Chapter 2
Embolization Materials, Catheters, and Intra-Arterial Ports

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2.1 Introduction

Catheter-directed embolization therapies for oncologic indications are increasingly gaining importance. Basically, these minimally invasive therapies include locoregional, tumoricidal therapies, pre- or postoperative adjunctive treatments as well as palliative management options. Although different materials are used depending on the indications, the interventional approach is in most of the cases similar: a diagnostic catheter is placed in the feeding, large artery, and through this guiding catheter a coaxial "microcatheter" is placed with its tip as close as possible to the target tumoral implants. Once the microcatheter is correctly positioned, chemotherapeutic agents can be carefully injected in order to obtain very high drug concentrations within the tumor and low(er) drug concentrations within the peripheral blood, resulting in high response rates and

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low(er) systemic toxicity rates. Additionally, occluding microparticles can be injected during or immediately after the chemotherapeutic infusion in order to add an ischemic effect or to create a slower wash-out phenomenon of the injected cytostatic agents. In case of emergency conditions of bleeding tumors, transcatheter injection of embolics without chemotherapeutic agents may be sufficient to stabilize the patient's condition.

In this chapter, an overview of different minimally invasive, transcatheter therapies for tumor treatment, including transarterial chemo-infusion with or without insertion of a permanent port system, transarterial (chemo-)embolization, yttrium-90 infusion, and isolated liver perfusion will be given. Also, a brief overview of interventional techniques to treat tumor-related hemorrhage will be presented, and finally, a short overview of percutaneous ablative devices will be given.

2.2 Transarterial Chemo-Infusion of Metastatic Liver Tumors [1–7]

1. *Rationale*

   (a) Liver metastases are perfused mainly by the hepatic artery, whereas normal liver tissue is primarily supplied by the portal vein.
   (b) Certain drugs have high hepatic extraction.
   (c) The liver is often the first site of metastases; eliminating liver metastases may prevent extrahepatic disease.
   (d) Many drugs have a steep dose-response disease.
   (e) Drugs with a high total body clearance are very effective.

2. *Indications*

   (a) Palliative chemotherapeutic treatment of liver-only or liver-predominant metastases, mainly as rescue for liver metastases refractory to all conventional intravenous chemotherapeutic lines.
   (b) Downstage the number and volume of liver metastases prior to surgical resection or any other percutaneous ablative therapy. This approach can be used as first, second, or as last chemotherapeutic line.

3. *Technique*

   (a) Repeat catheterization

   - Under local anesthesia, repeat catheterization of the feeding hepatic arteries with the use of a diagnostic catheter (4–5 French) and coaxial microcatheter.
   - Diagnostic catheter: 4–5 F cobra-shaped, Simmons I or Simmons II catheter.
   - Microcatheter: large-bore 2.5–3.0 F microcatheter.

   (b) Port catheter

   - Insertion of a permanent arterial port system from the femoral or axillary artery. Before each chemotherapeutic session, patency and position of the port have to be verified. Procedure under local anesthesia.

   (c) Choice of technique depends of:

   - Experience of the interventional radiologist
   - Short interval between two sessions (<2 weeks) and many sessions foreseen (>5 sessions): port system > repeat catheterization
   - Long interval (at least 2–4 weeks) between two sessions and potentially only a few sessions foreseen: repeat catheterization > port system

4. *Which chemotherapeutic agents for which metastases?*

   (a) Mitomycin C for breast cancer-related liver metastases
   (b) Oxaliplatin for colorectal-related liver metastases
   (c) Fotemustine for ocular melanoma-related liver metastases
   (d) 5-FU + floxuridine for colorectal-related liver metastases

2.3 Chemo-Embolization of Primary and Secondary Liver Tumors [8–18]

1. *Rationale*

   (a) See chemo-infusion of metastatic liver metastases.
   (b) Addition of embolic agents:

   - Reduce the washout effect of infused chemotherapeutic agents.
   - Ischemia may induce cellular pump destruction which may lead to better uptake of cytotoxic agents by the tumoral cells.
   - Persistent ischemia may induce tumor necrosis.

2. *Indications for primary liver tumors*

   (a) First-line therapy for unresectable, liver-only hepatocellular carcinoma
   (b) Rescue therapy for cholangiocarcinoma refractory to medical management

3. *Indications for secondary liver tumors*

   (a) Rescue therapy for liver-only or liver-predominant metastases refractory to most/all conventional chemotherapeutic lines

   - Colorectal metastases
   - Neuroendocrine metastases

- Pancreatic carcinoma metastases
- Malignant melanoma metastases
- Renal cell carcinoma metastases

(b) First- or second-line therapy for liver-only or liver-predominant metastases (experimental for colorectal metastases)
(c) Third-line therapy for liver-only colorectal metastases (drug-eluting beads with irinotecan)

4. *Technique of chemo-embolization*

(a) Conventional chemo-embolization

- Local anesthesia
- Selective catheterization of the hepatic artery and subsequently of the feeding arteries of the tumoral lesion(s)
- Slow injection under fluoroscopic guidance of the mixture of Lipiodol (Laboratoires Guerbet, Aulnay-sous-Bois, France) and chemotherapeutic agents, like:
  - Doxorubicin
  - Cisplatinum
  - Mitomycin C
  - Combination of abovementioned agents
- Injection of microparticles mixed with contrast medium
  - Polyvinyl alcohol (PVA) microparticles

    Contour (Boston Scientific Corp., Natick, MA, USA)
    PVA (Cook Medical, Bjaeverskov, Denmark)
  - Calibrated microspheres

    Embospheres (Merit Medical Systems Inc., South Jordan, UT, USA)
    BeadBlock (Terumo, Leuven, Belgium)

Embozene (CeloNova BioSciences Inc., San Antonio, TX, USA)

– Resorbable particles

Starch microspheres (EmboCept® S, PharmaCept, Berlin, Germany)
Spongostan (Ferrosan Medical Devices, Soeborg, Denmark)
Curaspon (P3 Medical Ltd., Bristol, UK)

(b) Chemoembolization with drug-eluting beads

- Local anesthesia, except when using irinotecan-loaded microparticles (epidural or general anesthesia)
- Selective catheterization of the hepatic artery and subsequently of the feeding arteries of the tumoral lesion(s)
- Slow injection under fluoroscopic control of the mixture of drug-eluting beads and contrast medium

– HepaSphere (Merit Medical, UT, USA)

Doxorubicin
Oxaliplatin
Cisplatinum

– DC-beads (Biocompatibles, UK)

Doxorubicin
Irinotecan

– Life Pearl (Terumo, Japan)

Doxorubicin
Irinotecan

– Embozene Tandem (CeloNova, USA)

Doxorubicin
Irinotecan

- Stop embolization when flow is slowing down or when stasis of contrast medium is obtained in the feeding artery.

5. *Exclusion criteria (absolute and relative contraindications)*

   (a) Absolute contraindication for chemo-embolization

   - >50% tumor involvement of the liver volume
   - Active infection
   - Liver function disturbances (bilirubin >2.5 mg/dL)
   - Macroscopic arterioportal fistula
   - Main portal vein thrombosis

   (b) Relative contraindication for chemo-embolization

   - Reduced liver function (bilirubin >1.5 > 2.5 mg/dL)
   - Child-Pugh B (drug-eluting beads are preferred)
   - Partial or distal portal vein thrombosis
   - Hepatic encephalopathy
   - ECOG >1
   - Renal insufficiency (contrast medium)

6. *Complications*

   (a) Common complications
   - Postembolization syndrome: >80%
     - Abdominal pain
     - Fever <38.5 °C
     - Nausea
     - Transient rise in liver function disturbances

   (b) Uncommon complications (<5%)

   - Liver abscess
     - Hepaticojejunostomy (Whipple operation)
     - Biliary stents

- Gallbladder necrosis
- Liver insufficiency
- Hepatorenal syndrome
- Biloma and liver necrosis with DC-beads

2.4 Radioembolization of Primary and Secondary Liver Tumors [19–25]

1. *Rationale*

   Yttrium-90 is a pure beta emitter with a half-life of 64.9 h. The radioactivity induces a tumoricidal effect when the radioactivity is >70 G (Gray). Yttrium-90 is incorporated in small resin-based (Sirtex, North Sydney, NSW, Australia) or glass-based (Therasphere, Nordion, Ottawa, Canada) microspheres with a diameter of 30–35 μm. These microspheres are infused through a microcatheter into the hepatic artery.

2. *Indications*

   Primary and secondary liver tumors in patients with liver-only or liver-predominant metastatic disease:

   (a) Hepatocellular carcinoma

   - Competitive technique to chemo-embolization
   - Presence of portal vein thrombosis
   - Presence of TIPS

   (b) Metastases

   - Salvage therapy for colorectal metastases in liver-only disease
   - Salvage therapy for neuroendocrine liver metastases
   - Metastases of ocular melanoma

3. *Palliative therapy to control the tumor burden*

   Downstaging to surgical resection, percutaneous radiofrequency ablation, or liver transplantation (HCC)
   Potentially curative in case of a small number of tumors: "radiation segmentectomy"

4. *Technique*

   The yttrium-90 infusion procedure is preceded by an angiographic work-up consisting in angiographic mapping of all hepatic arteries; in proximal coil occlusion of hepatoenteric arteries like the gastroduodenal artery, right gastric artery, and supraduodenal artery. Finally, a diagnostic concentration of Tc-99 is injected into the microcatheter to assess the liver-lung shunting, matching of the tumoral liver lesions and the presence or absence of extrahepatic Tc-99 uptake. In a next session, the yttrium-90 microparticles are infused through a microcatheter or an anti-reflux catheter (Surefire Medical, Westminster, CO, USA).

5. *Absolute contraindications*

   (a) Liver-lung shunt >20%
   (b) Mismatch between PET-CT and Tc-99 scintigraphy
   (c) Persistent extrahepatic TC-99 uptake
   (d) Reduced liver function (bilirubin >1.5 mg/dL)
   (e) Tumor volume >50% of the total liver volume
   (f) Significant extrahepatic disease

6. *Relative contraindications*

   (a) Liver-lung shunt >10% > 20%
   (b) Reduced liver function >1.0 > 1.5 mg/dL
   (c) Discrete extrahepatic disease

7. *Complications*

   (a) Common complications

   - Abdominal pain, fatigue (20–50%)
   - Gastroduodenal ulceration (5–10%) as a result of nontarget embolization

   (b) Uncommon complications (<5%)

   - Pancreatitis
   - Cholecystitis
   - Liver failure
   - Liver fibrosis and portal hypertension
   - Radiopneumonitis

2.5 Isolated Liver Perfusion ("Chemosaturation") [26, 27]

1. *Rationale*
   Perfusion of high concentration of chemotherapeutic agents through the liver and extraction once passed into the hepatic veins.
2. *Indications*
   Liver metastases responding to melphalan: ocular melanoma and some types of sarcoma.
3. *Technique*

   (a) General anesthesia.
   (b) Percutaneous placement of a catheter into the hepatic artery after coil occlusion of hepatoenteric arteries if required. Through this hepatic catheter: infusion of the chemotherapeutic drug: melphalan.
   (c) Placement of a double-balloon catheter into the inferior vena cava: one balloon is placed above the inflow of the

hepatic veins, and the other balloon is placed below the inflow of the hepatic veins. The occluded hepatic segment is connected through the inner lumen of the catheter with a filter device, extracting the residual amount of melphalan.

4. *Complications*

   (a) Device-related complications (vena cava wall dissection)
   (b) Complications related to general anesthesia
   (c) Complications related to temporary occlusion of the inferior vena cava (hypotension and related cardiac complications)
   (d) Complications related to melphalan:

   - Neutropenia
   - Thrombocytopenia
   - Anemia

   (e) Hepatic failure

2.6 Embolotherapy for Oncologic Hemorrhagic Conditions

1. *Indications*

   (a) Acute tumor-related bleeding

2. *Pathophysiology*

   (a) Intra- and peritumoral bleeding
   (b) Erosion of surrounding (large) vessel by the tumor

3. *Technique*

   (a) Distal embolization of the tumoral mass ("bland embolization") with the use of microparticles and microcoils

(b) Coil occlusion of the eroded artery
(c) Placement of a covered stent to exclude the erosion when coil embolization of the eroded vessel is not an option

- Aorta, iliac, or femoral arteries
- Subclavian, axillary, and carotid arteries
- Renal, superior mesenteric artery main branch

4. *Which tumoral lesions?*

(a) Primary and secondary liver tumors
(b) Pancreas carcinoma
(c) Renal and bladder tumor
(d) Gynecological tumors
(e) Carcinomas in head and neck region (Table 2.1)

Table 2.1 Summary of embolic agents for oncologic purposes

Embolic material	Brand name and manufacturer	Diameter of particles	Clinical indication
Non-resorbable microparticles			
Polyvinyl alcohol	Contour (Boston Scientific Corp.)	50–750 μm	Permanent occlusion adjunct for conventional chemoembolization; acute hemorrhagic conditions
Tris-acryl gelatin	PVA (Cook Medical) Embosphere—EmboGold (Merit Medical)	100–900 μm	Permanent occlusion adjunct for conventional chemoembolization; acute hemorrhagic conditions
Polyvinyl alcohol hydrogel m.	BeadBlock (Terumo)	50–900 μm	

Table 2.1 (continued)

Embolic material	Brand name and manufacturer	Diameter of particles	Clinical indication
Polyzene F-coated microspheres	Embozène (CeloNova)	50–1200 μm	
Resorbable microspheres			
Starch microspheres	EmboCept® S (PharmaCept)	35–50 μm	Mixture with chemotherapeutic drug/adjunct to conventional chemoembolization
Gelfoam	Spongostan (Ferrosan Medical Devices)		Slurry made by physician
Microspheres	Gel-bead (Vascular Solutions)		
Microcoils			
Fibered platinum coils	Target microcoils (Boston Scientific)	2–5.5 mm	Permanent vessel occlusion for acute bleeding
	Micro-tornado		
	Micronester (Cook Medical)	3–10 mm	Permanent vessel occlusion
Hydrogel-coated coils	AZUR microcoils (Terumo)	2–10 mm	Permanent vessel occlusion
Drug-eluting beads	HepaSphere (Merit Medical)	50–300 μm	Chemoembolization
	DC-beads (Biocompatibles)	50–300 μm	Chemoembolization
	Embozene tandem (CeloNova)	40–100 μm	Chemoembolization
	LifePearl (Terumo)	100–400 μm	Chemoembolization
Yttrium-90 microspheres			
Resin-based	SIR-spheres (Sirtex)	30–35 μm	Radioembolization of primary and secondary liver tumors
Glass-based	TheraSpheres (Nordion)	30–35 μm	Radioembolization of primary and secondary liver lesions

2.7 Percutaneous, Ablative Devices and Techniques [28–38]

Most of percutaneous, ablative techniques are based on the development of heat (radio-frequency ablation, laser ablation, microwave ablation, focused ultrasound, irreversible electroporation) or cold (cryoablation) to kill tumor cells. In general, these ablative techniques are performed with a needle-like device which is positioned under image guidance, such as ultrasound, computed tomography, or even magnetic resonance imaging, into the tumor. The only exception is high-intensity focused ultrasound (HIFU) ablation. This is a totally noninvasive technique consisting in the formation of ultrasound rays that are focused into the tumor. Additionally, these techniques are very suitable for small (less than 3–5 cm) and few (less than 5) lesions.

1. *Indications*
2. *Radio-frequency ablation*
   (a) Primary and secondary liver tumors
   (b) Lung tumors
   (c) Kidney tumors
   (d) Bone tumors
3. *Laser ablation*
   (a) Liver tumors
4. *Irreversible electroporation*
   (a) Pancreatic tumors
   (b) Liver tumors
5. *Microwave ablation*
   (a) Liver tumors

6. *High-intensity ultrasound*
   (a) Liver tumors
   (b) Pancreatic tumors
   (c) Uterine tumors
   (d) Bone tumors

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