Liver Radiation Therapy

(high dose-rate stereotactic ablative radiation therapy to the liver)

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Radiation Therapist, Wellington Blood & Cancer Centre
Background

Liver malignancies

- Incidence
  - 6th most common cancer diagnosis
  - 5.7% of all diagnoses

- Primary tumours
  - Hepatocellular carcinoma

- Liver metastases
  - Colorectal (~10-20% of patients)
  - Breast (~5% of patients)
  - Head & neck, lung, etc

Radiation therapy to the liver

- Limitation
  - Toxicity (*irradiated volume*)
  - Mean dose – 30Gy (TD5/5)
  - Emami et al. (1991)
Radiation therapy to the liver

- **Limitation**
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- **Radiation-induced liver disease (RILD)**
  - Fatigue
  - Weight gain
  - Increased abdominal girth
  - Hepatomegaly
  - Anicteric ascites
  - Elevated alkaline phosphatase

Radiation therapy to the liver

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- Reduce dose to normal liver tissue whilst maintaining therapeutic dose to tumour
Radiation therapy to the liver

- Limitation
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- Reduce dose to normal liver tissue whilst maintaining therapeutic dose to tumour
  - Increased precision in tumour volume definition (MRI/PET)
    - Increased conformity of dose to the tumour region (treatment planning)
    - Increased accuracy in tracking of tumour on-treatment (treatment delivery)
### Stereotactic Body Radiation Therapy (SBRT)

<table>
<thead>
<tr>
<th>Conventional RT</th>
<th>SBRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 1.8-2Gy per fraction</td>
<td>• 6-20Gy per fraction</td>
</tr>
<tr>
<td>• 25-30 fractions</td>
<td>• 1-8 fractions</td>
</tr>
<tr>
<td>• Total dose 45-60Gy</td>
<td>• EQD2 80-120Gy</td>
</tr>
<tr>
<td>• Maximum dose &lt;107% of prescribed dose</td>
<td>• Maximum dose &lt;140% of prescribed dose</td>
</tr>
<tr>
<td>• Allow function to return to targeted tissue</td>
<td>• Ablative treatment</td>
</tr>
<tr>
<td>• ‘Shape’ dose to spare adjacent organs at risk as achievable</td>
<td>• High maximum allows steepest possible dose fall-off, sparing adjacent tissue</td>
</tr>
</tbody>
</table>
University Hospital Zurich

- First Varian Truebeam treatment worldwide
  - March 16th, 2010
  - First FFF treatment

- Commence SBRT program
  - Thoracic (lung)
  - Abdominal (liver, renal)
SBRT from the RT’s perspective

- **Inter**fractional accuracy
  - Patient position reproducibility
  - Imaging (IGRT)

- **Intra**fractional accuracy
  - Patient position stability
  - Imaging (IGRT)
  - Respiratory motion
SBRT: Planning-CT

- CIVCO Body Pro-Lok
  - Wingboard
  - Vacuum Cast
  - Knee fix
- For lesions near diaphragm:
  - With/without abdominal compression
- 4DCT
  - Breathing curve amplitude
SBRT: Planning-CT (respiratory motion)
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ITV

SBRT: Planning-CT (respiratory motion)

ITV

• ↑Tumor motion = ↑ irradiated volume

• High biological dose of SBRT

**SBRT: Planning-CT (respiratory motion)**

**ITV**

- ↑Tumor motion = ↑ irradiated volume
- High biological dose of SBRT
- **Reduce respiratory motion**
- **Reduce normal tissue component of ITV**
- **Stabilise GTV**

SBRT: Planning-CT (respiratory motion)

Respiratory motion of the liver with/without abdominal compression:

- 10 abdominal SBRT patients
- 3 excluded (N=7)
- 4DCT scans with/without AC
- Liver contoured at inhale/exhale
SBRT: Planning-CT (respiratory motion)

Respiratory motion of the liver with/without abdominal compression:

- 10 abdominal SBRT patients
  - 3 excluded (N=7)
- 4DCT scans with/without AC
- Liver contoured at inhale/exhale

- MATLAB analysis
  - Comparative motion of whole liver
  - Comparative motion of liver segments
Results: Baseline respiratory motion (without AC)

Whole liver displacement (all patients)

Results: Baseline respiratory motion (without AC)

Segmental motion (mean)

Mean motion range (mm) w/o AC

Results: Reduction with AC

Segmental motion (mean)

Results: Reduction with AC

Segmental motion (mean)

<table>
<thead>
<tr>
<th>Segment</th>
<th>Ant</th>
<th>Post</th>
<th>Right</th>
<th>Left</th>
<th>Cran</th>
<th>Caud</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean reduction</td>
<td>2.25</td>
<td>1.36</td>
<td>1.03</td>
<td>-0.08</td>
<td>2.77</td>
<td>1.72</td>
</tr>
<tr>
<td>STD</td>
<td>1.14</td>
<td>2.66</td>
<td>1.68</td>
<td>0.63</td>
<td>2.00</td>
<td>1.21</td>
</tr>
</tbody>
</table>

*p<0.05

Key findings

- Liver segments demonstrate variable respiratory motion (with and without AC)
  - Left segments appear inherently stable
- Cranial, caudal and anterior segments become more stable with AC
- Other segments benefit more variably, or not at all
- Requires validation with treatment data
Inter-patient variation
Alternative immobilisation methods

Body fix
www.elekta.com
SBRT: Planning

- Eclipse (v11)

- Standard: 4x12Gy or 3x18Gy (adapted to individual patients)

- VMAT (~2 Arcs)
  - Complete arcs or-
  - Partial arcs (i.e. 30°-180E°) for peripheral lesions
    - Consideration of gantry clearance

- Optimisation/normalisation (adapted from RTOG 0915)
  - 40% inhomogeneity within PTV is allowed (ablative therapy)
    - Dmax ~120-130%
    - Steep dose gradient beyond PTV
  - 95% of PTV receives 100% prescribed dose
SBRT: Planning

- Truebeam STx
- HDMLC (2.5mm)
- Flattening filter free (FFF) mode
  - 10MV FFF: 2400MU/min
- CBCT imaging
- Sub-mm corrections
- Real-time Position Management (RPM)
  - Optical tracking/gating system
Dose rate

Effect of high dose per pulse flattening filter-free beams on cancer cell survival

Ines Lohse, Stephanie Lang, Jan Hrbacek, Stephan Scheidegger, Stephan Bodis, Nadia S. Macedo, Jianhua Feng, Urs M. Lütholf, Kathrin Zaugg

*Department of Radiation Oncology, University Hospital Zürich, Switzerland; †Institute of Radiation Oncology, Kantonsspital Aarau, Switzerland; ‡Centre of Applied Mathematics and Physics, Zurich University of Applied Science, Switzerland

Fig. 4. Surviving fraction of T98G-glioblastoma cells at different dose rates. For 24 Gy/min, the 1-LQ-model can fit the experimental data with \( \alpha = 0.03 \text{ Gy}^{-1} \), \( \beta = 0.04 \text{ Gy}^{-2} \) and \( \gamma = 0.556 \text{ min}^{-1} \); for 4 Gy/min, \( \gamma \) has to be adapted to 0.361 min\(^{-1}\); and for \( R = 0.2 \text{ Gy/min} \), a good fit can only be achieved by adapting the kinetic constant to \( \gamma = 0.0313 \text{ min}^{-1} \).
SBRT: Planning
SBRT: Planning

Dmax = 128%
SBRT: Planning

D_{max} = 128\%
SBRT: Treatment delivery

1. Patient positioning
2. Breathing curve verification
3. PreRT-CBCT (consultant present)
   - GTV Match (when visible) + correction
4. Breathing curve verification
5. Treatment delivery + respiratory tracking
6. PostRT-CBCT
   - Repeat match
   - Intrafractional motion assessment
SBRT: Treatment delivery

- Patient set up
- Check stability/breathing
SBRT: Treatment delivery

CBCT
SBRT: Treatment delivery

Matching
SBRT: Treatment delivery
SBRT: Treatment delivery (respiratory tracking)

- After matching...

  - Patient relaxation vs change in respiratory pattern
  - What is an ‘acceptable’ change?
  - When to repeat CBCT/match (extending treatment time)
  - Thresholds to ‘gate out’ changes during beam on

**Correlation between block position and tumour position...?**
SBRT: Treatment delivery

- 4 x 12Gy
- 2 partial arcs
  - 180.1°-30°
  - A1: 1802MU
  - B1: 1828MU
- 54 seconds/arc
- Max dose rate: 2400MU/Min
- 10MV FFF
SBRT: Treatment delivery

Stereotactic radiotherapy
Clinical application of flattening filter free beams for extracranial stereotactic radiotherapy
Stephanie Lang, Binaya Shrestha, Shaun Graydon, Frederique Cavelaars, Claudia Linsenmeier, Jan Hrbacek, Stephan Klöck, Gabriela Studer, Oliver Rieinterer *

Department of Radiation Oncology, University Hospital Zurich, Switzerland

Fig. 1. Total treatment time, separated into patient setup inside the room, CBCT acquisition, matching of the CBCT and actual beam on time.
SBRT: Treatment delivery

'Student' intrafractional motion (bone match)
SBRT: Treatment outcomes

Safety of high-dose-rate stereotactic body radiotherapy

Sonja Stieb, Stephanie Lang, Claudia Linsenmeier, Shaun Graydon and Oliver Risterer

Table 2: Acute and late lung toxicity in 75 patients with lung lesions

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Grade</th>
<th>I</th>
<th>II</th>
<th>≥III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute toxicity</td>
<td></td>
<td>11%</td>
<td>8%</td>
<td>-</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td></td>
<td>3%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td></td>
<td>8%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Atelectasis</td>
<td></td>
<td>44%</td>
<td>6%</td>
<td>-</td>
</tr>
<tr>
<td>Late toxicity</td>
<td></td>
<td>14%</td>
<td>2%</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3: Local Control Rate (LCR) 12 months after start of radiotherapy for all lesions and lung lesions

<table>
<thead>
<tr>
<th>LCR - 12 months</th>
<th>All (N = 100)</th>
<th>Lung (N = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BED ≤ 100 Gy</td>
<td>90.7% (N = 55)</td>
<td>93.5% (N = 61)</td>
</tr>
<tr>
<td>BED &gt; 100 Gy</td>
<td>100% (N = 55)</td>
<td>89.7% (N = 39)</td>
</tr>
<tr>
<td>GTV ≤ 14 cm³</td>
<td>98.1% (N = 58)</td>
<td>100% (N = 22)</td>
</tr>
<tr>
<td>GTV &gt; 14 cm³</td>
<td>84.9% (N = 25)</td>
<td>97.9% (N = 51)</td>
</tr>
<tr>
<td>Cox regression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BED</td>
<td>p = 0.36 (0.994)</td>
<td>p = 0.21 (0.986)</td>
</tr>
<tr>
<td>GTV</td>
<td>p = 0.72 (1.013)</td>
<td>p = 0.16 (0.986)</td>
</tr>
</tbody>
</table>

p-values indicate significance determined by log-rank test. Cox Regression is shown with p-values and hazard ratio in brackets. (BED: Biologically Effective Dose, GTV: Gross Tumor Volume).
SBRT: Treatment outcomes

Summary

• New treatment possibilities and clinical benefit from modern technology

However…
Summary

• New treatment possibilities and clinical benefit from modern technology

However…

• **Technology is only as good as the application by the user**
• RTs are key in this role:
  • Patient education and positioning at CT
  • Breathing coaching
  • Plan optimisation/evaluation
  • Patient education and positioning at the linac
  • Image matching protocols / intrafractional motion assessment
Thank you.

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