Transcatheter Therapies for NSCLC

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Transcatheter Therapies for NSCLC

Learning Objectives

• 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
Transcatheter Therapies for NSCLC

- Basics

- Technical considerations:
  - transbronchial arterial embolization
  - transbronchial arterial perfusion
  - transvenous pulmonary arterial
    - embolization
    - perfusion

- Indications

- Results

- Conclusion

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• **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%  
  Adenocarcinoma  30%  
  5-y-survival: 10%  
  Alveolar cell carcinoma  2-5%  
  5-y-survival: 10%

*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®

- Results: efficacy – tumor necrosis:
  - chemoembolization > intravenous chemotherapy
  - chemoembolization = isolated lung perfusion
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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Established ~ 1950
Cannulation of the pulmonary vessels: closed circulation → isolated perfusion
Application of high-dosed cytostatic agents, without systemic side effects
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

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**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: Technique II

| Step IV: balloon protection: | - diameter: 6-8 cm  
<table>
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<th>- length: 20-30 cm</th>
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| Step V: locoregional perfusion and embolization: | - Mitomycin C (Gemcitabine) 5-10 mg/m² b.s.  
|                                          | - Lipiodol ≤ 5 ml/m² b.s.  
|                                          | - Embocept ≤ 300 mg |
| Step VI: repetitive embolization: | 1-5 treatment courses |
| Step VII: post-interventional evaluation: | - clinical status  
|                                         | - blood parameters  
|                                         | - CT - MRI |

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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)

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## 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

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TPCE: Indications

Primary lung cancer & lung metastases

Unresectable

Size/diameter: ≤ 4 cm

Palliative intention

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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

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Tumor Entities

- Pleuramesothelioma (n=2)
- Squamous cell carcinoma (n=1)
- Small cell carcinoma (n=1)
- Adeno carcinoma (n=6)
- Non-small cell carcinoma (n=10)
Frankfurt – Ongoing Study: TPCE of Pulmonary Lung Tumors

- **TPCE technique:**

  ⇒ Transvenous pulmonary arterial chemoembolization (TPCE):
  - Mitomycin (Gemcitabine) 5-10 mg/m² b.s.
  - Lipiodol ≤ 5 ml/m² 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% - \( \bar{x} = 12 \text{ ml} \)
  - stable disease: 50%
  - progressive disease: 30% - \( \bar{x} = 24.2 \text{ ml} \)

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• 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

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- 55 y/o male patient
- Adenocarcinoma
- Three treatments
- Low Lipiodol uptake
- Progress
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: Number of Treatments

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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

- Moderate: 35.5%
- Low: 64.5%
TPCE: Results II

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

- Stable disease: 50%
- Progressive disease: 30%
- Response: 20%

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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 μm
  - 1 ml beads: 18.9 mg Doxorubicin
  - 8 ml beads: 150 mg Doxorubicin

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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

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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 μm
  3 cycles at 3-week intervals
- Follow-up: MRI
- Treatment of 5 patients: 3 females, 2 male
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

\[ \text{tumor volume} \downarrow \text{– 18.9\%} \]

- **Conclusion:**
  - Transpulmonary chemoembolization with doxorubicin-loaded beads is a feasible novel therapeutic regime
  - Further studies are necessary

*Prospective Phase I Study – Clinical Trial*

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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®

Interventional Oncology Group: University of Frankfurt

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