Knowledge-Based Planning for SRS: From Quality Control to Full Automation

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Disclosure Statement

- 2012 and 2014 patent filings
- Varian Medical Systems
  - Licensing Agreement
  - Master Research Agreement
  - Consulting
  - Honoraria
Outline

- Treatment plan quality control
- What is knowledge-based planning (KBP)?
- Case study: KBP for SRS at UCSD
- The future of treatment planning for SBRT/SRS (and everything else)
**Do IMRT planning goals ensure “safe” plans?**

<table>
<thead>
<tr>
<th>H&amp;N</th>
<th>Bilateral Neck Treatment</th>
<th>Ipsilateral Neck Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>PTV</strong></td>
<td><strong>95% of PTV &gt; 95% of Rx; Max dose &lt; 110% of Rx</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Spinal Cord</strong></td>
<td>Max dose 40 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Spinal Cord + Margin</strong></td>
<td>Max dose 52 Gy; &lt; 1% (or 1 cc) exceeds 50 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Optic Nerves, Optic Chiasm</strong></td>
<td>Max dose 54 Gy; &lt; 1% exceeds 60 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Brainstem</strong></td>
<td>Max dose 54 Gy; &lt; 1% exceeds 60 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Brain</strong></td>
<td>Max dose 60 Gy; &lt; 1% exceeds 65 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Retina</strong></td>
<td>Max dose 50 Gy; &lt; 5% exceeds 45 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Larynx</strong></td>
<td>Max dose 50 Gy; &lt; 5% exceeds 45 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Upper Esophagus</strong></td>
<td>As low as possible; mean dose &lt; 45 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Parotid</strong></td>
<td>As low as possible; mean dose &lt; 45 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Pharyngeal Constrictors</strong></td>
<td>As low as possible; mean dose &lt; 26 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Submandibular</strong></td>
<td>As low as possible; V60 &lt; 60 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Oral Cavity</strong></td>
<td>As low as possible; mean dose &lt; 39 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Mandible</strong></td>
<td>As low as possible; mean dose &lt; 35 Gy</td>
</tr>
<tr>
<td></td>
<td><strong>Unspecified Tissue</strong></td>
<td>Max 70 Gy; &lt; 5% exceeds PTV Rx</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than PTV Rx; &lt; 5% exceeds PTV Rx</td>
</tr>
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</tbody>
</table>
Do IMRT planning goals ensure “safe” plans?

- This plan was QA’d at the treatment machine, passed all standard criteria.
Do IMRT planning goals ensure “safe” plans?

- (Dotted line plan was approved but not treated)
- Treatment plan was safe with respect to PTV coverage (TCP), but decidedly unsafe with respect to critical OARs (NTCP)
Do IMRT planning goals ensure “safe” plans?

- Unless planning systems make trade-offs explicit, ignorance of what’s possible can result in unsafe plan
- IMRT QC can addresses this problem on both input and output
The need for IMRT quality control

Goal is a system that can identify sub-optimal plans (most typically manifested as insufficient OAR sparing)

With the model prediction, we can catch suspected outliers, take corrective action (i.e. more appropriate IMRT planning objectives), and bring the OAR doses back toward expected values.

\[
\delta = \frac{D_{\text{mean}} - D_{\text{pred}}}{D_{\text{pred}}}
\]

\(\delta\) (prior) = 0.28 ± 0.24
\(\delta\) (after) = 0.12 ± 0.13

KL Moore et al, IJROBP 81, 545-551 (2011)
Salvageable parotids: 3 mos. before QC vs 3 mos. after

<table>
<thead>
<tr>
<th>clinical plans</th>
<th>clinical plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>prior to feedback</td>
<td>after feedback</td>
</tr>
<tr>
<td>$D_{\text{mean}}$ (Gy)</td>
<td>$D_{\text{pred}}$ (Gy)</td>
</tr>
<tr>
<td>18.9</td>
<td>11.6</td>
</tr>
<tr>
<td>16.1</td>
<td>12.3</td>
</tr>
<tr>
<td>16.9</td>
<td>13.3</td>
</tr>
<tr>
<td>14.9</td>
<td>15.2</td>
</tr>
<tr>
<td>24.7</td>
<td>18.0</td>
</tr>
<tr>
<td>26.6</td>
<td>18.8</td>
</tr>
<tr>
<td>26.4</td>
<td>19.6</td>
</tr>
<tr>
<td>36.6</td>
<td>21.0</td>
</tr>
<tr>
<td>27.4</td>
<td>23.6</td>
</tr>
<tr>
<td>46.8</td>
<td>24.2</td>
</tr>
<tr>
<td>43.4</td>
<td>27.7</td>
</tr>
<tr>
<td>40.5</td>
<td>29.1</td>
</tr>
<tr>
<td>52.3</td>
<td>29.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Avg $D_{\text{mean}}$</th>
<th>Avg $D_{\text{pred}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>33.6 Gy</strong></td>
<td><strong>22.4 Gy</strong></td>
</tr>
<tr>
<td>Avg $D_{\text{mean}}$</td>
<td>Avg $D_{\text{pred}}$</td>
</tr>
<tr>
<td><strong>20.3 Gy</strong></td>
<td><strong>18.8 Gy</strong></td>
</tr>
</tbody>
</table>

KL Moore et al, IJROBP 81, 545-551 (2011)
The need for treatment plan quality control

1. Need system that can identify sub-optimal plans (most typically manifested as insufficient OAR sparing)

2. Requirement is quantitative knowledge of what trade-offs must be made on the Pareto optimal frontier.

3. Absence of such a “system” will inevitably rely on subjective quality assessments and user experience/alertness... classic safety hazard!
Treatment Plan Quality Control:

1. eliminates plans that will fail IMRT QA at the treatment machine
2. highlights dose calculation errors due to inhomogeneities
3. guarantees that patients will not receive dose to critical structures that exceeds tolerance levels
4. ensures no prescription dose penetrates into PTV-OAR overlap regions
5. can flag clinically significant excess dose to critical structures
Correct Answer: 5

Can flag clinically significant excess dose to critical structures

Experience-Based Quality Control of Clinical IMRT Planning
Moore, Kevin L.; Brame, R. Scott; Low, Daniel A.; Mutic, S.; INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY * BIOLOGY * PHYSICS Volume: 81 Issue: 2 Pages: 545-551

Radiotherapy Dose-Volume Effects on Salivary Gland Function
Deasy, Joseph O.; Moiseenko, Vitali; Marks, Lawrence; Chao, K.S. Clifford; Nam, Jiho; Eisbruch, Avraham; INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY * BIOLOGY * PHYSICS Volume: 76 Issue: 3 Pages: S58-S63
0D knowledge-based (single-variable) dose prediction

Step 1
- Identify a set of site similar training patients

Step 2
- Correlate mean dose with input geometry

Step 3
- Utilize prediction to obtain mean dose estimation for new patients

Patient 1

SS_{13}  
SS_{11}  
SS_{12}  
D_1(x)

Patient N

LT PAROTID Overlap
Volume = 13.5454 cc
- PTV 5400 overlap volume = 0.967021 cc
  Suggested Mean Dose = 1912.86 cGy
  Current Mean Dose = 2038.5 cGy

Moore KL et al, IJROBP 81, 545-551 (2010)
0D $\rightarrow$ 1D (DVH) knowledge-based dose prediction

Step 1
- Identify a set of site similar training patients

Step 2
- Generate pDVH model from training cohort

Step 3
- Utilize pDVH model to obtain DVH prediction for new patient

Patient 1

Patient N

Step 1
- Identify a set of site similar training patients

Step 2
- Generate 3D prediction model

Step 3
- Utilize model to obtain 3D dose prediction

0D → 1D → 3D knowledge-based dose prediction

Patient 1

SS_{11}  SS_{12}  SS_{13}

D_1(x)

?\

Patient N

Shiraishi and Moore, MO-FG-303-03, Manuscript under review
IMRT QC = knowledge-based plan assessment

Key features of a “knowledge base”:

1. Must be quantitative

1. Must have discernable correlations
   - e.g. larger bladder = lower bladder DVH

3. Must provide a sufficient range of previous experience

With these ingredients, one has everything needed to make patient-specific predictions
Knowledge-based planning “by hand”

- Knowledge-based planning involves nothing more than incorporating the dose-volume predictions directly into the optimization loop.
Treatment plan quality:

1. cannot be predicted using previously treated patient plans
2. cannot be improved by retrospective and objective plan review
3. metrics can be developed using previous plans to alert the user that their current plan is suboptimal
4. is already standardized throughout the industry and needs no improvement
5. is always guaranteed when using modern treatment planning systems
Metrics can be developed using previous plans to alert the user that their current plan is suboptimal.
KBP in SRS: The UCSD experience

• For several years, standard treatment for SRS/SRT at UCSD has been multi-arc non-coplanar RapidArc
UCSD SRS experience

- SRS: Target size, shape, and location show enormous variation
  - PTV volume (0.1 cc - 60 cc)
  - Malignant vs. benign disease
  - Fractionation schedule and clinical priorities
  - Proximity to OARs (brainstem, optic nerves, cochlea) highly variable (0-10cm)
  - Multiple PTVs

![Diagram of SRS VMAT 235 pts]

- PTV far from OAR
  - 163 (69%)
- PTV near OAR
  - 39 (17%)
- Multiple PTVs
  - 21 (9%)
- Others*
  - 12 (5%)

* Overlapping retreatment, staged approach for AVM
KBP in SRS

1. Structure & dose

2. DVH at varying distances from PTV

3. Fit with skew-normal PDF

\[ f(p_1, p_2, p_3; D) = \frac{1}{\pi p_2} \exp \left( -\frac{(D - p_1)^2}{2p_2^2} \right) \]
\[ \times \int_{-\infty}^{\frac{p_3(D - p_1)}{p_2}} \exp(-t^2/2) \, dt, \]

Three fit parameters: location, scale, shape

4. Parameterize fit parameters

Fits include:
Distance from PTV
PTV volume

KBP in SRS

N training plans

Structure & dose

Model DVH

1.5mm
4.5mm
3mm

PTV

k = 1

k = 2

k = 3

k = 4

k = 5

Predict DVH

PTV

Body

Brain

D_{Rx} = 21 Gy

Clinical

Prediction

Subvolume

PTV

Structure

SRS plan quality metrics are DVH-based

Gradient measure (GM) = \((3/4\pi)^{1/3}(V_{50\%}^{1/3}-V_{100\%}^{1/3})\)

\[\delta QM = QM_{\text{clin}} - QM_{\text{pred}}\]

\[D_{Rx} = 21 \text{ Gy}\]

Accurate QM predictions and outlier identification

\[ \delta_{GM} > 1.35 \text{ mm} \]

\[
\begin{array}{|c|c|c|c|}
\hline
 & \text{Training} & \text{Excluded} & \text{p-value} \\
\hline
\delta \text{GM (mm)} & 0.2 \pm 0.3 & 1.1 \pm 0.5 & <0.001 \\
\delta V_{10\text{Gy}}/V_{10\text{Gy}} & 0.04 \pm 0.12 & 0.20 \pm 0.11 & <0.001 \\
\delta CI & -0.02 \pm 0.12 & -0.03 \pm 0.10 & 0.19 \\
\hline
\end{array}
\]
KBP replanning confirms predicted clinical gains

<table>
<thead>
<tr>
<th>(\delta)QM</th>
<th>Clinical</th>
<th>Replan</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\delta GM) (mm)</td>
<td>1.6 ± 0.2</td>
<td>0.5 ± 0.5</td>
</tr>
<tr>
<td>(\delta V_{10Gy}/V_{10Gy})</td>
<td>0.27 ± 0.11</td>
<td>0.04 ± 0.06</td>
</tr>
<tr>
<td>(\delta CI)</td>
<td>1.12 ± 0.09</td>
<td>1.08 ± 0.11</td>
</tr>
<tr>
<td>Max dose</td>
<td>1.10 ± 0.03</td>
<td>1.18 ± 0.04</td>
</tr>
</tbody>
</table>

Improved QMs, Higher max dose

KBP SRS in Eclipse

- Use original plan’s arc arrangement
- DVH predictions feed two different optimization routines, coded as patient-specific templates
  - HOT: for brain metastases, reduces penalty for hot spots and prioritizes GM
  - COLD: for use in benign disease and retreatments where hot spot is clinically important
- All plans are normalized to the same PTV coverage (V100%=98% typically)
Tuning up autoplanning routines

GM: Hot < Clinical ≤ Cold
HI: Cold ≤ Clinical < Hot

$HI = \frac{D_{\text{max}}}{D_{Rx}}$
Single-blind study of autoplans vs. manual plans

**Study schema:**

1. Automatically replan 200+ SRS cases with *HOT* and *COLD* routines
2. Clinically approved plan and autoplans are de-identified (A, B, C randomly)
3. SRS physicians review plans with relevant clinical information and selects the preferred plan

A vs. B vs. C
Preliminary results

13%: Clinical and auto plans even
15%: Relatively close to OAR
2%: Near previous treatment site

<table>
<thead>
<tr>
<th></th>
<th>Clinical</th>
<th>Auto: Hot</th>
<th>Auto: Cold</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Sanghvi</td>
<td>18 (26%)</td>
<td>43 (61%)</td>
<td>9 (13%)</td>
<td>70</td>
</tr>
<tr>
<td>Dr. Hattangadi</td>
<td>25 (34%)</td>
<td>39 (53%)</td>
<td>10 (14%)</td>
<td>74</td>
</tr>
<tr>
<td>TOTAL</td>
<td>43 (30%)</td>
<td>82 (57%)</td>
<td>19 (13%)</td>
<td>144</td>
</tr>
</tbody>
</table>
Preliminary results

- Autoplan sequences took ~15 minutes on average

- In the (17%) 24/144 cases where the manually-planned treatments were preferred
  - 21 plans were selected because of more aggressive OAR sparing (brainstem, cochlea, or optic nerve) at max dose level
  - 3 plans were selected because the manual plans better spared a nearby volume that received prior radiotherapy
Summary of current KBP system in SRS

• Already have solution that yields superior or equivalent results for 83% of SRS cases

• Focusing on that remaining 17%...
  o Robust multi-met solution (forthcoming)
  o Robust neighboring OAR solution (underway)
  o Prior tx solution (underway)
  o Clinical “go live” after completion of blind study

• When possible, such a benchmarking study should be used before clinical implementation of automated planning
Knowledge-based planning in SRS:

1. can predict plan quality metrics and automate the planning process based on accurate dose-volume predictions
2. automatically loads standard planning templates for patients
3. guides the planning process by continually adjusting dose objectives during optimization
4. can only be used for inverse optimized planning
5. saves time but likely at the expense of plan quality

78% 4% 16% 1% 1%
Correct Answer: 1

1. Can predict plan quality metrics and automate the planning process based on accurate dose-volume predictions

Knowledge-based prediction of plan quality metrics in intracranial stereotactic radiosurgery
S Shiraishi, J Tan, LA Olsen, KL Moore
Medical physics 42 (2), 908-917
Conclusion

• SRS and SBRT* are extremely well suited to knowledge-based techniques

• Knowledge-based quality metric prediction is useful for both quality control and planning automation

• Clinical KBP is still in its infancy, but in some form these techniques will be part of the treatment planning process

• KBP can also help inform clinical decision making (when to fractionate, benefits of different treatment techniques, e.g. $4\pi$ vs. static field vs. coplanar VMAT vs. protons)

*Abstracts at AAPM 2015:*
  • Foy et al SU-ET-97
  • Snyder et al MO-F-CAMPUS-T-04