Clinical uncertainties: what is the magnitude?

BrachyNext
Miami 2014

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The 6 steps of 3D image guided brachytherapy

Applicator implant
3D imaging
Contouring
3D dose planning
Reconstruction of applicator
Dose delivery
Organ/applicator movement

Contouring uncertainties not yet handled in ICRU reports
Set-up uncertainties
Important publications!

- **Radiotherapy and Oncology 107 (April 2013):**
  - Special issue on uncertainties in brachytherapy (mainly gyn)
  - 16 original papers (contouring, inter-fraction, intra-fraction, applicator, vagina dose reporting)
  - 1 editorial

- **Radiotherapy and Oncology**

Uncertainties in the high gradient BT dose distribution

**Radial dose profile**

![Image of radial dose profile](image)

- Dose profile at level of point A
- Dose gradient per mm
  - 6% pr mm at point A
Contouring uncertainties
HR-CTV on MRI

- **HR CTV:**
  - Mean deviation <4mm
- **GTV, IR CTV:**
  - Mean deviation <6-7mm

Impact of contouring uncertainties (MRI) on dose

**10%**

**5%**

**8%**

**11%**

Hellebust et al, Vol 107, April 2013
Contouring uncertainties on CT
(interstitial brachytherapy)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Coefficient of variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>16% ± 10%</td>
</tr>
<tr>
<td>Rectum</td>
<td>7% ± 2%</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>34% ± 19%</td>
</tr>
</tbody>
</table>

Reconstruction uncertainties
MRI based intracavitary/interstitial brachytherapy

Reconstruction uncertainties in mm (SD):
~ 0.5mm in lateral and ant-post directions
~ 1-2mm in longitudinal directions

<table>
<thead>
<tr>
<th></th>
<th>Longitudinal SD (mm)</th>
<th>Lateral SD (mm)</th>
<th>Ant-posterior SD (mm)</th>
<th>Rotation SD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ring (plastic)</td>
<td>1.4</td>
<td>0.6</td>
<td>0.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Tandem (plastic)</td>
<td>1.7</td>
<td>0.6</td>
<td>0.5</td>
<td>-</td>
</tr>
<tr>
<td>Titanium Needle</td>
<td>2.2</td>
<td>0.4</td>
<td>0.3</td>
<td>-</td>
</tr>
</tbody>
</table>

S Haack et al., Radiother Oncol 2009
Impact of reconstruction uncertainties on DVH parameters

![Graph showing displacement](image)

K Tanderup et al., Radiother Oncol, 2008

Evaluation of needle displacement over 2 days
Prostate HDR implantation

![Graph showing needle displacement](image)

Fig. 1. Frequency histograms displaying the caudal movement in mm of each catheter at fractions 2 and 3 (326 in total).

Simnor, RO 2009
Impact of needle movement

- Needle movement has significant impact on target coverage

Kolkman-Duerloo, RO 2011

Random dosimetric variations during Brachtherapy

Same plan used for 4 fractions, anatomical changes between irradiations may lead to large random dosimetric uncertainties

Lang et al. 2013, Radioter Oncol

Results of a multicentre study between 6 centres with different treatment/application techniques (Nesvaci et al. 2013, Radiother Oncol 107 and references therein):

De Leeuw et al.; Hellebust et al.; Anderson et al.; Mohamed et al.; Lang et al.; Jamema et al.

<table>
<thead>
<tr>
<th>fraction 1</th>
<th>fraction 2</th>
<th>fraction 3</th>
<th>fraction 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder SD D2cc</td>
<td>2.7</td>
<td>1.5</td>
<td>20.3%</td>
</tr>
<tr>
<td>Rectum SD D2cc</td>
<td>3.3</td>
<td>3.8</td>
<td>20.5</td>
</tr>
<tr>
<td>Sigmoid SD D2cc</td>
<td>3.8</td>
<td>0.0</td>
<td>22.3</td>
</tr>
<tr>
<td>IRR CTV SD D90</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Changes correspond to physical dose change between 2 time points during course of BT. Effect on total EQD2 (EBRT+BT) depends on fractionation schedule (PDR, HDR, ...)

Courtesy Nicole Nesvaci
Gradients in brachytherapy

- **Longitudinal direction**
  - Gradients can be manipulated
  - Dependent on application

- **Radial direction**
  - Gradients cannot be manipulated
PTV margins in lateral direction?

Impact of uncertainties on total dose
Examples total dose and uncertainty

- HR CTV: \( D_{90} = 90 \pm 4\text{Gy} \)
- Bladder: \( D_{2\text{cm}^3} = 85 \pm 7\text{Gy} \)
- Rectum: \( D_{2\text{cm}^3} = 70 \pm 4\text{Gy} \)
- Sigmoid: \( D_{2\text{cm}^3} = 70 \pm 7\text{Gy} \)

Simulating dose-response curves for HR CTV \( D_{90} \)

Simulated data with 10% uncertainty (SD per BT fraction, for EBRT+4xHDR BT).
Error bars: +/-1SD of response probabilities calculated for individual patients

Negligible systematic differences between simulated „observed“ curve and assumed dose-response curve.
Ranges of response probability uncertainties around 85Gy EQD2 are around 2.5% for individual patients (1 SD of all simulated values \( n=10000 \)).

Courtesy Nicole Nesvacil
Simulating dose-response curves for OAR

Simulated data with 20% uncertainty (SD per BT fraction, for EBRT+4xHDR BT). Error bars: +/-1SD of response probabilities calculated for Individual patients

- Small systematic offset around rectum dose constraint of 70-75Gy
- Range of response probability uncertainty for individual patients ~4-6%

Courtesy Nicole Nesvacil

Dosimetric margin
Interventions to decrease uncertainties

- **Target**
  - Contouring training
    - ESTRO contouring workshops
  - Re-imaging for assessment of catheter position (interstitial)

- **OARs**
  - Re-imaging
  - Re-planning

- **What do we need?**
  - Tools for quick plan adaptation
  - Alternative imaging modalities (CBCT, US)

Conclusion

- Major clinical uncertainties are related to:
  - Contouring
  - Needle movement
  - Organ movement

- Geometrical PTV margins are not generally applicable for brachytherapy

- In brachytherapy ”dosimetric margins” may be the ”secret of success” even in the presence of considerable uncertainties