State of the art treatment options for primary liver malignancies and metastatic disease

Peter Huppert
Prof. of Radiology and Neuroradiology
Klinikum Darmstadt
Disclosure

Speaker name:

Peter Huppert, M.D.

☐ I have the following potential conflicts of interest to report:
  ☐ Consulting
  ☐ Employment in indstr
  ☐ Stockholder of a healthcare company
  ☐ Owner of a healthcare company
  ☐ Other(s)
  x I do not have any potential conflict of interest
Interventional Trx. Options in Liver Tumors

transhepatic
• Tumor ablation
• Portal vein embolization
• Biliary drainage

transarterial
• Conventional TACE
• Drug-eluting TACE
• Radioembolization
Liver Tumor Ablation

Basic Principle

- Thermocoagulation by heating
- Energy delivery by RF, MW, laser light, FUS...

Approach/Method

- perc. transhepatic access
- monopolar-multipolar probes
- various probe designs
Liver Tumor Ablation

Indication

- HCC: n ≤3; size ≤ 5 cm
- Mts.: n ≤3; size ≤ 3 cm
- Resection not preferred

Outcome/Limitations

- Local control >85% (<3 cm size)
- New lesions 50-70%/1-3a
- Limitations:
  - critical structures < 1cm
  - heat sink effect of vessels > 3mm
Liver Tumor Ablation

**Indication**
- HCC: n ≤ 3; size ≤ 5 cm
- Mts.: n ≤ 3; size ≤ 3 cm
- Resection not preferred

**Outcome/Limitations**
- Local control >85% (<3 cm size)
- New lesions 50-70%/1-3a
- Limitations:
  - critical structures < 1cm
  - heat sink effect of vessels > 3mm
Liver Tumor Ablation

Indication

• HCC: n \( \leq 3 \); size \( \leq 5 \) cm
• Mts.: n \( \leq 3 \); size \( \leq 3 \) cm
• Resection not preferred

Outcome/Limitations

• Local control >85% (<3 cm size)
• New lesions 50-70%/1-3a
• Limitations:
  - critical structures < 1cm
  - heat sink effect of vessels > 3mm
Portal Vein Embolization

Basic Principle
- flow redistribution into FRL
- induction of hyperplasia

Approach/Method
- percut. transhep. PV catheter.
- selectiv segmental PV embx.
- Particles, glue, coils
Portal Vein Embolization

**Indication**
- Prior to liver resection
- Insufficient FRLV

**Outcome/Limitations**
- + 20-30% of FRLV
- Limited in cirrhosis

+ 4 weeks
Transhepatic Biliary Drainage

Basic Principle

- recanalization of biliary obstruction
- reconstitution of internal biliary flow

Approach/Method

- percutaneous transhepatic access
- unilateral/bilateral drainage
- stenting, silicon-prosthesis
Transhepatic Biliary Drainage

Indication

- failed ERCP
- Hilar and extrahepatic biliary obstruction
- cholangitis

Outcome/Limitations

- effective in hilar and distal obstructions
- limited in multiple intrahepatic obstructions by mts.
Conventional TACE

Basic Principle
• local intraarterial chemotherapy
• embolization of tumor feeding arteries
• accumulation of drugs and embolics within tumor vessels

Approach/Method
• transfemoral selective catheter.
• microcatheter if needed
• various drugs and embolics combined
**Conventional TACE**

**Indication**
- HCC: non-resectable, intermediate stage – multinodular, PS 0, Child A/B
- CCC: non-resectable, PD after systemic treatment
- Mts.: palliative for various types

**Outcome/Limitations**
- HCC: survival benefit 6-12 mo. in selected cases
- limited effects in all others with no proven survival benefit
Conventional TACE

**Indication**
- HCC: non-resectable, intermediate stage – multinodular, PS 0, Child A/B
- CCC: non-resectable, PD after systemic treatment
- Mts.: palliative for various types

**Outcome/Limitations**
- HCC: survival benefit 6-12 mo. in selected cases
- limited effects in all others with no proven survival benefit
Radioembolization

Basic Principle
• internal radiation/brachytherapy
• catheter-directed application of microparticles emitting β-radiation
• minor embolic effects

Approach/Method
• bland embx. of non-target arteries in advance
• evaluation of av shunting
• appropriate dose application
Radioembolization

Indication

- HCC, Liver-Mts.
- advanced disease
- portal vein thrombosis

Outcome/Limitations

- tendency of better local response compared to TACE
- no proven survival benefit
- RILD, costs

Mts. CRC

+ 11 mo
Drug-eluting TACE

**Basic Principle**
- cytotoxic drug loaded into microspheres
- drug release after catheter-directed application and embx.
- sustained drug delivery and exposure

**Approach/Method**
- technique similar to conv. TACE
- today available for Doxorubicin, Epirubicin and Irinotecan
- today 3 types of microspheres

Interaction of irinotecan (Irt+) with SO₃⁻ groups by an ion-exchange process displaces water from the hydration shells

adapted from Biocompatibles
# Drug-Eluting Microspheres

## DC-BEADS™

![Image of DC-BEADS™]

- **Material:** Polyvinyl alcohol
- **Sizes:** 70-150μm..500-700μm
- **Loading:** 200 mg Irinotecan/4cc
  - 150 mg Doxorubicin/4cc

## HepaSphere™

![Image of HepaSphere™]

- **Material:** Sodium acrylate
- **Sizes:** 30-200 (x 4) μm
- **Loading:** 200 mg Irinotecan/50mg
  - 50 mg Doxorubicin/50 mg

## Tandem™

![Image of Tandem™]

- **Material:** Polyvinyl alcohol
- **Sizes:** 40μm, 75μm, 100μm
- **Loading:** 200 mg Irinotecan/4ml
  - 200 mg Doxorubicin/4cc

---

Images: Biocompatibles, Biosphere, Celonova
Drug-eluting TACE

**Indication**

- HCC (similar to conv. TACE)
- colorectal cancer liver mts. (salvage, downstaging)

**Outcome/Limitations**

- HCC: improved local efficacy and systemic toxicity however no proven survival benefit compared to conv. TACE
- CRC-Mts: TTP of 5-6 mo in salvage population; limited if >25% tumor load
Drug-eluting TACE

Indication

• HCC (similar to conv. TACE)
• colorectal cancer liver mts. (salvage, downstaging)

Outcome/Limitations

• HCC: improved local efficacy and systemic toxicity however no proven survival benefit compared to conv. TACE
• CRC-Mts: TTP of 5-6 mo in salvage population; limited if >25% tumor load

Table 3 Median time to progression and median survival after TACE in relation to liver tumor involvement and grade of tumor vascularization

<table>
<thead>
<tr>
<th>Liver tumor involvement (%)</th>
<th>Median TTP (mo)</th>
<th>Median survival (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>\ 25</td>
<td>10*</td>
<td>21*</td>
</tr>
<tr>
<td>26–50</td>
<td>4.5</td>
<td>7</td>
</tr>
<tr>
<td>51–75</td>
<td>3*</td>
<td>5*</td>
</tr>
<tr>
<td>Grade of vascularization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.5</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>7.5</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>12</td>
</tr>
</tbody>
</table>

* p ≤ 0.005

Transcatheter Arterial Chemoembolization (TACE) of Colorectal Cancer Liver Metastases by Irinotecan-Eluting Microspheres in a Salvage Patient Population

Peter Huppert · Thorsten Wenzel · Hubertus Wietholtz
Summary

• Thermal ablation, transhepatic biliary drainage and portal vein embolization are established techniques with well defined indications.

• cTACE is limited to HCC, CCC and NET, however deTACE and radioembolization have potential to improve results of transarterial treatment in selected patients with primary liver tumors and liver metastases.
State of the art treatment options for primary liver malignancies and metastatic disease

Peter Huppert
Prof. of Radiology and Neuroradiology
Klinikum Darmstadt