Palliative Care and Interventions in liver disease, biliary obstruction

Interventional and minimal invasive techniques

C. Kim-Fuchs
Outline

1. Advanced tumours: Interventional and minimal invasive techniques to treat patients
   – Percutaneous CT guided microwave ablation (MWA)
   – Irreversible electroporation (IRE)
   – Hepatogastrostomy (HGS)

2. Liver transplantation: which patients with advanced malignancies or benign diseases are good candidate?
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Advanced Pancreatic Cancer

• 46 year old female patient

• Abdominal pain, weight loss

• CA 19-9: 424 kU/l

• CT scan
Advanced Pancreatic Cancer

• 46 year old female patient

• Pancreatic cancer (adenocarcinoma), ED 05/2015
  – CA19-9: 424 kU/l
  – CT Abdomen 18.05.2015: Pancreas corpus cancer with infiltration of fat tissue, enclose splenic vein, portal vein and hepatic artery

  –> surgical resection not possible
  –> start with a palliative chemo
• 06/15-12/15: 9 cycle of FOLFIRINOX; stable tumour situation (images) with normal tumour markers

• 12/15-02/16 Radio-/Chemotherapy with a total of 50.4 Gy and Gemcitabin; stable tumour situation

• 12/2016 Possible new liver lesion
• 08/2017 Percutaneous CT guided microwave ablation (MWA) of the liver lesion with biopsy (adenocarcinoma)
• 07/18 CT: Local tumour progression and possible recurrent liver metastasis
• Start with a pre interventional chemo (FOLFIRINOX-Schema (4 cycle))

• 12/18 Irreversible electroporation (IRE) for local recurrence and liver metastasis
04/19: stable tumour situation
• 20.06.2019 CT: local tumour progression with intra and extrahepatic cholestasis and progressive duct ectasia. Invasion of the hepatic artery, lineal artery

• 21.06.2019: EGD und EUS: Hepatogastrostomy (HGS)
Interventional and minimal invasive techniques

• Percutaneous CT guided microwave ablation (MWA) of liver lesions

• Irreversible electroporation (IRE) for local recurrence and liver metastasis

• Hepatogastrostomy (HGS)
Percutaneous CT-guided microwave ablation (MWA)

- Ablation is an energy-based destruction of liver tumours

- Ablation is a minimal-invasive & tissue sparing treatment of liver lesions

- Ablation can be used as an alternative to resection or in combination with resection (e.g. multinodular disease or 2-stage procedures)

- Ablation can often still be performed for lesions irresectable due to the degree of the underlying liver disease or significant co-morbidities
Ablation Techniques

Radiofrequency ablation
- Monopolar RFA
- Multibipolar No touch RFA
- Active energy deposition: few mm
- Heat diffusion

Microwave ablation
- Active energy deposition: ~1 cm
- Heat diffusion

Cryoablation
- Ice ball: ~1–3 cm
- Cold diffusion

Irreversible electroporation
- Cell membrane

Thermal Ablation

Non-Thermal Ablation

EASL CPG HCC. J Hepatol 2018; doi: 10.1016/j.jhep.2018.03.019
Advantages of MWA

- Microwave ablation
  - Active energy deposition: ~1 cm
  - Heat diffusion
  - Higher and faster temperature picks reached than with RFA (less sensitive to heat sink effect than monopolar RFA)
  - No reliable endpoint to set the amount of energy deposition

- Cryoablation
  - Ice ball: ~1–3 cm
  - Cold diffusion
  - Easy monitoring with imaging of ice ball progression
  - Cryoshock with first device
  - Limited clinical data available with new devices

- Irreversible electroporation
  - Active energy deposition: few mm
  - Heat diffusion
  - Limited risk of thermal injury to neighbouring critical structures
  - Unsensitive to heat sink effect
  - Advantage of multibipolar mode
  - Only preliminary clinical data
  - General anaesthesia using curare and major analgesic drugs is mandatory

- Monopolar RFA
  - Active energy deposition: few mm
  - Heat diffusion
  - Thermal injury of adjacent structure
  - Heat sink effect (near major vessels)
  - Multibipolar mode is less sensitive to heat sink effect

- Multibipolar RFA
  - Active energy deposition: ~1 cm
  - Heat diffusion
  - Well-evaluated treatment (reference)
  - Multibipolar mode: increases volume and predictability (margin) of ablation zone
  - Heat sink effect (near major vessels)

- Radiofrequency ablation
  - Active energy deposition: few mm
  - Heat diffusion
  - Thermal injury of adjacent structure
  - Heat sink effect (near major vessels)
  - Multibipolar mode is less sensitive to heat sink effect

EASL CPG HCC. J Hepatol 2018; doi: 10.1016/j.jhep.2018.03.019
Microwave Ablation vs. Radiofrequency Ablation

Chris Brace, University of Wisconsin-Madison
Microwave Ablation (MWA)

Percutaneous Ablation

Laparoscopic Ablation

Open Ablation
Indications for Ablation

Hepatocellular Carcinoma (HCC)

Colorectal Liver Metastases (CRLM)

NET Liver Metastases

Liver Metastases

Cholangiocarcinoma?

Other Indications? (Lung, kidney, thyroid, etc.)
NAVIGATION PHASE
PROBE PHASE

ABLATION PHASE
VALIDATION PHASE
Percutaneous CT-guided microwave ablation (MWA)

- Good treatment option for hepatocellular carcinoma, liver metastasis (CR, NET, Pancreas and others), curative
- Good option to reduce symptoms in hormone active NET; palliative
- Can be used safely
- Possible to treat several metastasis simultaneously without losing a lot of healthy liver tissue

Filippiadis DK et al. J Gastrointest Cancer 2017
Poggi G et al. World J Hepatol. 2015
Irreversible electroporation (IRE)

- IRE leads to cell death mainly through a non-thermal technique.

- High voltage (max of 3000 V) electrical pulses of 70–90 μs duration.

- Electrical field leads to a disruption of the cell membrane.
  -> Collapse of intracellular homeostasis and an activation of apoptotic pathways, finally resulting in cell death.
• Advantages:
  – Preservation of structural components like collagen and elastin as thermal damage does only occur in the very close proximity to the ablation needles
  
  – Nonexisting “heat sink effect,” which means that the efficiency of IRE will not be reduced in proximity to large vessels
• IRE cannot be applied:
  – Presence of metallic material in close proximity to the placed IRE needles
  – Tumour size >5 cm
  – Patients with cardiac arrhythmias and pacemakers should be evaluated by a cardiologist prior to IRE
  – Patients with history of epilepsy or recent myocardial infarction
  – No data exist about the use of IRE in pregnancy
Indications for IRE

• Margin accentuation pancreas cancer (effect on local recurrence, ongoing study)

• Liver metastasis, unsuitable for thermal ablation
HGS

• 2001: First endoscopic ultrasound (EUS) drainage
  – Additional option to percutaneous drainage and endoscopic retrograde choalangiopancreatography (ERCP)

• Treatment option in patients with malignant biliary obstruction when ERCP fails.

Kim TH, World J Gastroenterol. 2012 May
• Indications:
  – Patients with malignant biliary obstruction when ERCP fails
  – Hepatolithiasis

• Complications:
  – Stentdislocation
  – Stentocclusion
  – Cholangitis
Not always possible
Outline

1. Advanced tumours: Interventional and minimal invasive techniques to treat patients
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2. Liver transplantation: which patients with advanced malignancies or benign diseases are good candidate?
Liver-Transplantation (OLT)

• Which patients benefit from a transplantation?
• Are there limitations?
Waiting List and Transplantations in 2018

Warteliste und Transplantationen | 2018

<table>
<thead>
<tr>
<th>Warteliste</th>
<th>Transplantationen</th>
</tr>
</thead>
<tbody>
<tr>
<td>148 + 12</td>
<td>50</td>
</tr>
<tr>
<td>Herz</td>
<td>Herz</td>
</tr>
<tr>
<td>87 + 4</td>
<td>42</td>
</tr>
<tr>
<td>Lunge</td>
<td>Lunge</td>
</tr>
<tr>
<td>407 + 29</td>
<td>156</td>
</tr>
<tr>
<td>Leber</td>
<td>Leber</td>
</tr>
<tr>
<td>1518 + 25</td>
<td>352</td>
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<tr>
<td>Niere</td>
<td>Niere</td>
</tr>
<tr>
<td>93 + 6</td>
<td>17</td>
</tr>
<tr>
<td>Pankreas</td>
<td>Pankreas</td>
</tr>
<tr>
<td>1 + 0</td>
<td>0</td>
</tr>
<tr>
<td>Dünndarm</td>
<td>Dünndarm</td>
</tr>
</tbody>
</table>

1 Anzahl Patienten
2 Die Zahlen setzen sich zusammen aus der Anzahl Patienten auf der Warteliste per 31.12.2017 plus der Anzahl Patienten, die 2018 neu gelistet wurden.
3 Anzahl verstorben Patienten auf der Warteliste
Lebertransplantationen und Warteliste | 2018

1 Zahlen setzen sich zusammen aus der Anzahl Patienten auf der Warteliste (Stand 31. Dezember 2017) plus der Anzahl Patienten, welche 2018 neu gelistet wurden.
2 davon im Urgent-Status

www.swisstransplant.org
### Indications for Liver Transplantation

<table>
<thead>
<tr>
<th>Acute Liver Failure</th>
<th>Metabolic Disorders Originating from the Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute viral hepatitis</td>
<td>Hyperoxaluria</td>
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<tr>
<td>Drug or toxin induced hepatotoxicity</td>
<td>Familial Amyloidosis</td>
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<tr>
<td>Acetaminophen overdose</td>
<td>Urea cycle defects</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>Branched-chain amino acid disorders</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>Familial homozygous hypercholesterolemia</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Cirrhosis from Chronic Liver Disease</th>
<th>Malignancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic viral hepatitis</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Alcoholic liver disease</td>
<td>Cholangiocarcinoma (limited)</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>Hepatoblastoma</td>
</tr>
<tr>
<td>Cholestatic liver disease</td>
<td>Fibrolamellar hepatocellular carcinoma</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>Metastatic neuroendocrine tumors</td>
</tr>
<tr>
<td>Hereditary and neonatal hemochromatosis</td>
<td>Hemangioendothelioma</td>
</tr>
<tr>
<td>Alpha-1-antitrypsin deficiency</td>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>Non-alcoholic steatohepatitis</td>
<td>Polycystic liver disease</td>
</tr>
<tr>
<td>Cryptogenic liver disease</td>
<td>Hereditary hemorrhagic telangiectasia</td>
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<tr>
<td>Budd-Chiari syndrome</td>
<td>Erythropoietic protoporphyria</td>
</tr>
<tr>
<td>Tyrosinemia</td>
<td></td>
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<tr>
<td>Glycogen storage diseases</td>
<td></td>
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</tbody>
</table>
HCC

• One of the most frequent cancers

• Associated with multiple risk factors

• 80% in cirrhotic liver

• 1/3 of all patients with liver cirrhosis develop HCC
59 year old male patient, HCV, liver cirrhosis
BCLC treatment guidelines

Hepatocellular carcinoma

Very early stage (0)
Single ≤2 cm
Preserved liver function,
ECOG PS 0

Potential candidate for liver transplantation

Early stage (A)
Single or up to 3 nodules ≤3 cm
Preserved liver function,
ECOG PS 0

Solitary

Up to 3 nodules (≤3 cm)

Intermediate stage (B)
Multinodular
Preserved liver function,
ECOG PS 0

Associated diseases

Advanced stage (C)
Portal invasion
Extrahepatic spread
Preserved liver function,
ECOG PS 1-2

Systemic therapy

Terminal stage (D)
End-stage liver function*,
ECOG PS 3-4

Best supportive care

Prognosis

No

Yes

Portal pressure Bilirubin

Normal

Increased

Survival

>5 years

>2-5 years

>1 year

3 months

Effective treatments with impact on survival

Ablation

Resection

Transplantation

Ablation

Chemoembolisation

Forner et al. Lancet 2018
Criteria for liver transplantation in HCC: Milano-Criteria

- Tumour < 5 cm
- Max 3 Tumours < 3 cm
- No extrahepatic manifestation

85% survival (4y) If the criteria correspond to the pathological findings
50% survival (4y) If the criteria doesn’t correspond to the pathological findings

Mazzaferro 1999 NEJM
• Bridging to transplantation
  – MWA
  – Resection
  – TAE

• Down staging
59 year old male patient, HCC, liver cirrhosis
• Lap. resection of Seg II/III
• MWA 2 HCC, follow up no other suspicions lesion

• OLT 12.06.2019

• Histology: 5 HCC (3-6mm), G2 pT2 (m) pNx L0 V0 Pn0 G2 R0
Conclusion for patient with liver cirrhosis / HCC

• Treatment / controls by a hepatologist with connections to a transplant centre

• Early discussion about possible transplantation, different treatment options
Liver metastasis from Neuroendocrine Tumours

Is a liver transplantation a good solution?
Indication for liver transplantation in NET

Mazzaferro et al. NET metastatic to the liver: how to select patients for LT, J. Hepatol, 2007

Inclusion criteria
• Low grade NET
• Primary tumor removed with a curative resection
• Metastatic diffusion to < 50% of the liver
• Good response or stable disease for at least 6 months
• Age < 55 Y
• Histological proliferation index < 10%

Exclusion criteria
• High-grade neuroendocrine carcinoma
• Carcinoma not drained by the portal system
07/2009; 50 year old female patient

- Diarrhea
- Vomitus
- Weightloss 8kg in 6 month
• Biopsy of the liver: Neuroendocrine tumour, G2, expression of cytokeratin, synaptosin and chromogranin A

• 31.07.09: Start with Sandostatin

• 06.08.09: Resection of pancreas corpus and tail with spleen, atypical liver resection segment III and V, reconstruction of the portal vein

• Histology: **Neuroendocrine tumour, pT3 pN1 (2/16) V2 L1 M1 (liver) G2 (ED 07/09)**, with gastrin production, SSR positive
• 16.11.2010: Embolisation of several liver metastasis

• Waiting list liver transplantation 09.11.2011

• 170 days later, successful transplantation
Not everything went well…
• Occlusion of the hepatic artery 36h after transplantation
• Re-canalisation

• Over time liver abscess (damage bile ducts), drainages, hemi hepatectomy

• 2nd transplantation 06/2011
• Primary non function
Stopp or go??????

• Death or again SU-List for a 3rd liver?
• 15.06.2011 3rd transplantation

• 17.06.11 Extubation

• 02.07.11 Patient went home
General Results

• Recurrence after liver transplantation 31.3% to 56.8%
• 1-, 3-, and 5-year overall survival: 89%, 69%, and 63%

• Prognostic factors associated with worse long-term survival including transplantation
  – >50% liver tumour involvement
  – high Ki67
  – pancreatic neuroendocrine tumours
• 02/2013 Local tumour recurrence pancreas:
  – Tumorectomie retroperitoneal left, adrenalectomie

• 12/2013 Resection und IRE tumour recurrence local

• 04/2014
• 06-10/2014: Palliative treatment with Sunitinib; tumour progress

• 10/2014 – 04/2015: 6 cycle Temodal; partial tumour remission

• 05/2015 Sandostatin

• 06 - 08/2017: Temodal (3 cycle)
• 2018 PRRT
• 01/2019 MRI: Tumour progression
• 2018 PRRT

• 04/2019 MRI: Massive Tumour progression:
  – Liver biopsy: G3 tumour, Ki67>20%
  – Patient declined Everolimus
  – First contact with our palliative care team, 10 years after diagnosis of a metastasised neuroendocrine tumour of the pancreas
Conclusion OLT in NET

• Liver transplantation may provide a survival benefit among patients with diffuse neuroendocrine tumours metastases to the liver.

• High recurrence rates
  -> Strict selection of patients is critical.
Conclusion

• Also in palliative situation good treatment options next to chemotherapy

• Discussion

• Patient with liver disease: Present early in a transplant centre
Thank you for your attention