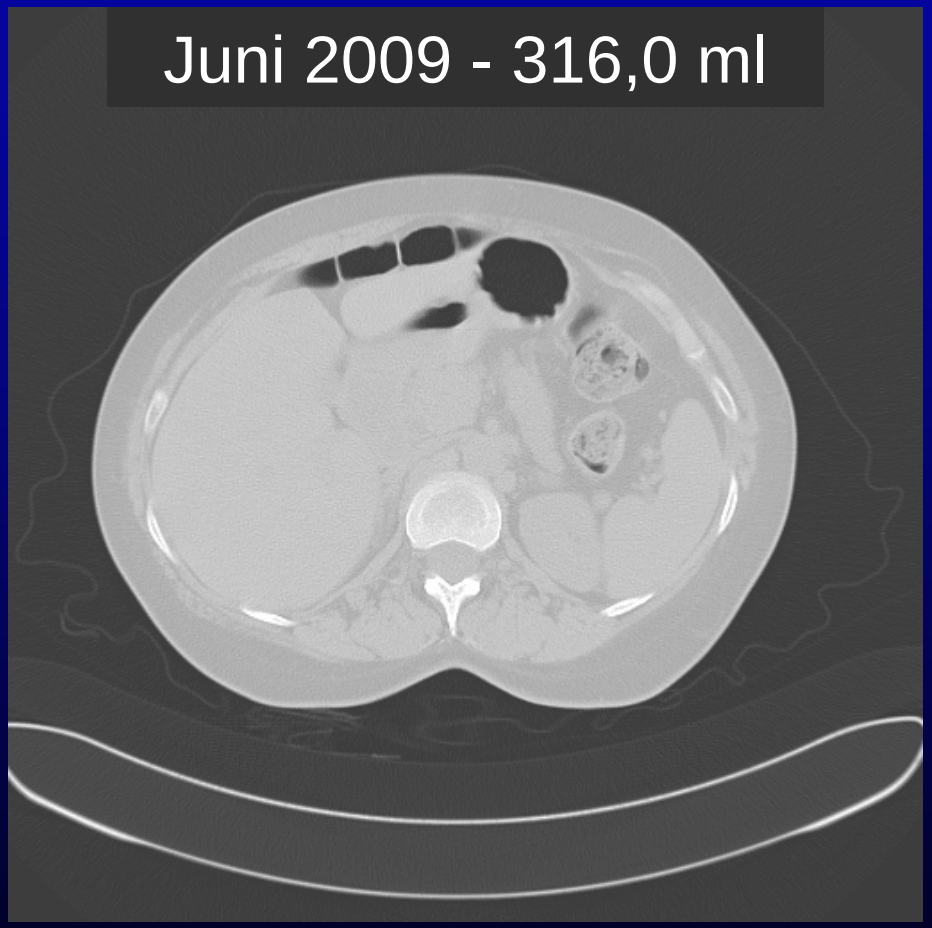
- Tumorvolumen nach der Behandlung: ∅ = 41,10 ml
  [Range: 0,69 ml – 66,90 ml]

- Volumenzunahme: ∅ = 47,6% (=13,45 ml)
  [Range: 2,9% (=0,02 ml) – 115,5% (=26,90 ml)]

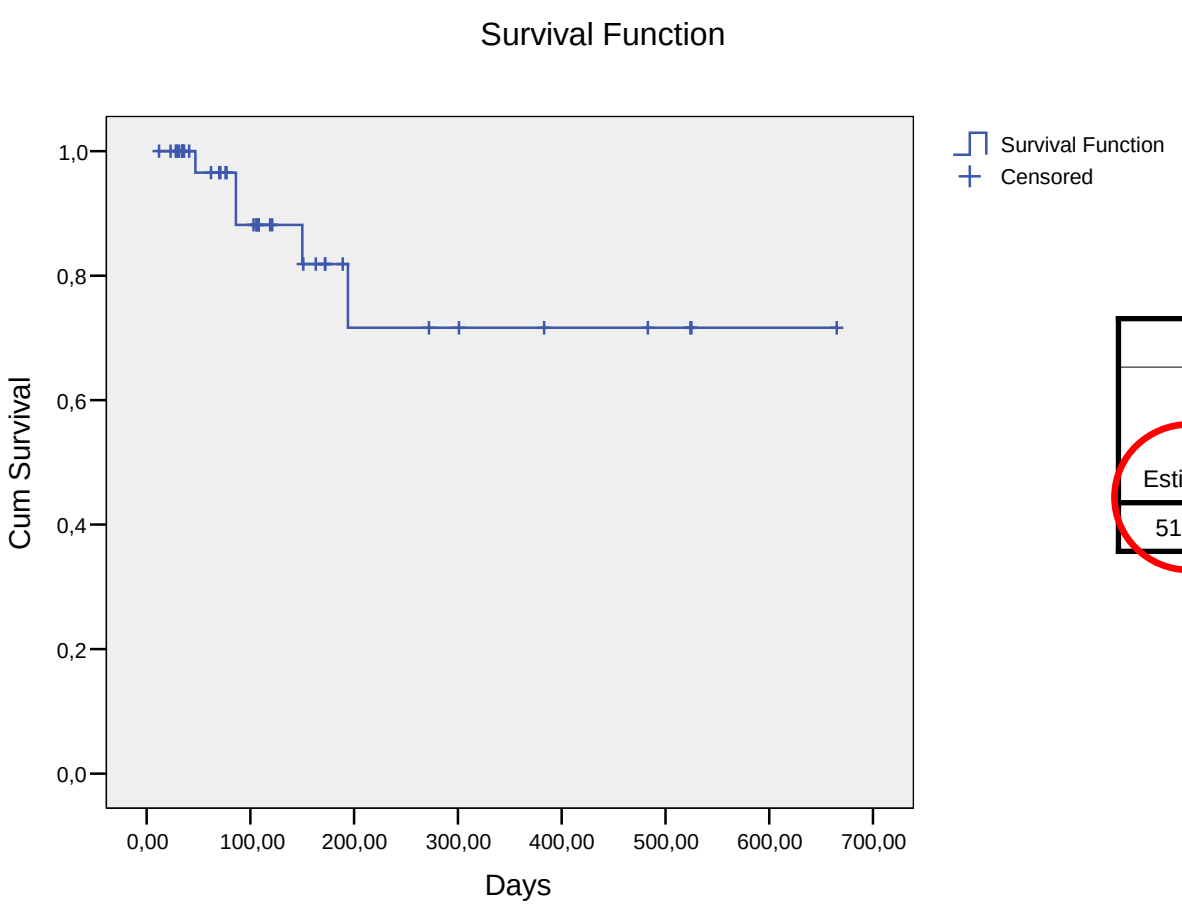
Chemoperfusion: Pleuramesotheliom

- Zeitraum: Januar 2007 – Januar 2010
- n = 46 Patienten mit inoperablem malignen Pleuramesotheliom (Stadien III / IV)
  - Verhältnis männlich zu weiblich: 37:9
  - Mittleres Alter: 64,0 Jahre (26 - 89 J.)
  - Follow-up: n = 39 Patienten
  - Kein Follow-up („drop-out“): n = 7 Patienten
- Ausschließlicher Einsatz dieser Behandlungsmethode bei Nicht-Ansprechen auf systemische Chemotherapie oder Radiatio

51-jährige Patientin mit malignem Pleuramesotheliom: 6 Chemoperfusionen



Chemoperfusion von malignen Pleuramesotheliomen: Überleben



Mean(a)			
		95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound
514,455	61,906	393,118	635,791

Kaplan-Meier

Unser Team

Institut für Diagnostische und Interventionelle Radiologie, Goethe-Universität, Frankfurt

MWA > RFA

- Schneller
- Mehr Energie
- Größeres Ablationsvolumen
- Differente Reaktion entlang von vaskulären Leitstrukturen
- Längere geometrische Ablationszonen
- Höhere Effizienz

Take Home Message

1. Indikationsstellung einer Ablationstherapie im Rahmen eines interdisziplinären patienten-individuellen Therapiekonzepts.

2. Die Ablation ist eine minimal invasive Technik mit weitgehender Schonung des umliegenden gesunden Gewebes.

3. Maximale Anzahl von Metastasen:
$\leq$ 3 pro Lungenflügel

4. Das Behandlungsergebnis einer Ablation wird vornehmlich durch die initiale Tumorgröße bestimmt.

5. Zentral und parahilär gelegene Läsionen haben eine signifikant höhere Inzidenz eines Lokalrezidivs nach Ablation, was auf den “current sink effect” zurückzuführen sein könnte.

6. Die Histologie einer Läsion hat keinen signifikanten Einfluss auf das Ablationsergebnis.

FISI 2013

14. Frankfurter Interdisziplinäres Symposium für Innovative Diagnostik und Therapie

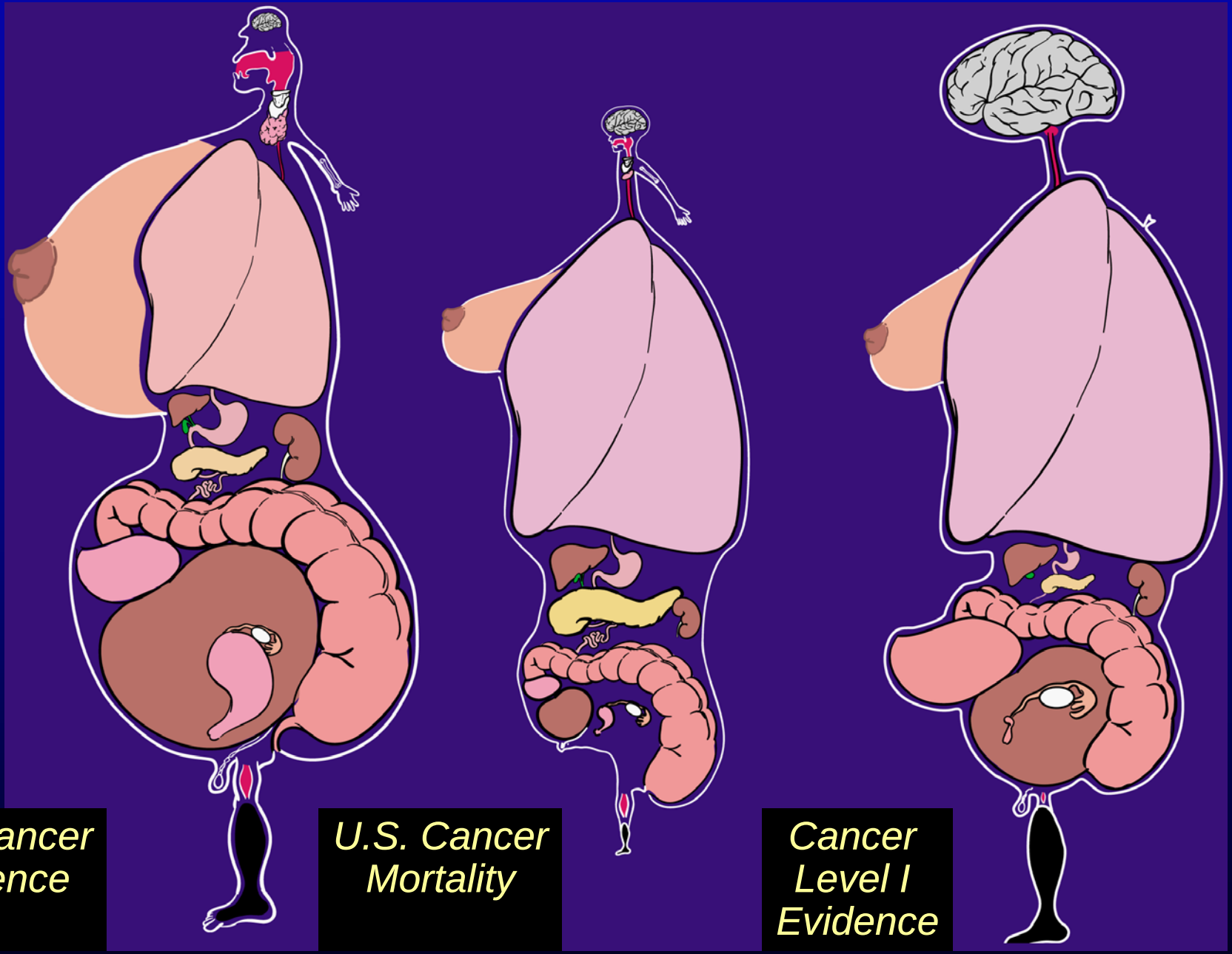
Computertomographie:
Vom Bild zum Befund

Frankfurt/Main, 8. – 9. November 2013

www.fisi-frankfurt.de

New Technologies in Frankfurt

The Onculus


U.S. Cancer Incidence
U.S. Cancer Mortality
Cancer Level I Evidence

Tumorablation Lunge: Technik

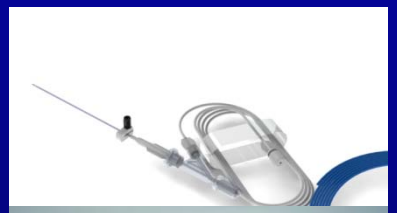
Hosten N, Röfo 2003 175 (3): 393-400
Vogl TJ, Radiology 2004 230: 450-8
Rosenberg C, Am J Roentgenol 2009 192 (3): 785-92

Laserablation (LA, LITT)

- Licht 1064 nm

Knappe, Berlin

μ_a	Absorptionskoeffizient [mm^{-1}]
μ_s	Streukoeffizient [mm^{-1}]
$p(s,s')$	Streu-Phasenfunktion



Lungenkarzinom: Outcome

Nicht-invasive oder minimalinvasive Alternativverfahren (St.-I-NSCLC)

- Konventionelle Strahlentherapie

  (3 JÜR um 25-45 %)
- Stereotaktische Bestrahlung

  (3 JÜR um 45-70 %), limitiert bei zentraler Lokalisation
- Thermoablation (LA; RFA)

  (3 JÜR um > 60 % für T1-Tumore)

American College of Surgeons Oncology Group

ACOSOG Z4033

Haasbeek CJA, Cancer 2010

Lanni TB, AJClinOncol 2010