





# Transcatheter Therapies for NSCLC

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# Transcatheter Therapies for NSCLC

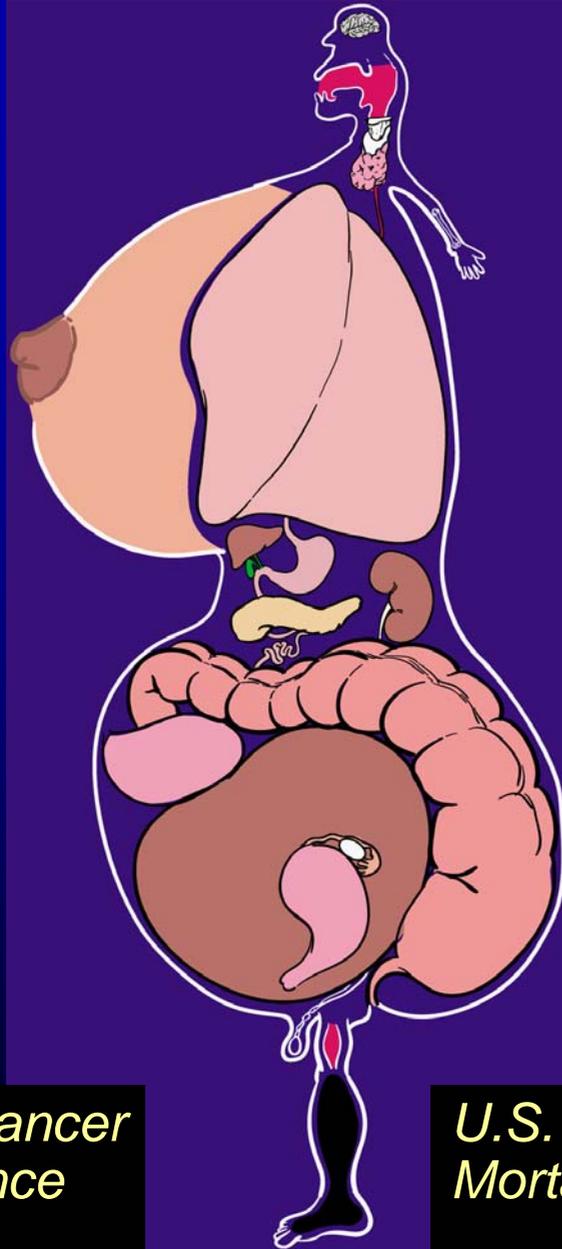
## Learning Objectives

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- To describe different transcatheter techniques for therapy of NSCLC such as transbronchial embolization, chemo-perfusion and transpulmonary chemoembolization (TPCE)
- To identify indications such as palliative treatment of bronchial carcinoma in symptomatic situations such as bleeding or mediastinal compression
- To define current and future developments



# The Onculus



*U.S. Cancer Incidence*



*U.S. Cancer Mortality*



*Cancer Level I Evidence*



# Transcatheter Therapies for NSCLC

- Basics

- Technical considerations:

- ▶ transbronchial arterial embolization
- ▶ transbronchial arterial perfusion
- ▶ transvenous pulmonary arterial

- embolization
- perfusion

- Indications

- Results

- Conclusion



# BC: Classification\*

- Small cell carcinoma (SCLC) – 25%

Limited disease

Extensive disease

5-y-survival: <1%

- Non-small cell carcinoma (NSCLC) – 75%

PLE carcinoma	40-45%	5-y-survival: 15%
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Adenocarcinoma	30%	5-y-survival: 10%
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Alveolar cell carcinoma	2-5%	5-y-survival: 10%
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*\*WHO 1982, ACS 1998, Johnson 1993*



# Chemoembolization of the Lung Improves Tumor Control in a CC531 Rat Model

- Unilateral chemoembolization: - degradable starch microspheres  
- cytotoxic drugs
- Solitary metastasis (rat model – CC531 adenocarcinoma)
- Applications: - control groups  
- intravenous carboplatin (45 mg/kg)  
- isolated lung perfusion  
- chemoembolization:  
15 mg/kg carboplatin/0.5 ml/kg Spherex<sup>®</sup>
- Results: efficacy – tumor necrosis:
  - ▶ chemoembolization > intravenous chemotherapy
  - ▶ chemoembolization = isolated lung perfusion

*Schneider P et al, Clinical Cancer Research 2002; 8(7):2463-69*



# Chemoembolization of the Lung Improves Tumor Control in a CC531 Rat Model

Difference in tumor volumes  
7 days after therapy

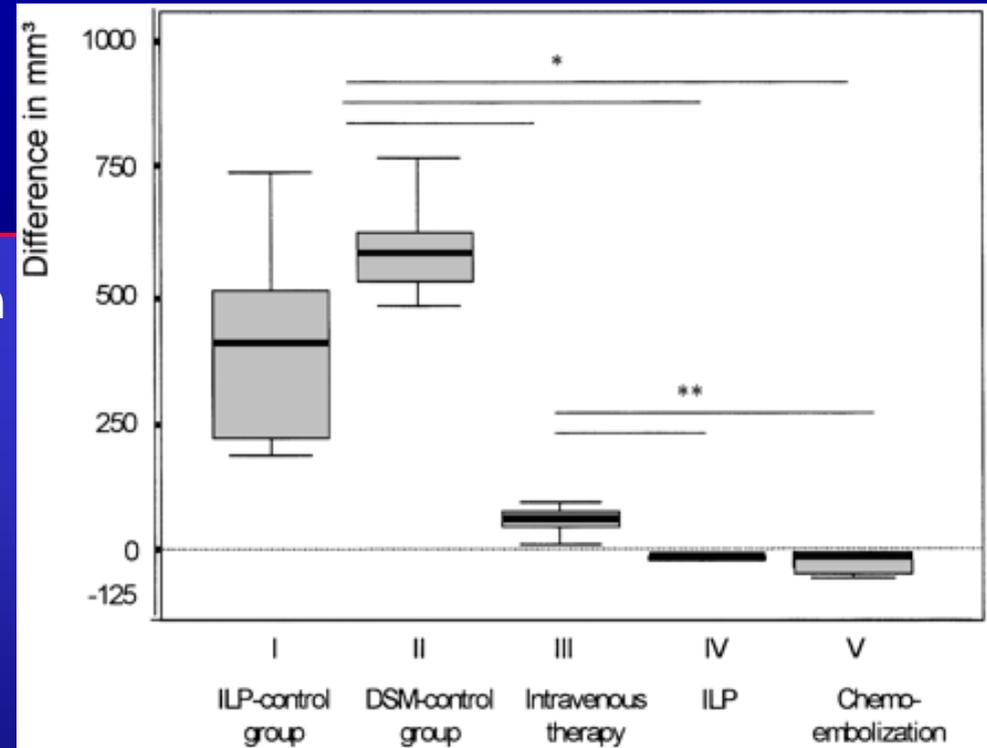
**Group I** : ILP – with 6% buffered starch solution without carboplatin

**Group II**: DSM – embolization with 0.5 ml/kg spherex without carboplatin

**Group III**: i.v. – 45mg/kg carboplatin

**Group IV**: ILP with 6% buffered starch solution and carboplatin

**Group V**: Chemoembolization with carboplatin + DSM



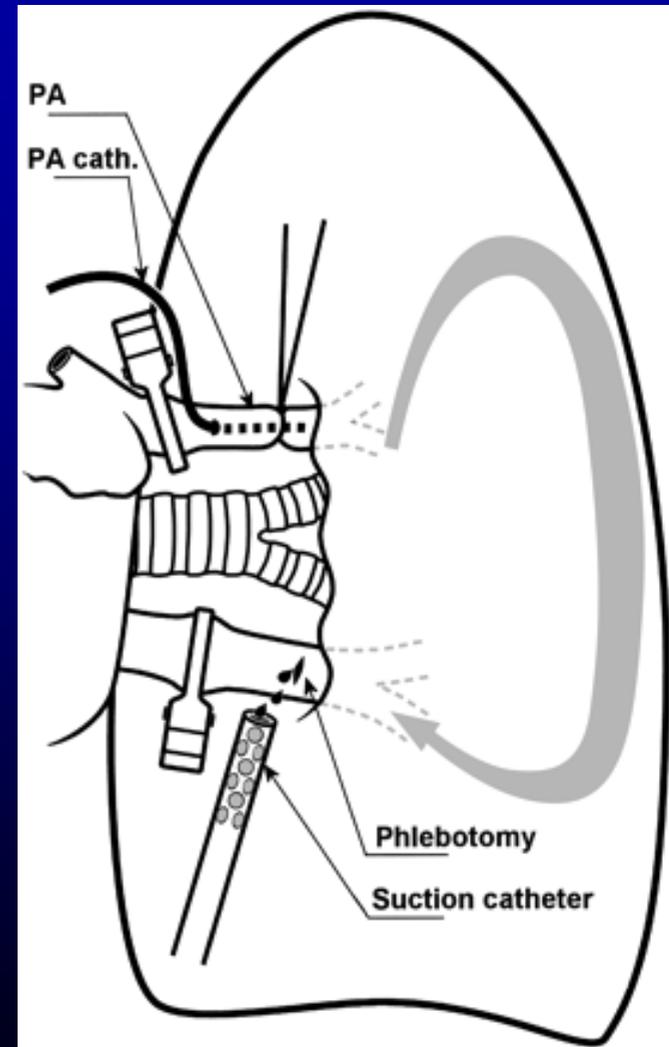
Schneider P et al, *Clinical Cancer Research* 2002; 8(7):2463-69

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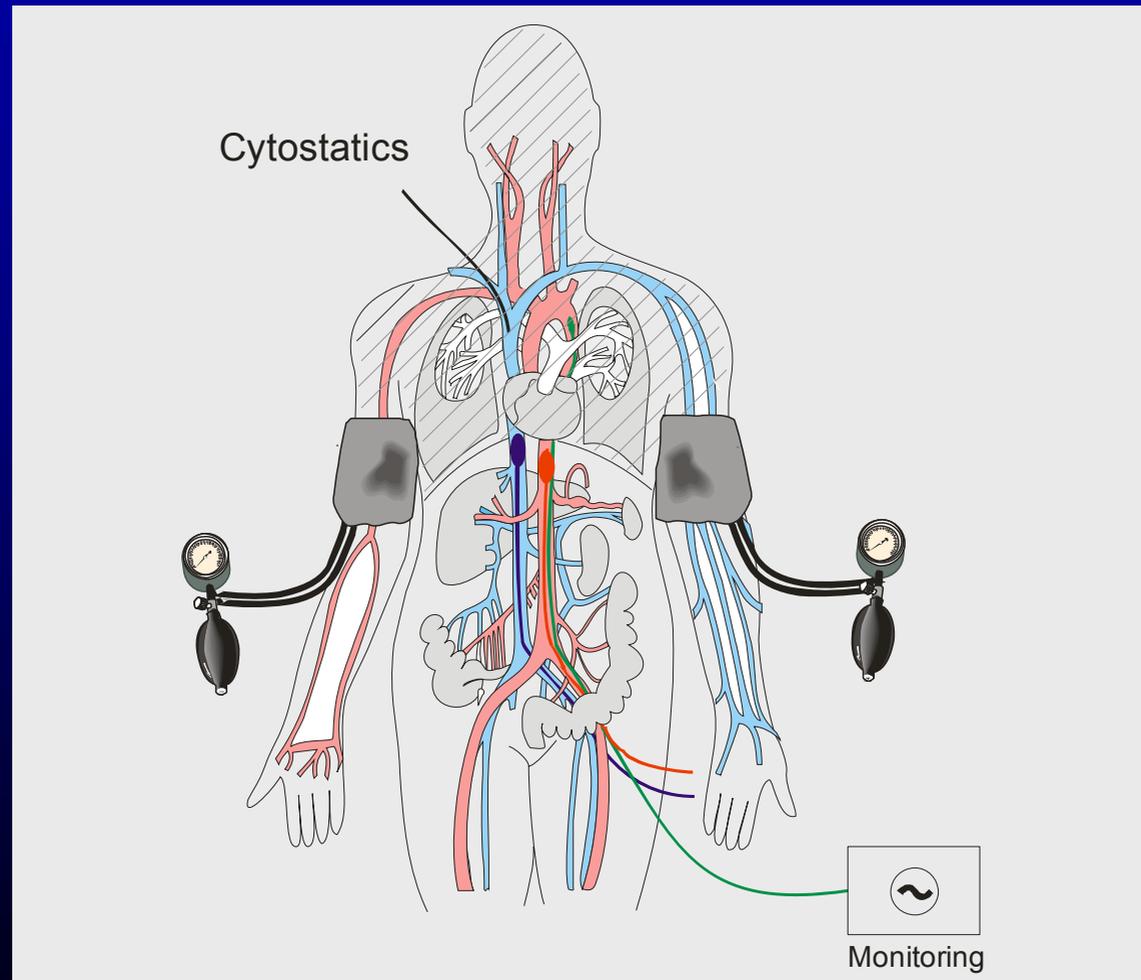


# Isolated Lung Perfusion

- Established ~ 1950
- Cannulation of the pulmonary vessels: closed circulation → isolated perfusion
- Application of high-dosed cytostatic agents, without systemic side effects



# Stop-flow Perfusion: Isolated Thoracic Perfusion



# Transpulmonary Chemoembolization

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- **Advantages of chemoembolization over isolated lung perfusion:**

- percutaneously applicable
- no thoracotomy required
- can be performed repeatedly
- no heart-lung machine necessary

- **Objectives:**

- dearterialization of the tumors with consecutive necrosis
- prolonged retention of the chemotherapeutic agent in the tumor



# TPCE: Technique I

- **Step I:** *preinterventional evaluation:*
  - blood parameters
  - clinical status
  - CT - MRI
- **Step II:** *7 F venous femoral access*
- **Step III:** *transvenous access to pulmonary artery:*  
⇒ selective/superselective pulmonary angiography:
  - ▶ evaluation: - feeding vessels
  - pulmonary arteriovenous shunts
  - two-plane evaluation



# TPCE



LUNGE  
14-Dez-01  
09:48:48  
Scene: 2  
W-B: 700  
W-C: 500  
X: 0.0  
Y: 0.0



# TPCE: Technique II

- **Step IV:** *balloon protection:*
  - diameter: 6-8 cm
  - length: 20-30 cm
- **Step V:** *locoregional perfusion and embolization:*
  - Mitomycin C (Gemcitabine) 5-10 mg/m<sup>2</sup> b.s.
  - Lipiodol ≤ 5 ml/m<sup>2</sup> b.s.
  - Embocept ≤ 300 mg
- **Step VI:** *repetitive embolization: 1-5 treatment courses*
- **Step VII:** *post-interventional evaluation:*
  - clinical status
  - blood parameters
  - CT - MRI



# TPCE: Post Treatment

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- 24 to 48 hours after initial treatment: unenhanced and contrast-enhanced CT scans, follow-up intervals of 4 weeks
- 4-row MDCT [Somatom Plus 4 VZ, Siemens Medical Solutions, Erlangen, Germany]
  - collimation: 4 x 2.5 mm
  - slice thickness: 2.5 mm, increment: 1.25 mm
- Comparison of images in the follow-up → detection of changes in size
- Calculation of tumor volumes via ellipsoid formula



# TPCE: Post Treatment

- Clinical examination and evaluation of health condition (questionnaire):
  - ▶ dyspnea
  - ▶ chest pain
  - ▶ coughing
  - ▶ elevated temperature
  - ▶ use of pain medication
- Complications: → Minor:
  - no or nominal therapy only required
  - overnight admission for monitoring→ Major:
  - therapy required
  - hospitalisation necessary
  - permanent damage
  - death

*Society of Cardiovascular & Interventional Radiology (SCVIR)*



# Bronchial Artery Embolization: Complications

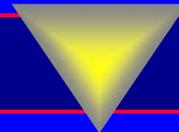
- Chest pain: 24 – 91%
- Dysphagia: 0.7 – 18.2% (2-7 days post embolization)
- Subintimal dissection of bronchial artery
- Pulmonary infarction
- Spinal chord ischemia
- Contrast-induced neurotoxicity:
  - bronchoesophageal fistula
  - bronchial infarction



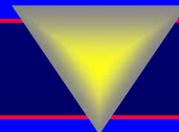
# TPCE: Indications

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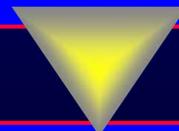
**Primary lung cancer & lung metastases**



**Unresectable**



**Size/diameter:  $\leq 4$  cm**



**Palliative intention**

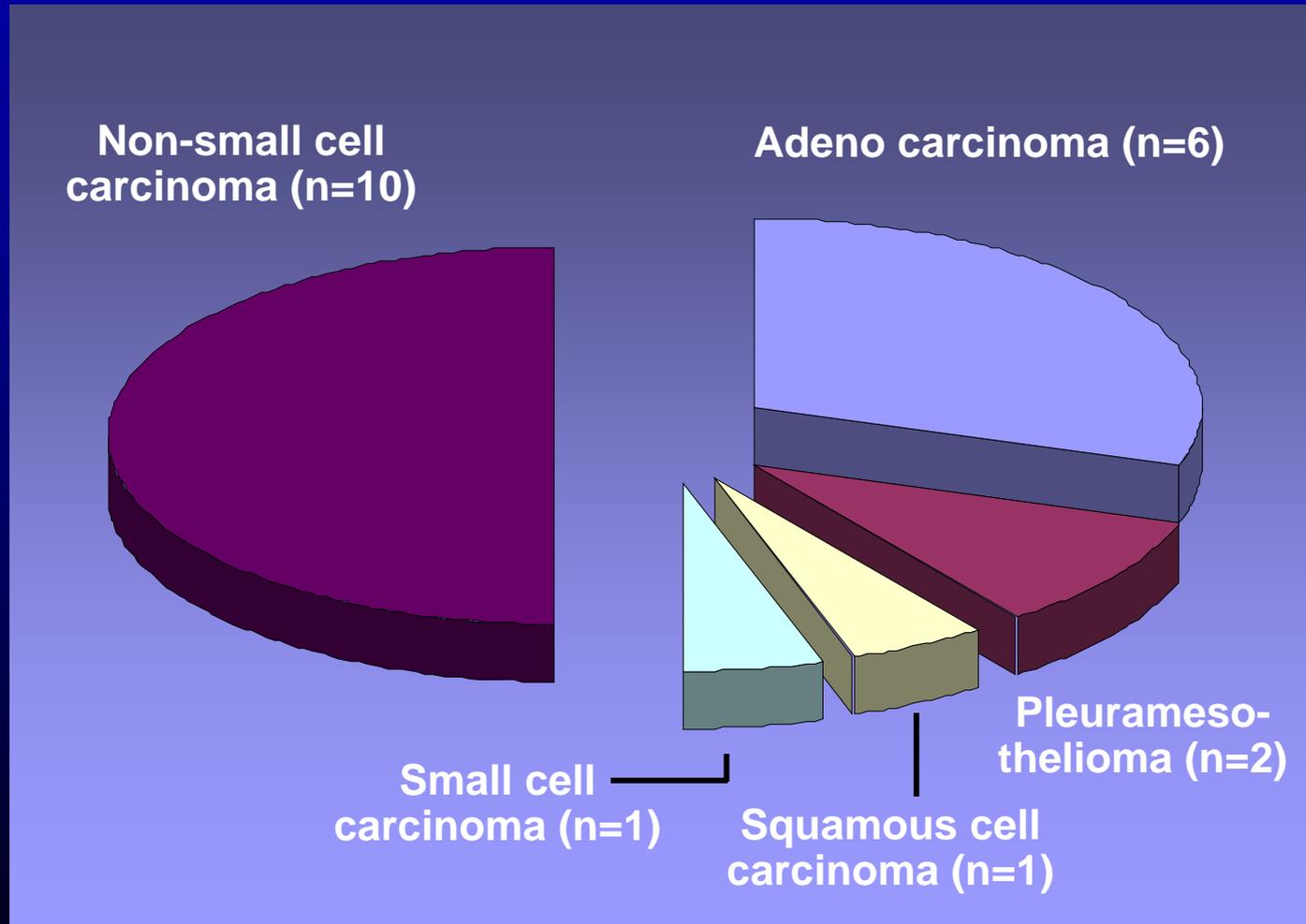


# Frankfurt – Ongoing Study: TPCE of Pulmonary Lung Tumors

- Time period: 2002 - 2006
- Materials & methods:
  - ▶ patients:  $n = 20$
  - ▶ age:  $\bar{x} = 63.7$  years
  - ▶ m:f = 16:4
  - ▶ # of tumors:  $\bar{x} = 2.1$
- Histologies:
  - ▶ adenocarcinoma:  $n = 6$
  - ▶ pleural mesothelioma:  $n = 2$
  - ▶ squamous cell carcinoma:  $n = 1$
  - ▶ small cell carcinoma:  $n = 1$
  - ▶ non-small cell carcinoma:  $n = 10$



# Tumor Entities



# Frankfurt – Ongoing Study: TPCE of Pulmonary Lung Tumors

- TPCE technique:

⇒ Transvenous pulmonary arterial chemoembolization (TPCE):

- ▶ Mitomycin (Gemcitabine) 5-10 mg/m<sup>2</sup> b.s.
- ▶ Lipiodol ≤ 5 ml/m<sup>2</sup> b.s.
- ▶ Embocept ≤ 300 mg

⇒ Number of cycles:

- ▶  $\bar{x} = 3.7$  (range, 2-8)



# Frankfurt – Ongoing Study: TPCE of Pulmonary Lung Tumors

- Results:

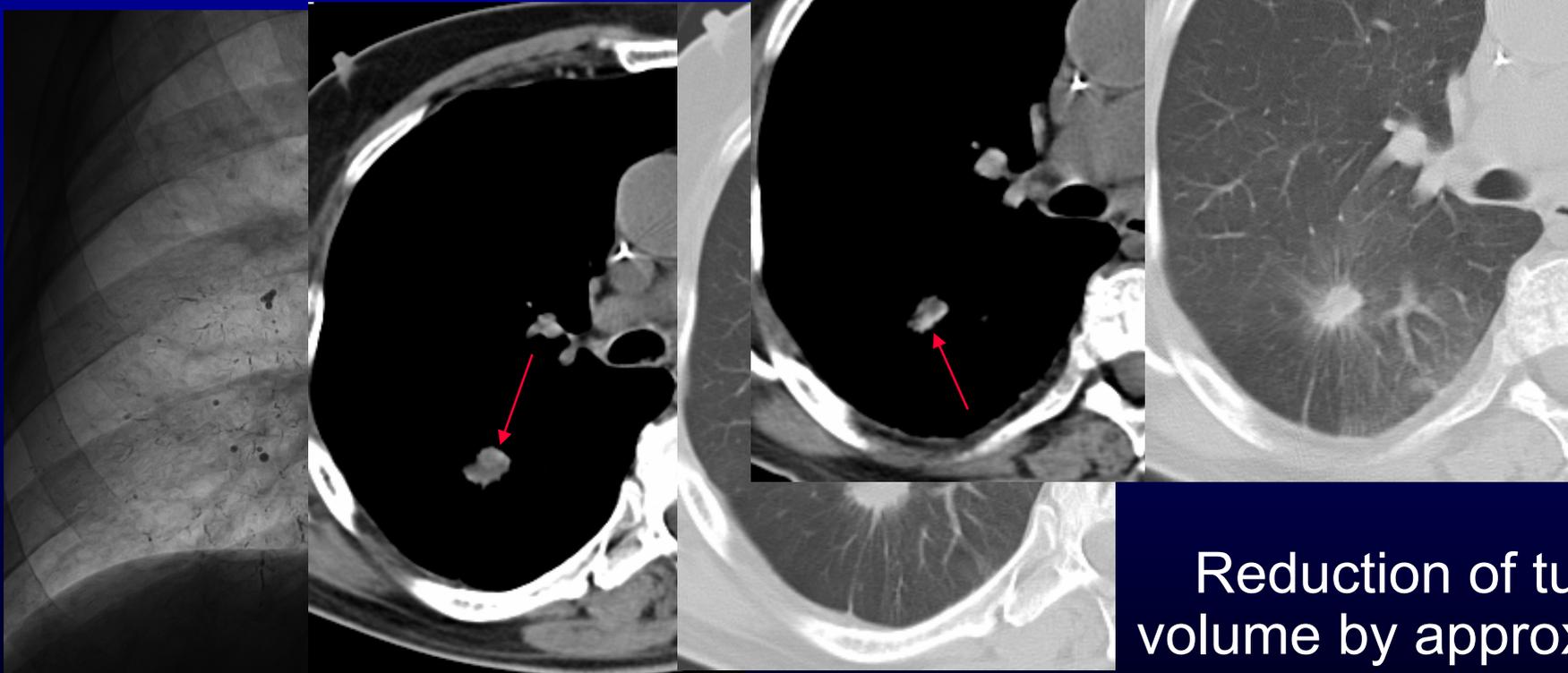
- ▶ no relevant side effects
- ▶ lipiodol enhancement: moderate - 35.5%  
low - 64.5%

- Response:

- ▶ volume reduction: 20% -  $\bar{x}$  = 12 ml
- ▶ stable disease: 50%
- ▶ progressive disease: 30% -  $\bar{x}$  = 24.2 ml

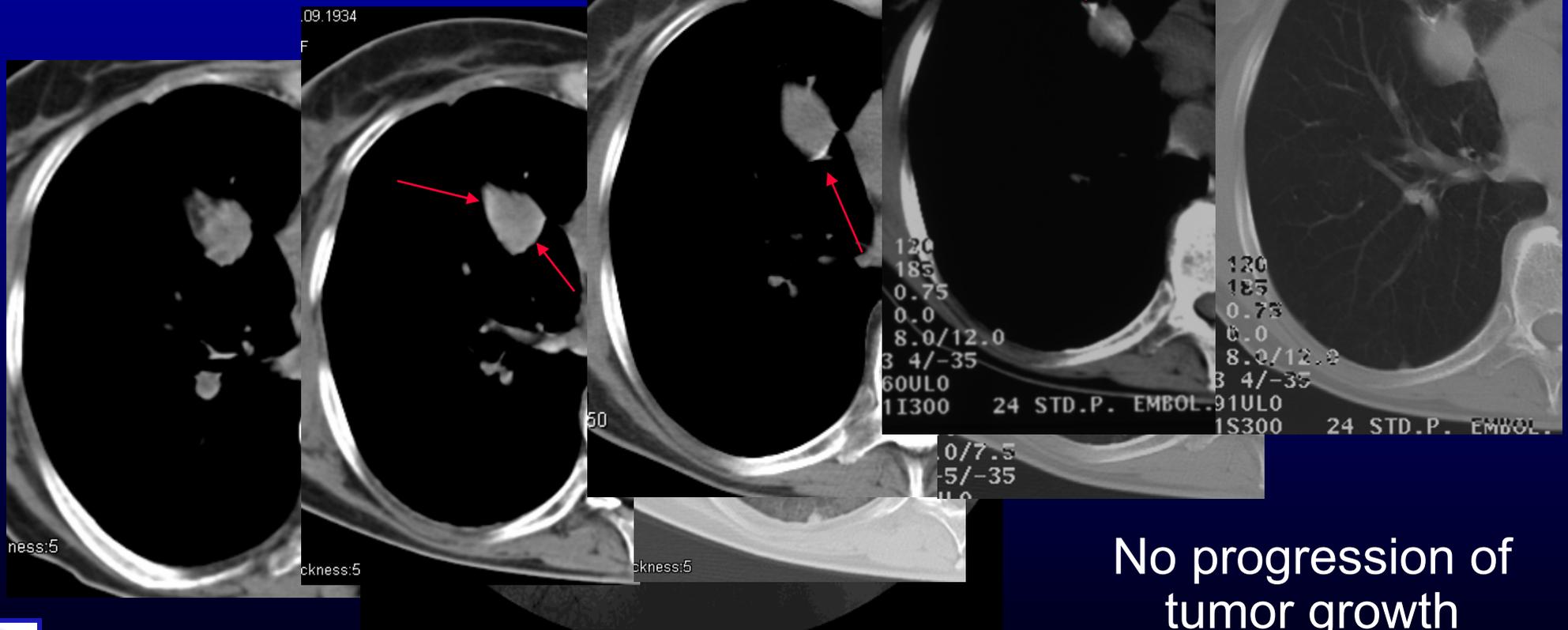


- 70 y/o male patient
- Adenocarcinoma of the right lung
- 2 treatments
- Moderate Lipiodol uptake
- Response to therapy



Reduction of tumor volume by approx. 50%

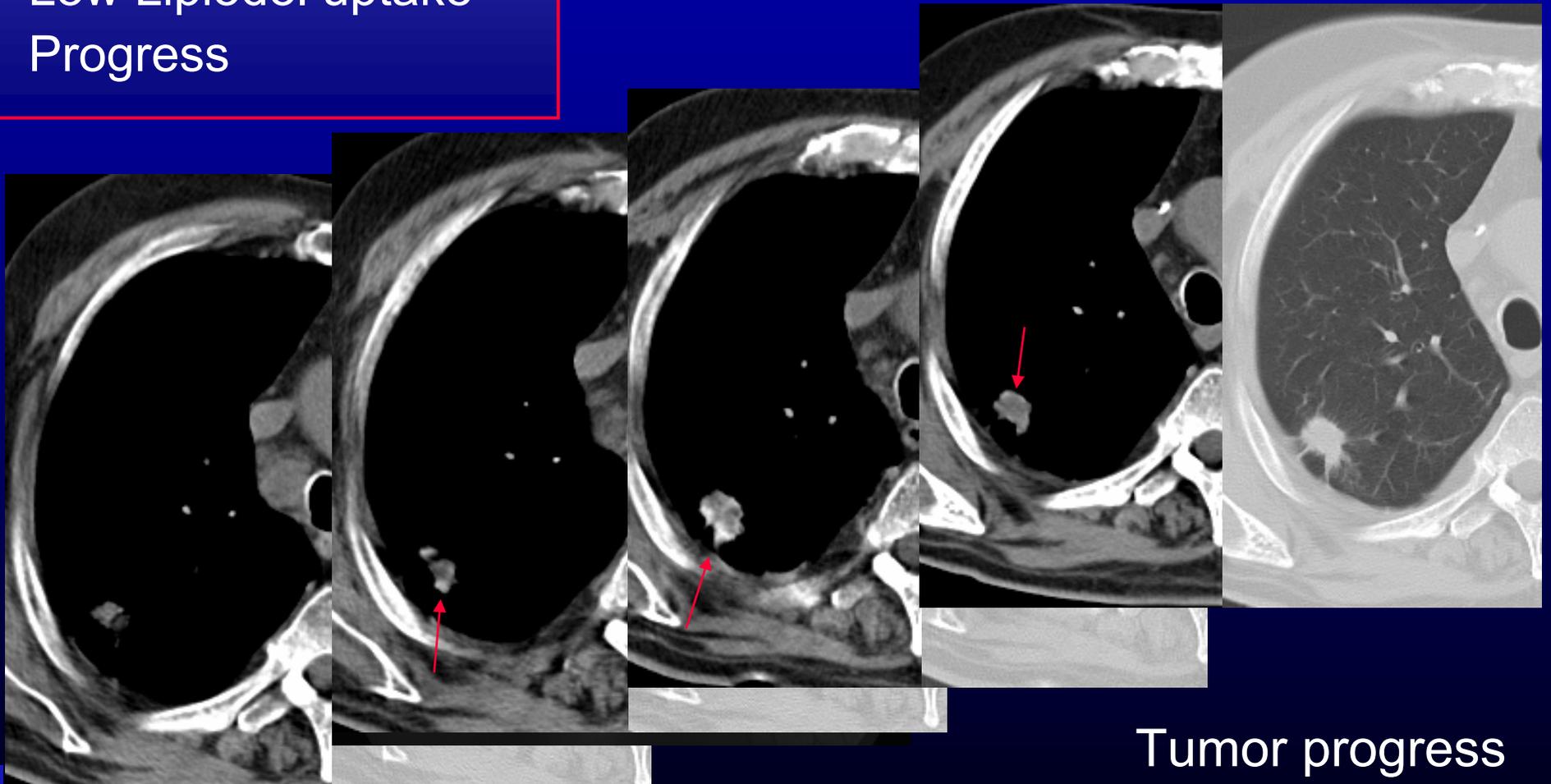
- 69 y/o patient
- Small cell carcinoma
- 3 treatments
- Low Lipiodol uptake
- Stable disease



No progression of tumor growth

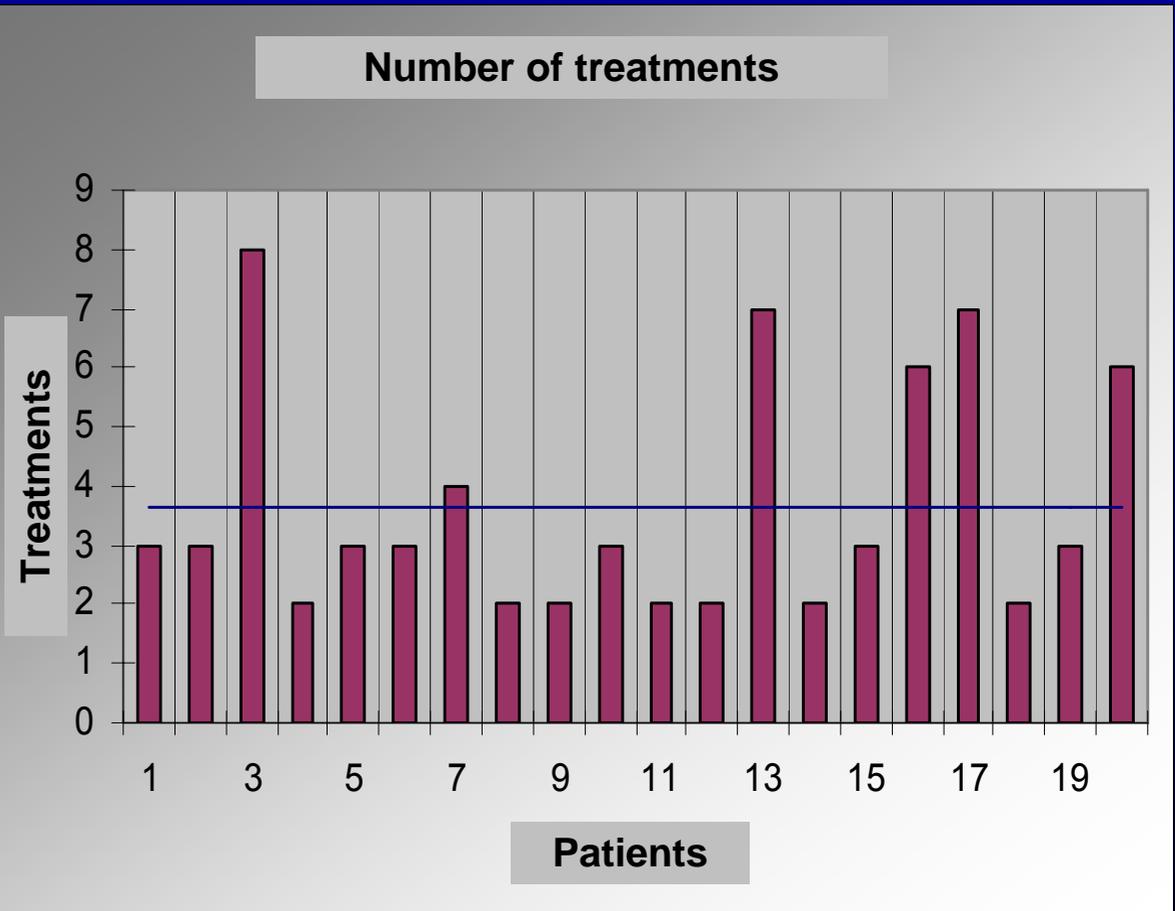


- 55 y/o male patient
- Adenocarcinoma
- Three treatments
- Low Lipiodol uptake
- Progress



# TPCE: Number of Treatments

- ▶ During one session only one segment of the lung was treated
- ▶ Treatment courses: between 2 and up to 8 times (mean 3.7 per patient)
- ▶ Sessions were repeated at 4-week intervals
- ▶ Follow-up: 6 up to 12 months

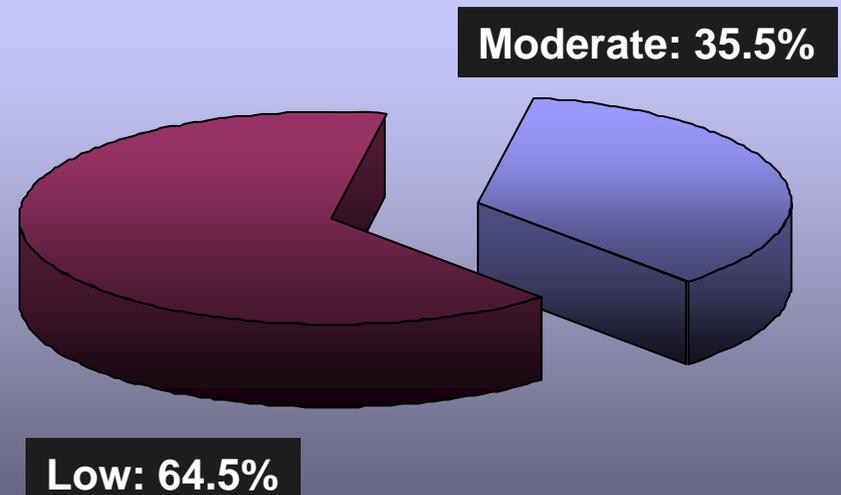


# TPCE: Results I

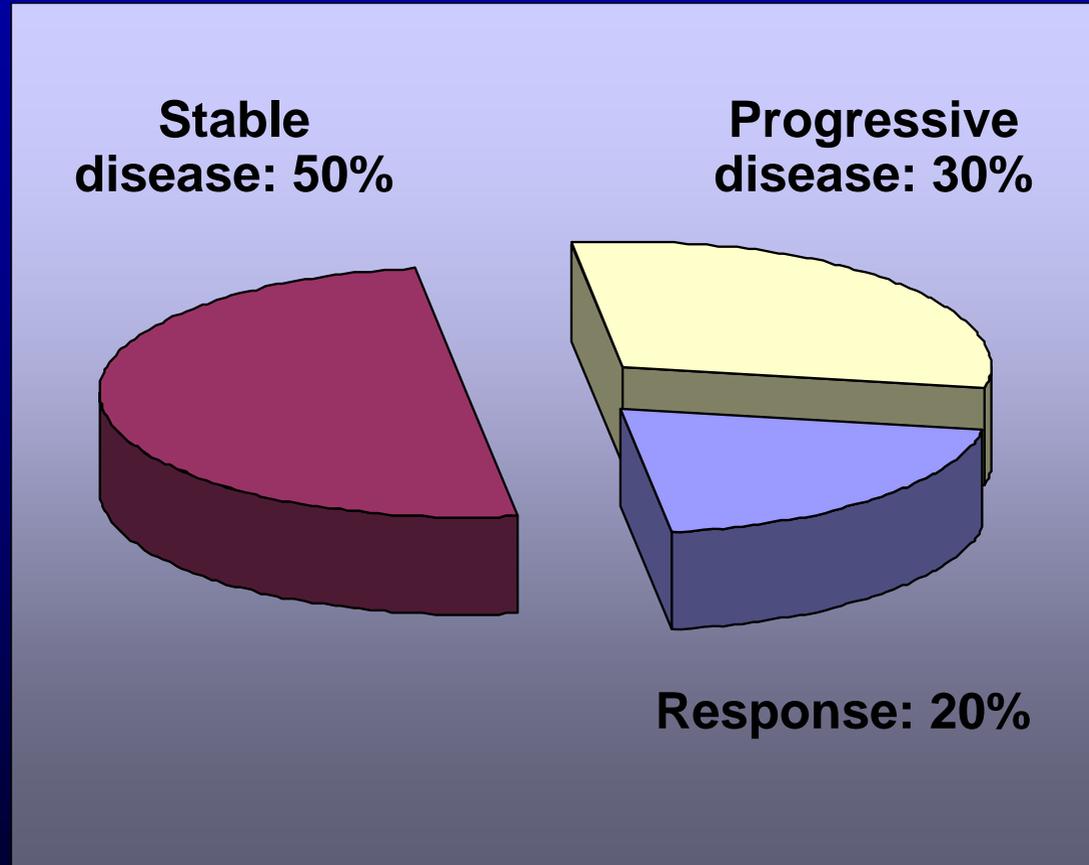
▶ All patients tolerated the procedure well and were released at the same day

- ▶ Major complications: n=0
- ▶ Minor complications: n=3
  - coughing: n=1
  - elevation of temperature: n=2
- ▶ No impact on laboratory parameters

## Lipiodol uptake



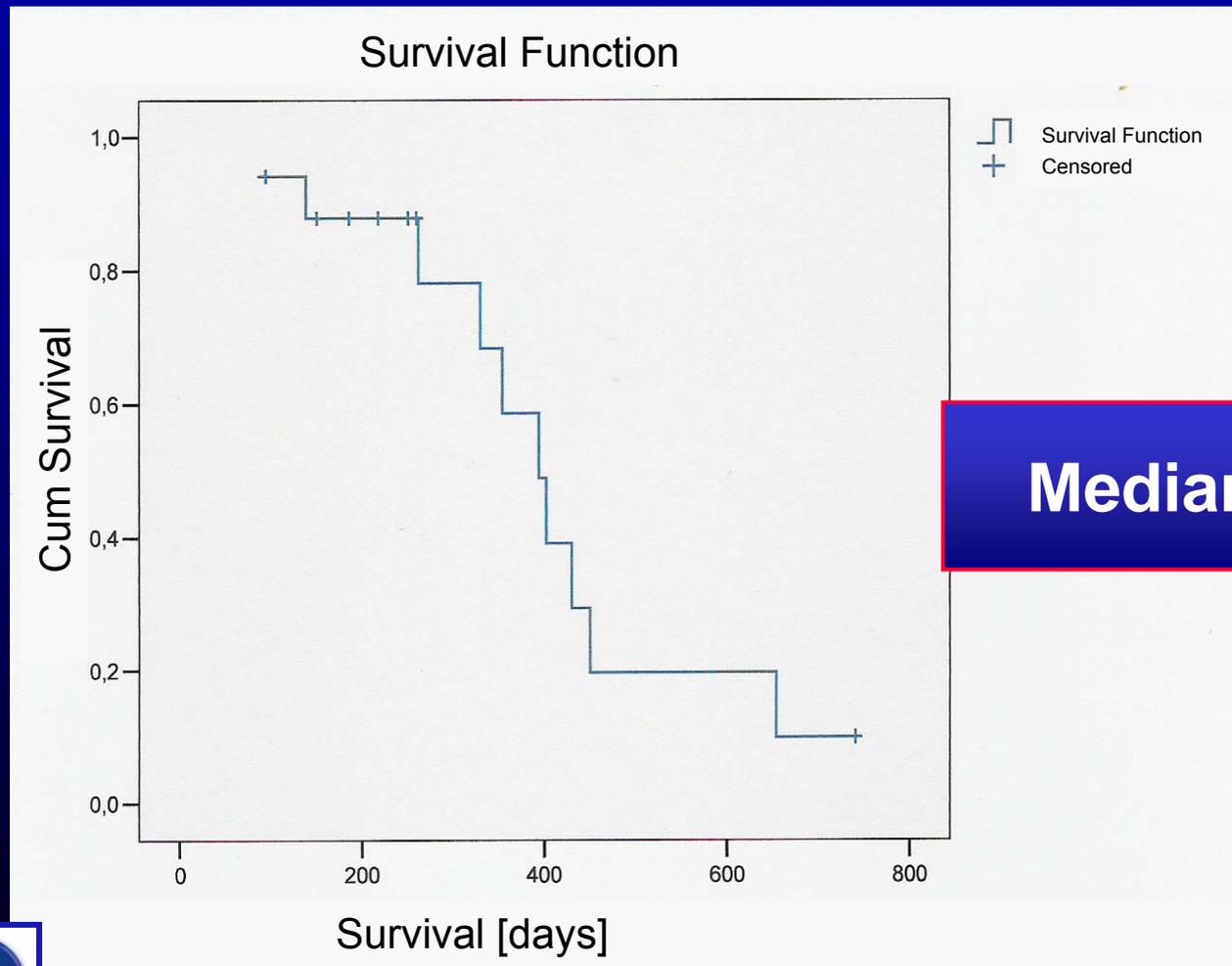
# TPCE: Results II



**Progression: after 2.4 months (mean; range, 0.7 to 6.1 mo)**



# TPCE: Survival – Primary Lung Cancer (Kaplan-Meier)



**Median survival: 394 days**



# Frankfurt – Ongoing Study: TPCE with Doxorubicin-loaded Beads

- Patients:

- ▶ planned: n = 20
- ▶ treated: n = 5
- ⇒ primary and secondary lung neoplasms

- Materials and methods:

- ▶ Doxorubicin-loaded beads (DC beads)
- ▶ size: 500-700  $\mu\text{m}$
- ▶ 1 ml beads: 18.9 mg Doxorubicin
- ▶ 8 ml beads: 150 mg Doxorubicin



# Frankfurt – Ongoing Study: TPCE with Doxorubicin-loaded Beads

- Side effects:

- ▶ pleural effusion n = 2
- ▶ nausea n = 2
- ▶ pneumonia n = 1
- ▶ pain n = 1

- Therapy response:

- ▶ stable disease n = 2
- ▶ progressive disease n = 2
- ▶ partial remission n = 1



# Transpulmonary Chemoembolization (TPCE) with Doxorubicin-loaded Beads for the Treatment of Primary and Secondary Lung Cancer

- Purpose: To evaluate the feasibility of TPCE using DC beads loaded with doxorubicin for the treatment of patients with lung tumors.
- Materials & methods: n = 20 patients treated in palliative intention
  - TPCE: max. 8 ml DC beads loaded with 150 mg doxorubicin  
size of the beads: 500 - 700  $\mu\text{m}$   
3 cycles at 3-week intervals
  - Follow-up: MRI
  - Treatment of 5 patients: 3 females, 2 male

*Prospective Phase I Study – Clinical Trial*



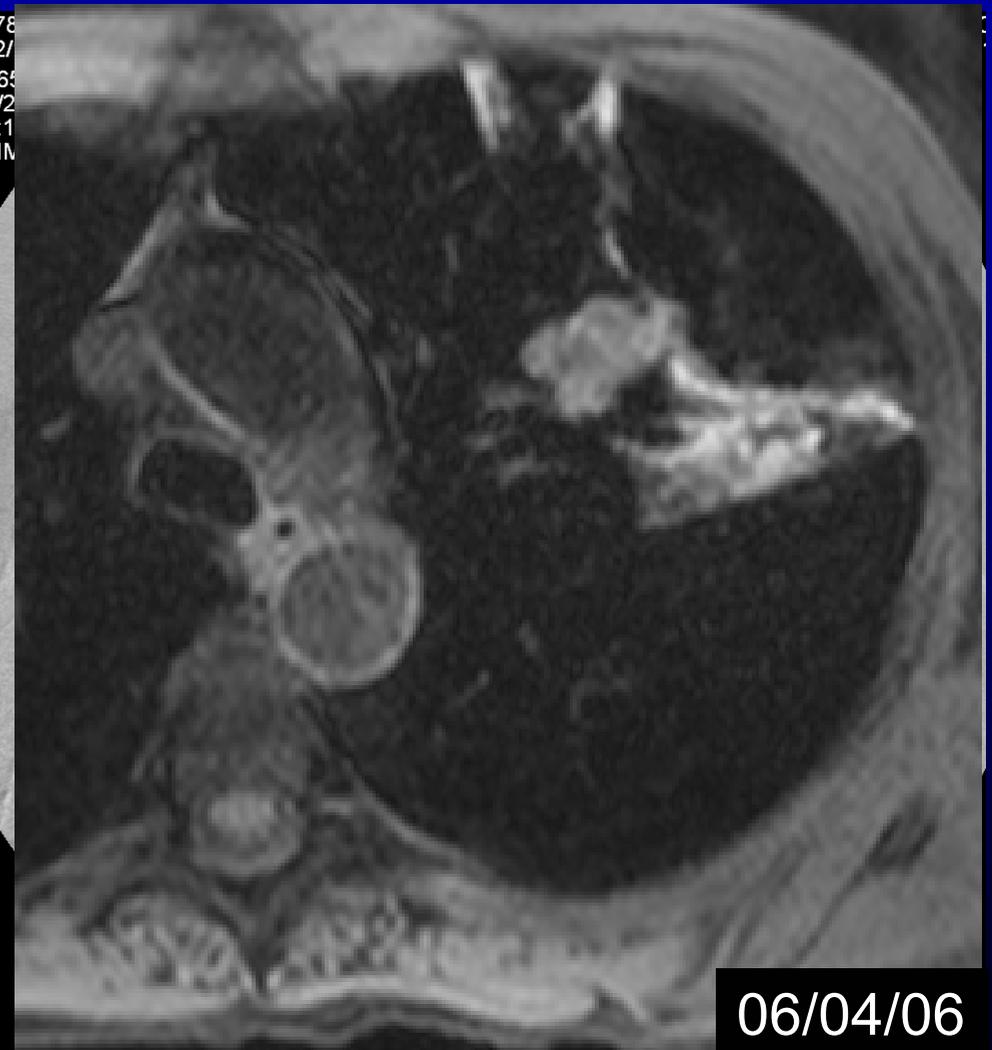
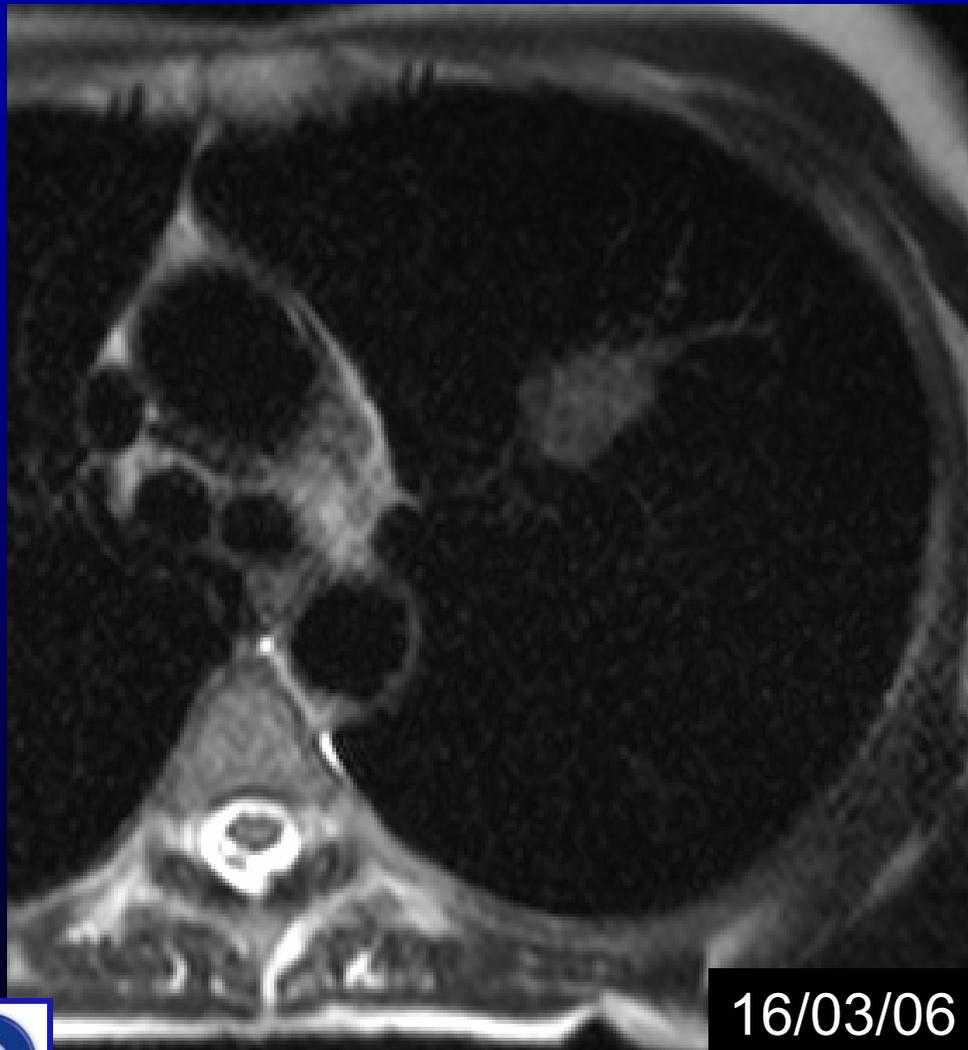
# Transpulmonary Chemoembolization (TPCE) with Doxorubicin-loaded Beads for the Treatment of Primary and Secondary Lung Cancer

- Results:
    - Partial response: n = 1
    - Stable disease: n = 2
    - Progression: n = 2
    - Side effects: pleural effusion  
increase of inflammatory parameters
- tumor volume ↓ - 18.9%
- Conclusion:
    - ▶ Transpulmonary chemoembolization with doxorubicin-loaded beads is a feasible novel therapeutic regime
    - ▶ Further studies are necessary

*Prospective Phase I Study – Clinical Trial*



# TPCE with Doxorubicin-loaded Beads



# Conclusions

## Transvenous pulmonary chemoperfusion & chemoembolization

- Low-risk procedure
- Minimal invasive therapy management possible
- Relevant response to therapy
- Combination with thermoablative procedures
- Further prospective clinical studies required

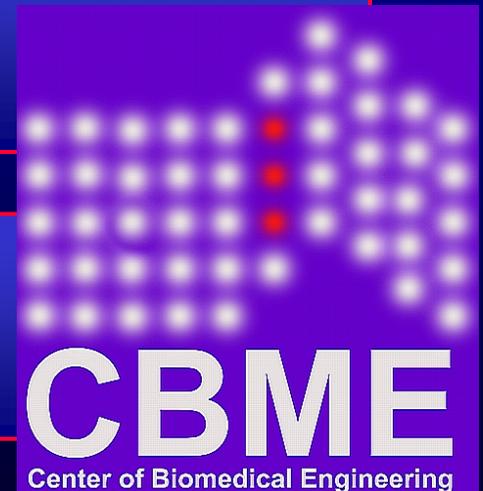


# TPCE: Current Studies

1. TPCE combined < *radiotherapy*  
*systemic chemotherapy*

2. TPCE combined — *thermal ablation*

3. TPCE *beads application: Doxorubicin<sup>®</sup>*



*Interventional Oncology Group: University of Frankfurt*



