Optimizing Global Liver Function in Stereotactic Body Radiotherapy

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Introduction

Stereotactic Body Radiation Therapy (SBRT)
- SBRT delivers up to 5 treatments of high dose from fixed directions to control liver tumors (targets) but this treatment also increases the risk of radiation-induced liver disease.
- Fact: Liver function is not homogeneous.
- Idea: Maximize post-treatment liver function using liver tissue dose-response based on liver function.
- Research questions: "How can we quantify important liver tissue dose-response behavior? Are currently-used surrogate representations sufficient?"
- Developed an optimization model that incorporates functionality to produce alternative treatment plans that prioritize high functioning areas of the liver.
- Using 2D (synthesized) and 3D (real patient) liver cancer examples, we compare treatment plans obtained conventionally and with two proposed objectives that consider liver function.

Liver Perfusion-based Dose-response
To quantify relative liver function we use venous perfusion, a good indicator of global and local liver function [2]. Perfusion maps were computed by dynamic contrast enhanced magnetic resonance image (DCE MRI).

Experiment: Notation and Metrics

Sets
Each beam is discretized into beamlets \( i \in \mathbb{N} \).
Patient is discretized into voxels \( j \in \mathbb{V} \).
Geometry is partitioned into structures \( s \in \mathbb{S} \).

Voxels in each structure \( s \in \mathbb{S} \) make up the set \( V_s \subset \mathbb{V} \).

Parameters
Dose matrix \( D \in \mathbb{N}^{\mathbb{N} \times \mathbb{V}} \) where an element \( D_{is} \) is the dose deposited from beamlet \( i \) to voxel \( s \).
Voxels have perfusion value \( f = \mathbb{R}^{V_s} \).

Decision Variables
Beamlet intensities are denoted \( \mathbb{V} \).

Objectives
We compare 3 objectives:
1) Reduce Dose (min, Gurobi):
\[
\text{fEUD}_{\text{min}}(z) = \frac{1}{|V_s|} \sum_{j \in V_s} f_j
\]
2) Avoid high perfusion [3] (min, Gurobi):
\[
\text{fEUD}_{\text{high}}(z; g)(t) = \frac{|V_s|}{|V_s|} \sum_{j \in V_s} g(t) f_j
\]
3) Preserve global liver function* (max, IpOpt, Fig 2c, blue):
\[
GLF(z; f) = \frac{1}{|V_s|} \sum_{j \in V_s} \left( 1 - \left( \frac{f_j}{D_{\alpha,t} f_j + 2} \right) \right)
\]

*Simple approximation used (Fig 2c, red).

Optimization Models

General Model (PTV = Planning Target Volume)

\[
\begin{align*}
\text{minimize} & \quad h(z) \\
\text{subject to} & \quad \alpha, \beta \geq 0, \quad \sum_{j \in V_s \cap \{\text{Liver}\}} z_r = \alpha_{\text{V}_s}, \quad \sum_{j \in V_s \cap \{\text{Liver}\}} z_r = \alpha_{\text{V}_s}, \\
& \quad z_r = \sum_{i \in \mathbb{N}} D_{is} x_i, \quad j \in \mathbb{V}, \quad s \in \mathbb{S} \cup \{\text{Liver}\}, \\
& \quad x_i \geq 0, \quad j \in \mathbb{V}, \quad s \in \mathbb{S} \cup \{\text{Liver}\},
\end{align*}
\]

where \( h(z) = \text{fEUD}_{\text{min}}(z), \text{fEUD}_{\text{high}}(z; g), \text{GLF}(z; f) \).

Patient Example Parameters:

<table>
<thead>
<tr>
<th>Structure</th>
<th>$</th>
<th>RHS bound (Gy)</th>
<th>Structure</th>
<th>$</th>
<th>RHS bound (Gy)</th>
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<td>BOWEL</td>
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<td>25</td>
<td>LIVER</td>
<td>4</td>
<td>30</td>
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</tbody>
</table>

Conclusions and Future Work

Conclusions
- Surrogate (linear) objective functions such as fEUD are not sufficient for capturing complex tissue dose-response behavior such as damage-resistant-saturated thresholds.
- Although GLF-based model optimizes global liver function, fEUD-based model can be optimized much more quickly tradeoff between treatment quality and time to obtain treatment.
- Because fEUD-based solutions typically achieve better GLF than fEUD-based solutions, fEUD solutions make good starting solutions for finding GLF-based solutions.

Future Work
- Incorporating uncertainty in perfusion values (image registration)
- Determine individualized parameters for a patient’s dose-response pathway through treatment and adapt accordingly.

Acknowledgements

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References

[1] VARIAN MEDICAL SYSTEMS, INC.