Interventional Radiology: Radiation lobectomy / segmentectomy.

International Course on Theranostics and Molecular Radiotherapy

IAEA-BELNUC-BORDET

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Introduction to SIRT

Sangro, J Nucl Med Radiat Ther 2011

Lobar level

Segmental level

Subsegmental level

http://www.therasphere.com/home_us/index.asp
Imaging Techniques for SIRT

Angio CT

Perfusion CT arterial map

MAA-SPECT-CT

Angiography

Cone Beam CT

Atassi al. Radiographics 2008

Planar scintigraphy
(Lung-shunt detection)
Resin microspheres:
Activity = (BSA - 0.2) + Tumor Involvement / (Tumor Volume + Normal Liver Volume)

Glass microspheres:
Dose (Gy) = Activity (GBq) X 50/Mass of treated liver (kg)
Hepatocellular Carcinoma

- Most frequent liver cancer
- Sixth most common malignancy worldwide
- Counts as the third cause of tumor-related death
- Increasing incidence in Western Europe (6.2 per 100,000 in 2002)
- Occurs in a context of cirrhosis in 90% of cases

Bosetti et al. Hepatology 2008
Parkin et al. CA 2005
El-Serag et al. NEJM 2011
K Thornton. Hepatitis C Online 2015
EASL-EORTC Clinical Practice Guidelines

(very) early stage  
Curative Treatment  
Transplantation Resection  
RFA

Intermediate stage  
TACE

Advanced stage  
Sorafenib

Terminal stage  
Best Supportive Care

Adapted from EASL-EORTC clinical practice guidelines. J Hepatol 2012

Dodd et al. RadioGraphics 2000
De Baere et al. Tech Vasc Interv Radiol. 2007
Y90 in the BCLC Algorithm
EASL-EORTC Clinical Practice Guidelines

(very) Early stage
Curative Treatment
Transplantation
Resection

Intermediate stage
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sorafenib

Terminal stage
Best Supportive Care

Adapted from EASL-EORTC clinical practice guidelines.
J Hepatol 2012
Metastatic Disease: Is the Patient a Candidate for LRT?

• Performance status / Life expectancy

• Tumor extent (site and tumor load of the extrahepatic disease)

• Tumor Biology (definition of oligo-metastatic disease)

• Functional liver reserve

• Aim of the LRT: palliative? Bridging-to-surgery?
Locoregional Therapies on Oligometastatic Disease

Hypothesis: Depth of response relates to OS

- **Consolidation** (oligoresistance)
- **Salvage** (oligoprogression)

- Lethal tumour load
- Tumour load at baseline

- ETS
- TTG
- DpR
- Tumour nadir
- PFS
- Time since start of treatment
- OS

+ molecular markers e.g. CEA, CA19-9

Resection?
Radiation Segmentectomy
Context: Limitations of RFA

- RFA is a current standard of care for unresectable HCC <2-3 cm.

- Above 3 cm, the efficacy of RFA is diminished.\(^1-3\) (tumor control and disease-free survival)

- Challenging tumor locations.\(^4\)

1. Kim et al. J Hepatol 2013
2. Livraghi et al. Radiology 2000
3. Lencioni. Hepatology 2010
The Concept of Radiation Segmentectomy

MRI arterial phase

MRI portal phase

Perfusion CT arterial map
The Concept of Radiation Segmentectomy

MRI arterial phase

Perfusion CT arterial map

Angiography
The Concept of Radiation Segmentectomy

MRI arterial phase  MRI portal phase  Perfusion CT arterial map

Yttrium-PET-CT
The purpose of this study was to assess:

- The safety
- The efficacy (response, radiology-pathology correlation, overall survival)

of radiation segmentectomy in solitary HCC≤5 cm not amenable to RFA.
Inclusion criteria:
1) Unresectable solitary \leq 5\text{cm} \text{HCC}
2) Absence of portal vein thrombosis/metastases
3) Treatment-naïve (except prior hepatectomy with R0 margins).

- No formal bilirubin cutoff.

- The analysis was performed on 102 patients.
**Baseline Characteristics**

<table>
<thead>
<tr>
<th>Lesion Location (Segment)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>2 + 3</td>
<td>1</td>
</tr>
<tr>
<td>4 + 8</td>
<td>1</td>
</tr>
<tr>
<td>5 + 8</td>
<td>2</td>
</tr>
</tbody>
</table>

- Median (IQR) administered dose (Gy): 242 Gy (173 – 369)
- Median follow-up: 27.1 months
Clinical Adverse Events and Laboratory Toxicities

- No major complication was observed.
- None required readmission.
- There was no change in the rate of laboratory toxicity compared to baseline.
Tumor Control: Alphafetoprotein (AFP)

% reduction in median AFP in patients with AFP >200 ng/mL at baseline (n=18).

% reduction AFP

baseline 1 mo 3 mo

-100

p<0.01

p<0.001
## Tumor Control: Imaging Outcome

- **Rate of disease progression:** 27/102 (26%)
- **Median (IQR) time-to-disease-progression:** 33.1 months (IQR: 10-35)

### Best Radiological Response (mRECIST)

<table>
<thead>
<tr>
<th>Response</th>
<th>Count/Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>47/99 (47%)</td>
</tr>
<tr>
<td>PR</td>
<td>39/99 (39%)</td>
</tr>
<tr>
<td>SD</td>
<td>12/99 (12%)</td>
</tr>
<tr>
<td>PD</td>
<td>1/99 (1%)</td>
</tr>
</tbody>
</table>

### Type of Progression

<table>
<thead>
<tr>
<th>Type of Progression</th>
<th>Count/Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New intrahepatic lesions Only</td>
<td>15/27 (56%)</td>
</tr>
<tr>
<td>+ Local progression</td>
<td>1/27 (3%)</td>
</tr>
<tr>
<td>+ Vascular invasion</td>
<td>1/27 (3%)</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>5/27 (19%)</td>
</tr>
<tr>
<td>Local progression</td>
<td>4/27 (15%)</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td>1/27 (3%)</td>
</tr>
<tr>
<td>Isolated extrahepatic metastases</td>
<td>0/27 (0%)</td>
</tr>
</tbody>
</table>
Pathological Outcome by Radiation Dose

- 33/102 (32%) patients were transplanted.
- Median (IQR) time-to-transplantation: 6.3 months (3.6-9.7).

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>PN</th>
<th>CPN</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;190 Gy</td>
<td>9</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>&gt;190 Gy</td>
<td>7</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>17</td>
<td>33</td>
</tr>
</tbody>
</table>

*P = 0.03 (Fisher’s exact test).*
## Radiological-Pathological Analysis by Lesion Size and Radiation Dose

<table>
<thead>
<tr>
<th>Lesion Size</th>
<th>Rate of mRECIST CR</th>
<th>Rate of CPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 – 1.9 cm</td>
<td>2/3 (66%)</td>
<td>3/4 (75%)</td>
</tr>
<tr>
<td>2.0 – 2.9 cm</td>
<td>8/16 (50%)</td>
<td>8/16 (50%)</td>
</tr>
<tr>
<td>3.0 – 4.9 cm</td>
<td>3/13 (23%)</td>
<td>6/13 (46%)</td>
</tr>
</tbody>
</table>
Conclusions

- Radiation segmentectomy is a safe and effective technique with favorable risk profile and radiology-pathology outcomes for solitary HCC ≤5 cm.

- These data support its use as a second choice if RFA or resection is not feasible.
Radiation Lobectomy
Context

- **Tumor Control:** A progressive disease is a contra-indication to hepatic resection

- **HCC:** Transplant shortage

- **mCRC:** Curative liver surgery may imply extensive liver resection.

- **Future Liver Remnant (FLR):** A sufficient FLR is requested to avoid post-resection hepatic insufficiency.

- **Standard technique:** Portal Vein Embolization (PVE).

Selection for hepatic resection of colorectal liver metastases:
- expert consensus statement. HPB 2013
- Madoff et al. J Vasc Interv Radiol 2005

De Baere et al. Tech Vasc Interv Radiol 2007
Introduction

- Rising controversies on PVE:
  - Enhanced tumor growth on the embolized side.
  - Appearance of new metastases in the FLR.
  - Is a rapid FLR growth requested?


Radiation lobectomy: Time-dependent analysis of future liver remnant volume in unresectable liver cancer as a bridge to resection
Clinical Case
Volumetric Changes and Tumor Control

FLR (%)

% FLR hypertrophy

R²=0.92

Right lobe tumor burden

R²=0.95

p<0.001

p=0.22

p=0.02
Tumor Control (HCC) and Impact on the Liver Function

Median AFP

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 Month</th>
<th>1-3 months</th>
<th>3-6 months</th>
<th>6-9 months</th>
<th>&gt; 9 months</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh Score (all tumors)</td>
<td>n=77</td>
<td>n=69</td>
<td>n=26</td>
<td>n=32</td>
<td>n=16</td>
<td>n=13</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>6 (5-10)</td>
<td>6 (5-12)</td>
<td>7 (5-11)</td>
<td>7 (5-13)</td>
<td>6.5 (5-10)</td>
<td>6 (5-10)</td>
<td></td>
</tr>
</tbody>
</table>

p=0.03  p=0.05
Conclusions

- Radiation lobectomy by Y90 is a safe and effective technique to hypertrophy the FLR.

- Volumetric changes are time-dependent and synchronous with an homolateral tumor control.

- This technique is of particular interest in the bridge-to-resection setting.
Radiation lobectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>RE Mean (median)</th>
<th>SD</th>
<th>PVE Median (median)</th>
<th>SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLR baseline (mL)</td>
<td>368.7 (339)</td>
<td>142.2</td>
<td>381.7 (323)</td>
<td>166.0</td>
<td>0.763</td>
</tr>
<tr>
<td>FLR post treatment (mL)</td>
<td>470.6 (435)</td>
<td>203.6</td>
<td>589.5 (535)</td>
<td>221.9</td>
<td></td>
</tr>
<tr>
<td>Change from baseline (mL)</td>
<td>101.9 (80)</td>
<td>106.5</td>
<td>207.9 (176)</td>
<td>114.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change from baseline (%)</td>
<td>29 (25.3)</td>
<td>22.9</td>
<td>61.5 (50.6)</td>
<td>37.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P value (change from baseline within treatment, both mL and %)</td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Liver Function Assessment: A Key Point

FDG-PET-CT

99Tc Mebrofenin SPECT-CT

Liver Clearance = 7.7%/min/m²
Inferior Limit: 2.7 (Cieslak et al.)
Work in Progress

- How is the hypertrophy related to the administered dose?

- What is the underlying pathophysiological mechanism of FLR hypertrophy? (portal flow redirection? Radiation-induced Fibrosis?)

- How is the liver function impacted in the irradiated lobe?
General Conclusions: Clinical Implications HCC

(very) Early Stage → Intermediate Stage → Advanced stage → Terminal stage

Curative Intent → TACE → Sorafenib → Best Supportive Care

Transplantation → Resection

RFA → TACE → Sorafenib

Radiation Lobectomy
Radiation Segmentectomy

Adapted from EASL-EORTC clinical practice guidelines. J Hepatol 2012
General Conclusions: Clinical Implications: Oligometastatic Disease

Hypothesis: **Depth of response relates to OS**

- **Consolidation (Oligoresistance)**
- **Salvage (oligoprogression)**

- **Lethal tumour load**
- **Tumour load at baseline**

- **Time since start of treatment**

- **Radiation Segmentectomy**

**Additional markers**:
- + molecular markers e.g. CEA, CA19-9
General Conclusions: Clinical Implications: Oligometastatic Disease

Hypothesis: Depth of response relates to OS

Lethal tumour load

Tumour load at baseline

TTG

ETS

DpR

Tumour nadir

PFS

Time since start of treatment

OS

+ molecular markers e.g. CEA, CA19-9

Radiation Lobectomy

Resection?

Optimal tool for borderline resectable liver cancers?
Clinical Case: Combination

Baseline

Post-TACE
Clinical Case: Combination

Post-Radiation segmentectomy segment V

Post-Radiation lobectomy
Clinical Case: Combination

Before Radiation lobectomy

FLR = 23.7 %

3 months scan

FLR = 37.8%