Role of SBRT in the management of lung and liver metastases

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Oligometastatic RCC

• **mRCC**: Lung, Bone, Liver, Brain (Schlesinger-Raab, EJC2008)

• **Targeted therapies**
  – **Objective** response: 20-40% patients
  – **Complete** Response: 1 - 3% patients (Motzer, JCO 2009)
  – **Median OS**: 9-40 months (Heng DY, Lancet Oncol 2013)

• **Oligometastatic disease**
  – 25% metachronous mRCC / 10% synchronous mRCC (Alt, Cancer2011; Oddsson, Scand Journ Surg 2012)
  – Clinical benefit to local control of metastatic sites
Liver metastases

- **Colo-Rectal cancer**

Liver resection

- 5-yr OS: >35% vs 11% (all mCRC)
- Morbidity rates: 20-45%
- Mortality rates: 1-3%

- **Better results** nb M+, no extra hepatic M+, R0, response to systemic ttt
- **Limitations** Operability; Resectability: minimum size of future liver with adequate vascular function

- **For non CRC primitives** (Hatzaras, HBP 2012)

Lo, Nat Rev Clin Oncol 2011; Dabestani, Lancet Oncol 2014
SBRT

- **Dose escalation**: High dose per fraction
- **Different radiobiology**: no differential effect
  - Millimeter precision
  - Moving target tracking fiducials
  - Sharp dose gradient
    - Isodose prescription and
    - Multiple non-opposing and non-coplanar beams
• **Patients**
  - **Child-Pugh** < C, 1 – 3 lesions, **Size** < 6 cm, > 700cc liver spared

• **Dose**
  - **48Gy / 3 fractions on 70-80%**, at least > **36 Gy / 3** (Mc Cammon, IJROBP 2009)

• **Results**
  - **2-yr LC**: 60%-90%; **2-yr OS**: 30-83%; **Median OS**: 10-34 months

**Hoyer, IJROBP 2012**
**Lo, NRCO 2011**
Liver SBRT

• Toxicity
  – Radiation Induced Liver Disease: Veino-occlusive disease
    • Anicteric ascites and hepatomegaly
    • higher elevated liver enzymes, thrombocytopenia
    • 2 patients with grade 3 +/- 1 grade 5 on early studies
    • Child-Pugh ++, functional liver volume

  – Gastro-duodenal ulceration:
    • 4 patients with Grade 3 hemorrhagic ulcerations
    • Dosimetric constraints

Hoyer, IJROBP 2012
Lo, NRCO 2011
## Liver SBRT for mRCC

<table>
<thead>
<tr>
<th>Author/d</th>
<th>Liver target / total</th>
<th>Average marginal dose (Gy)</th>
<th>Median follow-up (months)</th>
<th>Crude/1y LC (%)</th>
<th>Median OS (months)</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Svedman, 2006</td>
<td>3 / 77</td>
<td>40Gy / 4</td>
<td>52</td>
<td>100/100</td>
<td>32</td>
<td>No RILD</td>
</tr>
<tr>
<td>Wersall, 2005</td>
<td>2 / 154</td>
<td>45Gy / 3</td>
<td>37</td>
<td>98/99</td>
<td>NR</td>
<td>23/58 GI-II 1 GV</td>
</tr>
<tr>
<td>Ranck, 2013</td>
<td>2 / 39</td>
<td>50y / 10</td>
<td>16</td>
<td>50%</td>
<td>NR</td>
<td>No RILD</td>
</tr>
</tbody>
</table>

G.Kothari, Acta Oncol 2015
Liver SBRT for mRCC

- Unsuitable for Surgery
- Unsuitable for ablative therapy
  - Size > 3-5 cm
  - Vascular / major biliary structure closeness
- Suitable for SBRT
  - Child-Pugh < C, > 700cc liver spared
Lung SBRT

• Medically inoperable stage I NSCLC (Chi,RO 2010)
  – 5-yr local control: 85% +/- 15%
  – 5-yr CSS: 60% +/- 17%
  – 5-yr OS: 47% +/- 20%
  – Toxicity < 10% G3
# Lung SBRT

<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>$n$</th>
<th>Number of lesions</th>
<th>Dose</th>
<th>Median follow up (months)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ernst-Stecken et al. (2006)</td>
<td>Prospective</td>
<td>18</td>
<td>36</td>
<td>7–8 Gy×5 fractions (90% coverage of 90% of PTV required)</td>
<td>NA</td>
<td>CR: 51%; PR: 33%; SD: 3% (including 3 patients with primary lung tumors); grade 4 or higher toxic effects: 0</td>
</tr>
<tr>
<td>Le et al. (2006)</td>
<td>Prospective</td>
<td>11*</td>
<td>11</td>
<td>15–30 Gy×1 fraction</td>
<td>NA</td>
<td>1-year FFP: &lt;20 Gy 54%, &gt;20 Gy 91% ($P=0.03$)<em>; grade 2/3 pneumonitis: 4 patients</em>; treatment-related deaths: 3 patients*</td>
</tr>
<tr>
<td>Rusthoven et al. (2009)</td>
<td>Prospective</td>
<td>38</td>
<td>63</td>
<td>16–20 Gy×3 fractions prescribed to isodose line covering PTV</td>
<td>15.4 for assessable lesions</td>
<td>LC: 100% and 96% at 1 and 2 years; OS: 39% at 2 years; grade 4 or higher toxic effects: 0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Author/date</th>
<th>Patient (target)</th>
<th>Location</th>
<th>Average marginal dose (Gy)</th>
<th>Median follow-up</th>
<th>Crude/1y LC/Gen LC (%)</th>
<th>Median OS</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Svedman, 2006</td>
<td>26 (77)</td>
<td>63 lung</td>
<td>40Gy / 4</td>
<td>52</td>
<td>98/100/79%</td>
<td>32</td>
<td>52% GI-II 0 G&gt;2</td>
</tr>
<tr>
<td>Wersall, 2005</td>
<td>50 (154)</td>
<td>117 lung</td>
<td>32Gy-40Gy / 4 45Gy/3</td>
<td>37</td>
<td>98/99</td>
<td>NR</td>
<td>40% GI-II</td>
</tr>
</tbody>
</table>
Prospects

• Association with targeted therapies?
  – Pre-clinical: RT / SBRT (Zeng, Lancet Oncol 2014; El Kaffas, Angiogenesis 2013)
  – Clinical: oligometastatic disease (J. Kao, Target Oncol 2014)
Conclusion

• Major advance in mRCC: **Targeted therapies**

• Oligometastatic state
  • Lung and Liver metastases
    – SBRT is a reliable and safe alternative for patients unsuitable for surgery
  • Spine and Brain metastases
    – SBRT: central treatment modality


