Radioembolization with Lipiodol for the Treatment of Hepatocellular Carcinoma and Liver Metastases
Malignant Tumours of the Liver
Histological Classification

* Hepatocellular carcinoma (liver cell carcinoma)
* Hepatocellular carcinoma (fibrolamellar variant)
* Cholangiocarcinoma (intrahepatic bile duct carcinoma)
* Mixed hepatocellular cholangiocarcinoma

* Undifferentiated

* Hepatoblastoma (children)
Continuum of disease: hyperplasia → dysplasia → carcinoma

+ Cirrhosis: tumour nodule and regenerative nodule

→ Multifocal: difficult diagnosis, necessity to treat the whole liver

+ Symptoms and prognosis mainly influence by the disease state of the liver (liver cirrhosis)

→ Death mostly by liver failure (distant metastases occur late):

In palliative treatment, underlying liver disease may limit the prognosis, even if good local control is achieved
HEPATOCELLULAR CARCINOMA Therapy

1. **Surgical:**
   - Liver transplantation
   - Tumour resection

2. **Non-surgical:**
   - **Loco-regional**
     - IT Alcohol injection
     - IT Radiofrequency ablation
     - IA chemo-/embolisation
     - External (/ brachy) radiotherapy
     - RNT: $^{131}$I-Lipiodol, $^{90}$Y-glass spheres, $^{188}$Re-Lipiodol
   - **General**
     - Chemotherapy
     - Immunotherapy
     - Hormonal therapy
     - RNT: $^{90}$Y-AFP
Selective Radionuclide Therapy

Catheterisation Procedure

- Transarterial embolization of the hepatic artery (arterial exclusive supply to liver tumours vs. portal predominant supply to normal liver)
  → Highly selective tumour uptake
- At the dept. Interventional Radiology
- Seldinger technique via femoral artery
Mechanisms

- Embolization (alone or associated with chemotherapy): ischemia
- Radioembolization: $\beta$ irradiation (> 90%) + ischemia (< 10%)

Therapeutic efficacy

- Lipiodol: direct irradiation (rapid diffusion into the tumour microenvironment, slow clearance)
- Micro-spheres: irradiation of tumour cells surrounding microvessels containing a high radioactive ligands concentration
Micro-Dosimetry in Explanted Livers

Liver Tolerance & Tumour Sensitivity to Radiation

RILD – Radiation-Induced Liver Disease

Effective Dose: Testicular Ca Lymphoma Myeloma

Curative Doses: Adenocarcinoma

Preoperative Radiation: Rectal Ca

Lipioci®

- Radiopharmaceutical
  - Supplied in ready to use 2 ml solution for injection
  - Stored in a 4 ml cone shaped glass vial
  - Specific activity: 1.1 GBq / ml at calibration

- Quality control:
  - Not usually required prior to therapy (< 5% free radio-iodine within 1 week of manufacturing at ambient temperature)
  - Radiochemical purity may eventually be checked with thin layer chromatography
  - The activity to be administered should be checked using an isotope calibrator
  - Shelf life: 3 days after the date of calibration (i.e. 7 days after the date of manufacturing)
• **Lipiocis®**
  – Palliative treatment of inoperable primary hepatocellular carcinoma.
  – Experimental:
    • liver metastases
    • adjuvant after liver tumour resection and neo-adjuvant before resection or liver transplantation

• **Microspheres**
  – Treatment of unresectable liver cancers, both primary and metastatic
  – Experimental:
    • adjuvant after liver tumour resection and neo-adjuvant before resection or liver transplantation
Specific Contraindications

• Absolute:
  – Pregnancy; breastfeeding
  – Life expectancy less than 1 month

• Relative:
  – High extrahepatic tumour burden
  – Acute or severe chronic pulmonary disease
  – Contra-indications to hepatic artery catheterization
    (i.e. coagulation disturbance, allergy to contrast media, vascular abnormalities …)
Specific Contraindications

- Contra-indications:
  - Clinically evident liver failure (hepatic encephalopathy or ascites)
  - Child-Pugh exceeding B7 (in case of whole liver or lobar treatment)

- Special warnings
  - 131I-Lipiodol **is not** contraindicated in case of partial or total thrombosis of the portal vein
  - Low uptakes in lungs (shunts), thyroid and gastro-intestinal tract (free iodine) are commonly seen and **do not represent problems** (thyroid protection?: low degree of uptake, grave prognosis of the patients, long duration of the treatment, possible side effects of stable iodide overload)
  - Relative contra-indication: medical risk for isolation (associated gamma-emission)
Facility and personnel

• Interdisciplinary team:
  – interventional radiology
  – medical, radiation, surgical oncology
  – transplant surgery
  – nuclear medicine
  – hepatology
  – medical physics
  – radiation safety
  crucial to the success of the treatment

• Facility must have radiation safety equipment, procedures for waste handling and disposal

• Treatment should be undertaken by trained medical staff with supporting physics and nursing staff
Prior to therapy, patients should receive both written and verbal information about the procedure.

Patients should be informed:
- that this therapy is a palliative treatment
- of the potential side effects of therapy
- that response rates are in the order of 25-40% (comparable to chemo-embolisation) but with rare occurrence of serious side effects

Patients must be advised to reduce unnecessary radiation exposure to family members and the public (especially with 131I-Lipiodol).
Administration

- Supplied in solution for use at room temperature
- May be diluted (viscous oil): high resistance to syringe dispensing and catheter injection
- **Caveat: use material which does not dissolve in lipiodol**
- Should be prepared in an appropriately ventilated cabinet (radio-iodine aerosol inhalation)
- Administered under fluoroscopy controlling flow:
  - Using a catheter in the **propria hepatic artery**
  - Exceptions:
    - anatomical variations: separate procedures of the right and left hepatic system
    - super- or hyperselective administration of more distally located hepatic branches
  - **Fixed activity of 2.22 GBq**
  - Exceptions:
    - medical reasons (tumour load)
    - dosimetric calculation
    - local legislation
Follow-up

• At 30 days and at 2- to 3-month in order to assess:
  – treatment-emergent side effects
  – tumour response

• Parameters to assess the result of treatment:
  – determination of tumour load, volume and serum tumour markers (AFP, CEA)

• Images
  • whole body scintigraphy (one week post therapy)
  • Lipiodol is also a contrast agent visible on CT (combined with SPECT images for dosimetry calculations)
Side effects

• Early side effects:
  – Moderate and temporary pyrexia (29%)
  – Hepatic pain on injection (12.5%)
  – Moderate and temporary disturbancies of liver enzymes (20%)
  – Thrombocytopenia and bone marrow suppression

• Delayed side effects:
  – Interstitial pneumonitis (0.5%)
  – Moderate, reversible leukopaenia (7%)
  – Hepatic insufficiency (in case of limited hepatic reserve: post-resection, cirrosis, irradiation)