CENTER FOR HEALTHCARE ENGINEERING & PATIENT SAFETY
UNIVERSITY OF MICHIGAN

2015 Healthcare Engineering and Patient Safety Symposium

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.

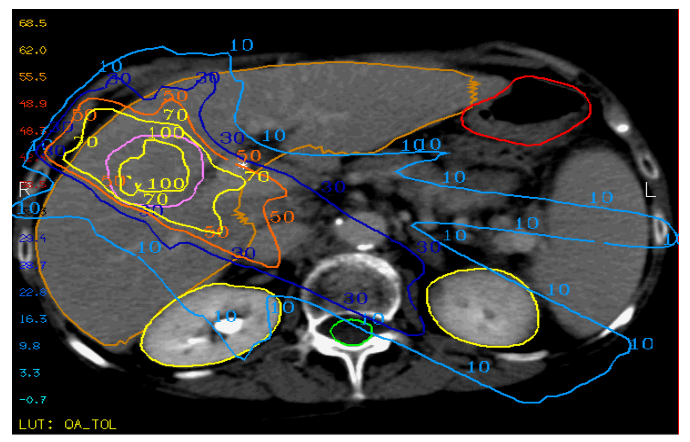
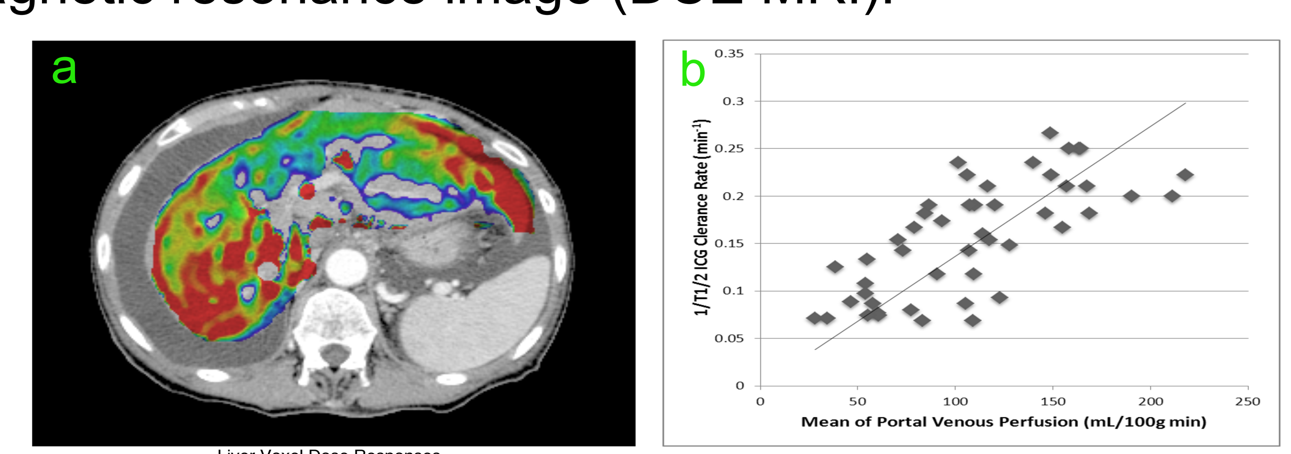


Figure 1. (left) Treatment setup.[1] (right) Goals of treatment planning: (i) eradicate tumor cells (pink) and (ii) spare surrounding critical organs to ultimately preserve functionality.

• 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).



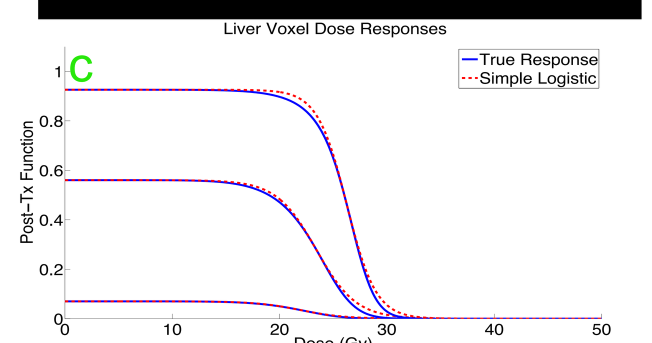


Figure 2. (a) Perfusion map. (b) Correlation between biomarker for global liver function and perfusion. [2] (c) Liver dose response.

The output of the true dose-response function is post-treatment liver function and the inputs are pre-treatment liver perfusion and dose delivered. This function contains two important dose thresholds: i) under the damage-resistant threshold, little damage is done and ii) above the damage-saturation threshold, no more damage is done.

Experiment: Notation and Metrics

Sets

Each beam is discretized into beamlets $i \in N$
Patient is discretized into voxels $j \in V$
Geometry is partitioned into structures $s \in S$
Voxels in each structure $s \in S$ make up the set $V_s \subset V$

Parameters

Dose matrix $D \in \Re^{|N|\times|V|}$, where an element D_{ij} is the dose deposited from beamlet i to voxel j, $\forall i \in N,\ j \in V$
Voxels have perfusion value $f \in \Re^{|V_{Liver}|}$

Decision Variables

Beamlet intensities are denoted $x_i\ \forall i \in N$
Voxels received dose $z_j\ \forall j \in V$

Objectives

We compare 3 objectives:

1) Reduce Dose (min, Gurobi):

$$\ell EUD_{Liver}(z) = \frac{1}{|V_{Liver}|}\sum_{j\in V_{Liver}} z_j$$

2) Avoid high perfusion [3] (min, Gurobi):

$$fEUD_{Liver}(z; g(f)) = \frac{1}{|V_{Liver}|}\sum_{j\in V_{Liver}} g_j(f) z_j$$

3) Preserve global liver function* (max, IpOpt, Fig 2c, blue):

$$GLF(z;f) = \frac{1}{|V_{Liver}|}\sum_{j\in V_{Liver}}\left(1+\left(\frac{F}{f_j^{pre}}\left(1+\left(\frac{z_j\left(\frac{\alpha}{\beta}+\frac{z_j}{T}\right)}{D\left(\frac{\alpha}{\beta}+2\right)}\right)^k\right)\right)^n\right)^{-1}$$

*Simple approximation used (Fig 2c, red)

Optimization Models

General Model (PTV = Planning Target Volume)

$$\begin{aligned}
&\underset{x,z}{\text{minimize}}\ h(z) \\
&\text{subject to}\ \alpha_{PTV}\frac{1}{|V_{PTV}|}\sum_{j\in V_{PTV}} z_j + (1-\alpha_{PTV})\min_{j\in V_{PTV}} z_j \ge l_{PTV} \\
&\qquad z_j \le u_s \qquad\qquad j\in V_s,\ s\in S\setminus\{Liver\} \\
&\qquad z_j = \sum_{i\in N} D_{ij}x_i \qquad j\in V \\
&\qquad x_i \ge 0 \qquad\qquad i\in N
\end{aligned}$$

where $h(z)$ is $\ell EUD_{Liver}(z)$, $fEUD_{Liver}(z; g(f))$, $-GLF'(z;f)$.

Patient Example Parameters:

Structure	S	RHS bound (Gy)	Structure	S	RHS bound (Gy)
PTV	0	**R_x dose=60**	KIDNEYS	3	15
PTV	0	80	STOMACH	4	27.5
NORMLIVER	1	Obj. Function	DUODENUM	5	30
CORD	2	25	BOWEL	6	30

Results

Figure 3 below contrasts a slice of the dose distribution obtained from using the three objective functions previously mentioned. Notably, the GLF- and fEUD-based plans are different from each other (Fig. 4e).

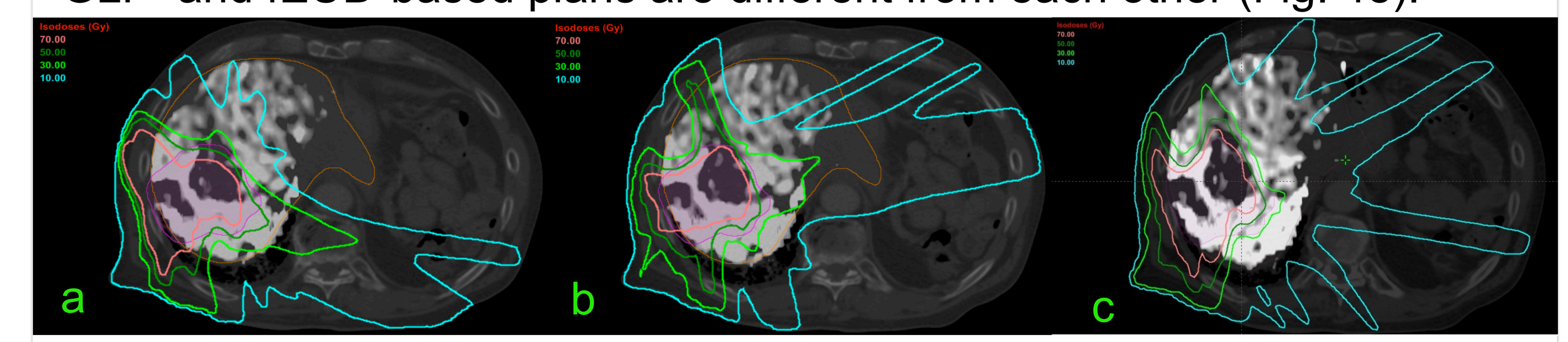


Figure 3. (a) Isodose lines (lEUD; **0.448 GLF**). (b) Isodose lines (fEUD, **0.459 GLF**). (c) Isodose lines (GLF, 0.**504 GLF**).

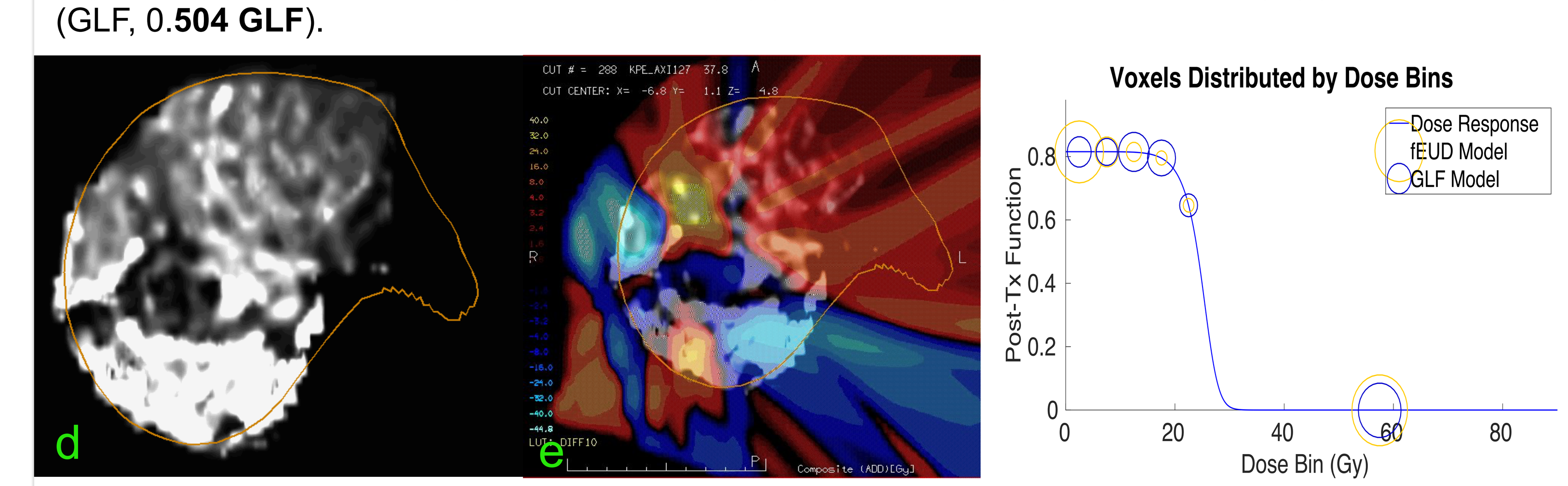


Figure 4.
(d) Grayscale perfusion map. (e) Dose wash diff.: (c) minus (a). (f) How GLF objective achieves higher post-treatment global liver function than the fEUD objective.

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 optmized much more quickly ➔ tradeoff between treatment quality and time to obtain treatment.
- Because fEUD-based solutions typically achieve better GLF than ℓEUD-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 partway through treatment and adapt accordingly

Acknowledgements

We would like to thank NIH (R01-CA132834) for funding this project.

References

[1] VARIAN MEDICAL SYSTEMS, INC.
[2] Yue Cao, Hesheng Wang, Timothy D Johnson, Charlie Pan, Hero Hussain, James M Balter, Daniel Normolle, Edgar Ben-Josef, Randall K Ten Haken, Theodore S Lawrence, et al. Prediction of liver function by using magnetic resonance-based portal venous perfusion imaging. International Journal of Radiation Oncology* Biology* Physics, 85(1):258263, 2013.
[3] Moyed M Miften, Shiva K Das, Min Su, and Lawrence B Marks. Incorporation of functional imaging data in the evaluation of dose distributions using the generalized concept of equivalent uniform dose. Physics in medicine and biology, 49(9):1711, 2004.