Sensitivity Analysis for Lexicographic Ordering in Radiation Therapy Treatment Planning

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Dosimetrists create plans for patients, with a number of goals for the treatment outcome of varying importance. Many models and methods have been developed to measure the quality of a plan’s dose distribution. Challenge - tradeoffs between criteria can be difficult to quantify because some structures are more important than others. Tradeoffs are patient specific, making tradeoff identification difficult as well.
Research Questions

- What are the tradeoffs between competing objectives in the treatment planning model?
- How can these tradeoffs be calculated efficiently and visualized or communicated in a manner valuable to physicians?
Multi-criteria optimization

- Many values are used to describe the treatment plan in the model
- Intuitive when there are many competing objectives
- Creates a many-dimensional Pareto frontier to realize tradeoffs
Lexicographic Ordering (LO)

- Multi-stage approach
- Uses clinical insights to prioritize treatment planning goals
  - Focuses the computational effort to clinically relevant tradeoffs
- For each stage
  - A Pareto-efficient tradeoff is plotted between competing criteria
  - The planner constrains the more important criteria accordingly, to be controlled for later stages
- Clinically, LO allows for easier interpretation of tradeoff results

Notation

- \( S \) = set of structures
- \( T \) = set of targets
- \( V_s \) = set of voxels in structure \( s \)
- \( K \) = set of all apertures (\( K^* = \) active apertures)
- \( D_{kj} \) = dose to voxel \( j \) from aperture \( k \) at unit intensity
- \( u_s \) = upper bound on dose to voxels in structure \( s \)
- \( \rho_s \) = bound on EUD\(_s\) after tradeoff for \( s \in S \) analyzed
- \( \alpha \) = weighting between structure EUD’s, \( \alpha \in [0, 1] \)
Decision Variables

- $z_j = \text{dose received by voxel } j \in V$
- $y_k = \text{intensity of aperture } k \in K$
- $\text{EUD}_s = \text{Linearly-approximated EUD to structure } s \in S$
Linearly Approximating the EUD

- Equivalent Uniform Dose (EUD) can be approximated using a linear combination of the mean and max dose to the structure (mean and min dose for targets)

\[
EUD_s = \gamma_s \cdot \frac{1}{|V_s|} \sum_{j \in V_s} z_j + (1 - \gamma_s) \cdot \max_{j \in V_s} z_j \quad (s \in S \setminus T)
\]

\[
EUD_s = \gamma_s \cdot \frac{1}{|V_s|} \sum_{j \in V_s} z_j + (1 - \gamma_s) \cdot \min_{j \in V_s} z_j \quad (s \in T)
\]

- Motivation
  - The optimization problem can be formulated as a linear program

General Model for LO Stage \( i \)

\[
\begin{align*}
\min \quad & \alpha \text{EUD}_{s_i} + (1 - \alpha) \text{EUD}_{s_{i+1}} \\
\text{s.t.} \quad & z_j = \sum_{k \in K} D_{kj} y_k \\
& z_j \leq u_s \\
& \text{EUD}_s = \gamma_s \cdot \frac{1}{|V_s|} \sum_{j \in V_s} z_j + (1 - \gamma_s) \cdot \max_{j \in V_s} z_j \\
& \text{EUD}_s = \gamma_s \cdot \frac{1}{|V_s|} \sum_{j \in V_s} z_j + (1 - \gamma_s) \cdot \min_{j \in V_s} z_j \\
& \text{EUD}_{s_j} \leq p_{s_j} \\
& \text{EUD}_{s_j} \geq p_{s_j}
\end{align*}
\]

\( \forall j \in V \) \\
\( \forall j \in V_s, s \in S \) \\
\( \forall s \in S \setminus T \) \\
\( \forall s \in T \) \\
\( s_j \in S \setminus T, \quad j \leq i - 1 \) \\
\( s_j \in T, \quad j \leq i - 1 \)
Generating Tradeoff Curves

- Two-phase approach
  - Phase 1 - Generate an aperture pool for $K^*$
  - Phase 2 - Sequentially solve LO optimization model, only allowing $y_k > 0$ when $k \in K^*$
Aperture Generation

**Generation goals**

- Generate a set of apertures large enough to produce clinically acceptable plans
- Limit the number of apertures to keep the computational costs in Phase 2 manageable
Aperture Generation Process

- We iteratively solve the master problem with aperture set $K^*$, adding apertures to $K^*$ each iteration $i$ using Direct Aperture Optimization (DAO).
- Each iteration, the best aperture per beam is added to $K^*$.
  - Adding only the best aperture overall produces less conformal plans.
- This process continues until a desired size of $K^*$ is reached.

Generating Tradeoff Curves

- For each stage $i$, there are two tasks:
  - Approximate tradeoff curve by solving the general stage model for various $\alpha \in [0, 1]$
    \[ \min \alpha \text{EUD}_{s_i} + (1 - \alpha) \text{EUD}_{s_{i+1}} \]
  - Select a bound for $\text{EUD}_{s_i}$ by analyzing tradeoff curve for structure $s_i$
    - Add constraint $\text{EUD}_{s_i} \leq p_{s_i}$ for later stages

Sensitivity Analysis for LO in Radiotherapy Treatment Planning

Troy Long\textsuperscript{1}, Dick Fraass\textsuperscript{3}, Martha Matuszak\textsuperscript{2}, Edwin Romeijn\textsuperscript{1}
Tradeoff Curve Approximation Process

- Goal is to generate a tradeoff curve that is clinically relevant while keeping computational effort to a minimum.
- We found that plotting about 8 or 9 strategically positioned solutions for different $\alpha$ values was sufficient.
Tradeoff Curve Approximation Example

Curve Drawing per Iteration Illustration

minimize $\alpha\text{EUD}_{\text{Rect}} + (1-\alpha)\text{EUD}_{\text{Blad}}$

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Tradeoff Curve Approximation Example

Curve Drawing per Iteration Illustration

minimize $\alpha EUD_{Rect} + (1-\alpha)EUD_{Blad}$

EUD$_{Blad}$ vs. EUD$_{Rect}$

Iteration 1
Iteration 2
Tradeoff Curve Approximation Example

\[ \text{minimize } \alpha \text{EUD}_{\text{Rect}} + (1-\alpha) \text{EUD}_{\text{Blad}} \]

Curve Drawing per Iteration Illustration

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Introduction and Motivation

Methodology

Application

Remarks and future research

Tradeoff Curve Approximation Example

Curve Drawing per Iteration Illustration

minimize $\alpha EUD_{Rect} + (1-\alpha)EUD_{Blad}$

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Selecting a Bound

- The physician examines the tradeoff and then chooses a value, $\rho_{s_i}$, at which to constrain $\text{EUD}_{s_i}$.
- This bound is added to the model for later stages.
Application - Prostate Case

Statistics
- 7 beams
- 796 beamlets
- 44390 voxels, .5cm × .5cm
**Approximate EUD Parameter $\gamma_s$**

$\gamma_s$ calibrated by comparing approximate EUD to actual EUD values using a clinically acceptable dose distribution for the application case.

$$EUD_s = \gamma_s \cdot \frac{1}{|V_s|} \sum_{j \in V_s} z_j + (1 - \gamma_s) \cdot \max_{j \in V_s} z_j$$

<table>
<thead>
<tr>
<th>Structure</th>
<th>PTV</th>
<th>Rectum</th>
<th>Bladder</th>
<th>Femora</th>
<th>PenileBulb</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUD Param</td>
<td>-5</td>
<td>8</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>$\gamma_s$</td>
<td>.3</td>
<td>.4</td>
<td>.85</td>
<td>.8</td>
<td>1</td>
</tr>
</tbody>
</table>
Sensitivity Analysis for LO in Radiotherapy Treatment Planning

**LO Model Structure**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Primary Structure</th>
<th>Secondary Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PTV</td>
<td>Rectum</td>
</tr>
<tr>
<td>2</td>
<td>Rectum</td>
<td>Bladder</td>
</tr>
<tr>
<td>3</td>
<td>Bladder</td>
<td>Femora</td>
</tr>
<tr>
<td>4</td>
<td>Femora</td>
<td>Penile Bulb</td>
</tr>
<tr>
<td>5</td>
<td>all non-PTV voxels</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Structure</th>
<th>PTV</th>
<th>Rectum</th>
<th>Bladder</th>
<th>Femora</th>
<th>Penile Bulb</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUD Goal</td>
<td>Max</td>
<td>Min</td>
<td>Min</td>
<td>Min</td>
<td>Min</td>
</tr>
</tbody>
</table>

- $K^*$ has 84 apertures
### Voxel Dose Upper Bounds, $u_s$

<table>
<thead>
<tr>
<th>Structures</th>
<th>PTV</th>
<th>Rectum</th>
<th>Bladder</th>
<th>Femora</th>
<th>Penile Bulb</th>
</tr>
</thead>
<tbody>
<tr>
<td>$u_s$ (Gy)</td>
<td>85.5</td>
<td>78</td>
<td>78</td>
<td>85.5</td>
<td>85.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Structures</th>
<th>NT 1.5cm</th>
<th>NT 3cm</th>
<th>Other Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>$u_s$ (Gy)</td>
<td>83</td>
<td>77</td>
<td>65</td>
</tr>
</tbody>
</table>
Stage 1 - PTV vs. Rectum

Minimize $-\alpha EUD_{PTV} + (1 - \alpha) EUD_{Rect}$, 133s draw time
Stage 2 - Rectum vs. Bladder

Minimize $\alpha EUD_{Rect} + (1 - \alpha) EUD_{Blad}$, 83s draw time
Stage 3 - Bladder vs. Femora

Minimize $\alpha \text{EUD}_{\text{Blad}} + (1 - \alpha) \text{EUD}_{\text{Fem}}$, 183s draw time
Stage 4 - Femora vs. Penile Bulb

- Minimize $\alpha EUD_{Fem} + (1 - \alpha) EUD_{PB}$, 200s draw time
Dose-Volume Histogram (with chosen bounds)
Dose-Volume Histogram (strict LO)
<table>
<thead>
<tr>
<th>Priority</th>
<th>Clinical Goals (Gy)</th>
<th>Actual</th>
<th>Strict</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>$\max_{Rect} &lt; 78$</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>0</td>
<td>$\max_{Blad} &lt; 78$</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>1</td>
<td>$\min_{PTV} &gt; 73.8$</td>
<td>75.8</td>
<td>76.7</td>
</tr>
<tr>
<td>2</td>
<td>$\text{mean}_{Rect} &lt; 40$</td>
<td>31.8</td>
<td>34.8</td>
</tr>
<tr>
<td>2</td>
<td>$\text{mean}_{Blad} &lt; 50$</td>
<td>20.7</td>
<td>22.3</td>
</tr>
<tr>
<td>3</td>
<td>$\min_{PTV} &gt; 77.7$</td>
<td>75.8</td>
<td>76.7</td>
</tr>
<tr>
<td>4</td>
<td>$\max_{Fem} &lt; 45$</td>
<td>56.3 (mean$_{Fem} = 25.0$)</td>
<td>48.6</td>
</tr>
<tr>
<td>4</td>
<td>$\text{mean}_{PB} &lt; 52.5$</td>
<td>46.4</td>
<td>48.5</td>
</tr>
<tr>
<td>4</td>
<td>$\max_{PB} &lt; 77.7$</td>
<td>84.0</td>
<td>85.5</td>
</tr>
</tbody>
</table>
Isodose Lines (84 Apertures)
Isodose Lines (161 Apertures)
Concluding remarks

- Exploring stage-by-stage tradeoffs can help identify beneficial treatment plan alterations.
- This process can be especially useful in cases with critical structures overlapping with targets.
- This focuses computational effort efficiently.
Future Research

- Apply technique to other regions with more impacting tradeoffs
- Study alternate means of tradeoff calculation and presentation
  - Multiple tradeoffs per stage
  - Comparing everything to PTV coverage
- Other aperture pool generation techniques
- Using GPU techniques to quicken tradeoff curve drawing process
Acknowledgements

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References


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Dose-Volume Histogram (strict LO), full

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