It’s All About Margins

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Why margins?

The smaller the better!
Short Introduction

- Erasmus MC has been using the CyberKnife® Robotic Radiosurgery System since 2005

- Current status
  - 2 CyberKnife® M6™ Series
  - 2 InCise™ 2 Multileaf Collimators
  - 1 in-room CT
  - Accuray Precision® TPS
  - 725 treatment plans in 2017

- Sites
  - lung
  - pancreas
  - oligometastases
  - liver
  - H&N boost
  - prostate
  - brain (metastases and radiosurgery)
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- “Accuray and The ErasmusMC have a research agreement in place”
Why do we need margins?

- **Tumor**
  - To compensate for deviations between the intended target position and the actual target position during treatment.
  - These deviations are estimated from population-based measurements of geometrical errors.

- **Healthy tissue**
  - To avoid unintended (high) dose to the healthy tissue and organs at risk (OAR) after alignment of a displaced tumor.
90% of patients in the population receives a minimum cumulative CTV dose of at least 95% of the prescribed dose - van Herk et al.

However, not directly suitable for hypofractionation: residual error

Compensate for this with larger margin

Margins for hypofractionation: Go Small

- High dose with large margin: high dose to OAR, only possible with fractionation
- For hypofractionation
  - Conformal plan
  - Small margins
- In radiosurgery often 0 mm margin are used, while there are always residual geometrical uncertainties
Margins: Go Small or Not

- Decreasing the margins is not without risk
- Conventional prostate treatment

<table>
<thead>
<tr>
<th>CTV to PTV</th>
<th>LR (mm)</th>
<th>AP (mm)</th>
<th>CC (mm)</th>
<th>Freedom from Biological Failure (p = 0.02)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No markers</td>
<td>6</td>
<td>10</td>
<td>10</td>
<td>91%</td>
</tr>
<tr>
<td>Implanted markers</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>58%</td>
</tr>
</tbody>
</table>

- Geometrical uncertainties not properly taken into account
- According to Van Herk margin recipe: 6 mm isotropic margin

Margins: Go Small or Not

- A 2 mm margin around the resection cavity for brain metastases improved local control without an increase in toxicity

<table>
<thead>
<tr>
<th></th>
<th>Local Failure (P = 0.042)</th>
<th>Toxicity Rate (P = 0.27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No margin</td>
<td>3 %</td>
<td>3 %</td>
</tr>
<tr>
<td>2 mm margin</td>
<td>16 %</td>
<td>8 %</td>
</tr>
</tbody>
</table>

Choi et al. Stereotactic Radiosurgery of the Postoperative Resection Cavity for Brain Metastases: Prospective Evaluation of Target Margin on Tumor Control, International Journal of Radiation Oncology*Biology*Physics, 84 (2), 2012
Margins vs OAR: Go Small

- Unambiguous: smaller margins are better for OAR
- Effect of increasing PTV margin on NTCP for H&N

Images courtesy of Rik Bijman & Tine Arts
Margins can fail: tumor

- In case of large individual changes, e.g. due motion
- When the shape of the target changes

Instead of increasing the margins, an online adaptive strategy can be used

- Bladder filling can be modelled to create a plan library for cervix

Margins can fail: OAR

- In case of large individual changes, e.g. due motion
- When the shape of the OAR changes
- Often motion of OAR with respect to tumor is harder to predict: pancreas

Images courtesy of Alba Magallon Baro
To see more: Today 16:25 OC-0184 Principal Component Analysis of Daily Changes in OAR Anatomy in Pancreatic Cancer Patients
Margins can fail: OAR

- LAPC study: Retrospective study quantifying movement of OAR
- Pancreas with fiducial markers (5 x 8 Gy, 80%), Synchrony® tracking
- In-room CT scan with contrast

- Accurate tumor tracking, but high frequency of OAR constraint violation during treatment fractions
Margins can fail: tumor and OAR

- Close vicinity of moving OAR: margin reduction unwanted → underdosage of tumor, online adaptive can bring a solution
- STEAL study: prospective
- Oligometastatic pelvic lymphnodes (5 x 9 Gy, 90%)
- In-room CT scan + plan of the day
- Library of plans with different snapshots of OAR

A: Conventional plan
B: Plan based on OAR delineation on diagnostic CT scan
C: Conventional plan prescribed to a lower isodose line
Summary

- We need margins
- Not necessarily the smaller the better for (local) control
- The smaller the better for OAR
- Using margins to ensure adequate target coverage and OAR sparing can fail in case of large individual differences and changes in shape
- In this case an online adaptive strategy can resolve the problem
- A pre-fraction in-room CT scan is used for individualizing treatment plans