LET-guided Plan Evaluation and Robust Optimization in Intensity-Modulated Proton Therapy

Wei Liu, PhD

Associate Professor, Department of Radiation Oncology
Research Director, Division of Medical Physics
Mayo Clinic Arizona

Supported by the National Cancer Institute (NCI) *Career Developmental Award K25-CA168984*, by *Arizona Biomedical Research Commission Investigator Award (R01 type)*, by The *Lawrence W. and Marilyn W. Matteson Fund for Cancer Research*, and by The *Kemper Marley Foundation.*

Disclosures

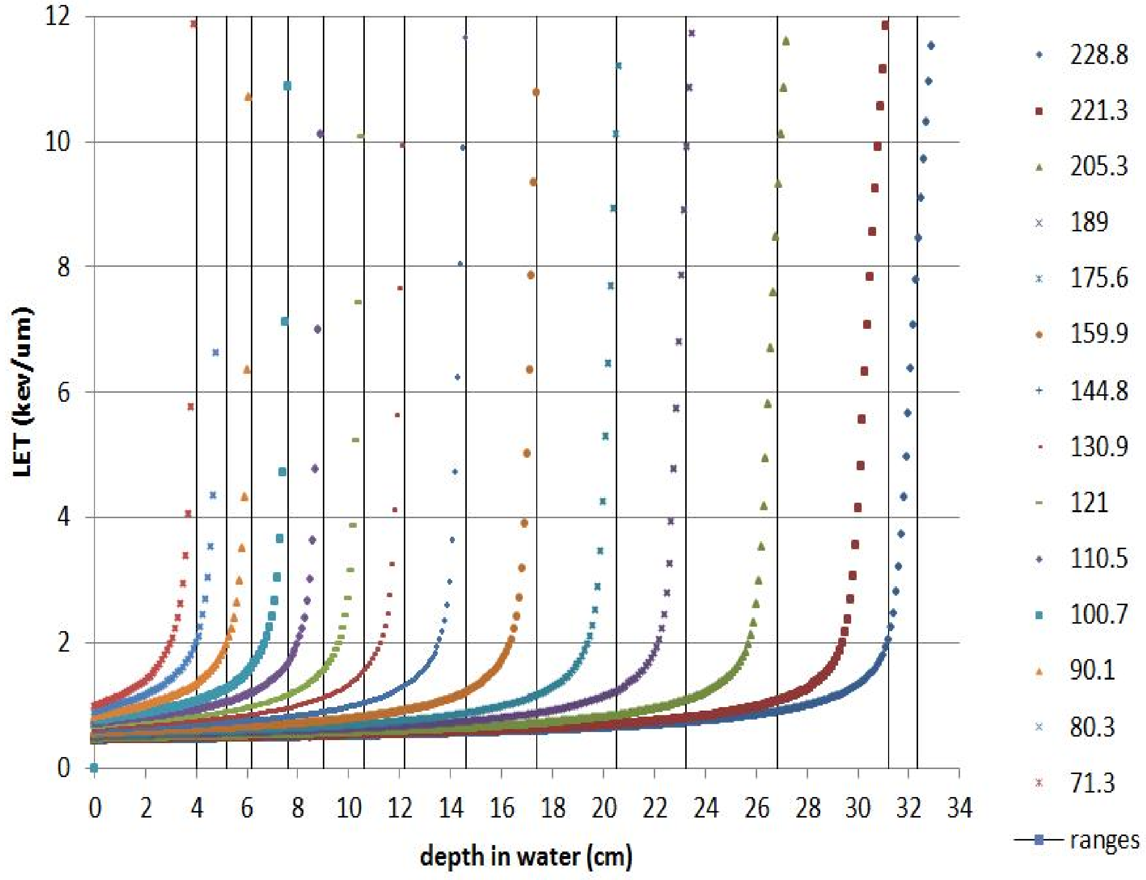
- I am a PI on a grant funded by NIH/NCI
- I am a PI on a grant funded by Arizona Department of Health Sciences (ADHS)
- The LET calculation software reported in this presentation has been licensed to .decimal LLC by Mayo Clinic

Objectives

1. How to calculate LET accurately and efficiently in IMPT
2. How to use LET in plan quality evaluation in IMPT
3. How to use LET to implement LET-guided robust optimization in IMPT

HOW TO CALCULATE LET ACCURATELY AND EFFICIENTLY IN IMPT

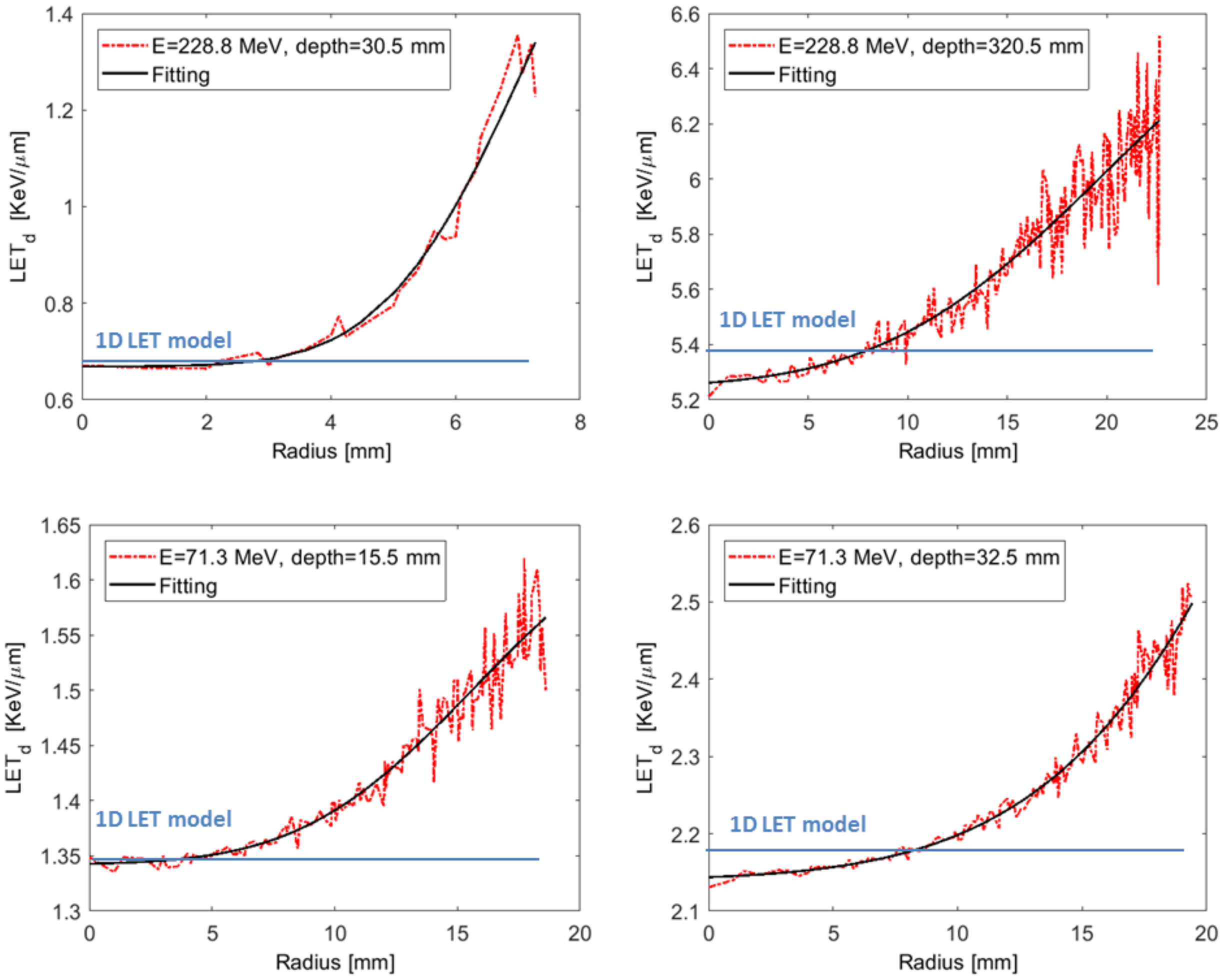
LET value in the middle as function of depth calculated using Geant4



Dose averaged LET:

$$LET_d(x,y,z) = \frac{\sum_i \int_0^\infty \varphi_{E_i}(x,y,z,E_i)\, SP_i^2(E)\, dE_i}{\sum_i \int_0^\infty \varphi_{E_i}(x,y,z,E_i)\, SP_i(E)\, dE_i}$$

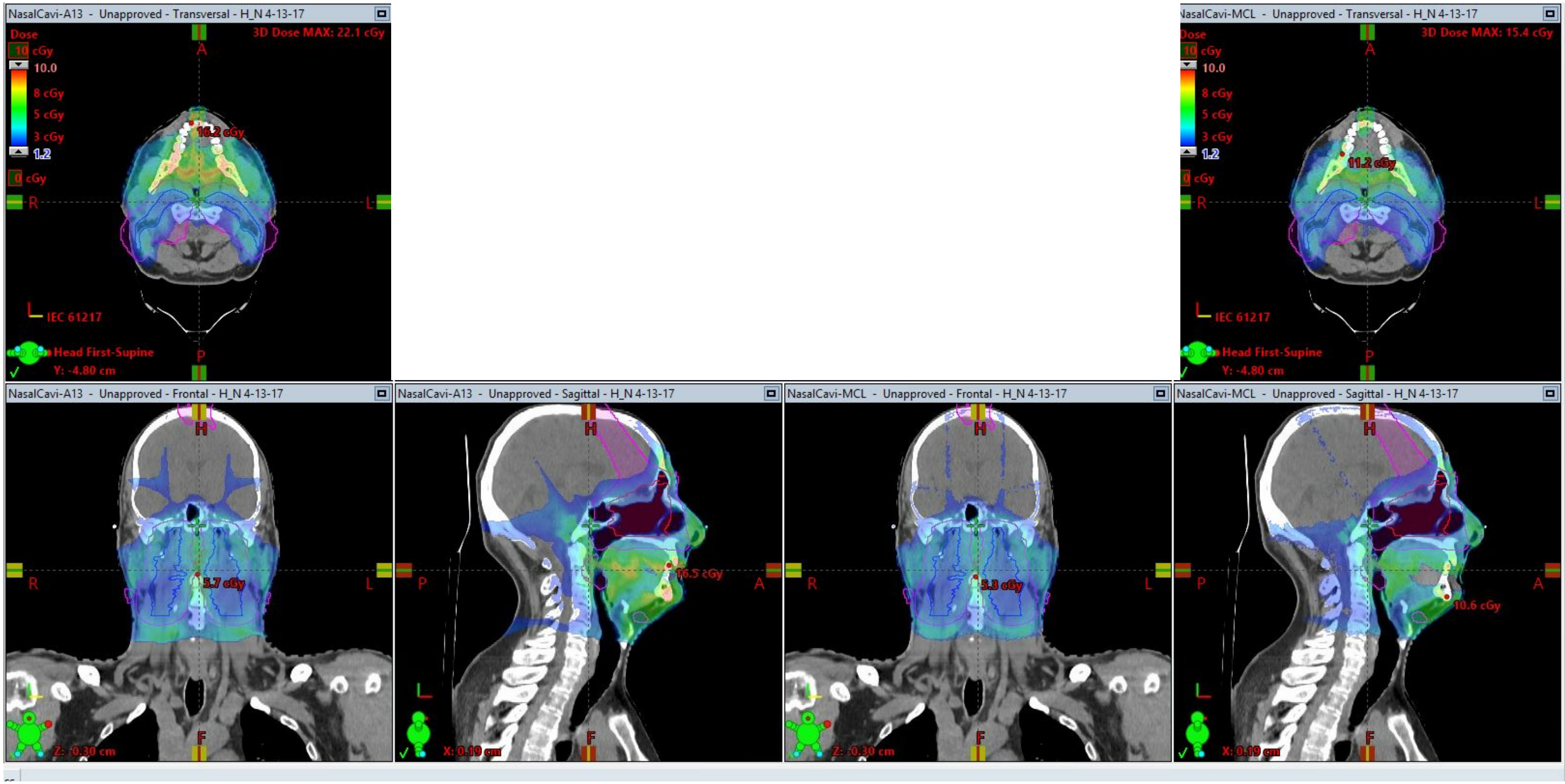
Sample LET lateral profile from Geant4 in water for 228.8 MeV and 71.3 MeV at different depths



- Red: Geant4 simulation
- Blue: 1D LET calculation model
- Black: Fitted results

$$LET_d(E, z_{WET}, r) = a_3(E, z_{WET}) + a_2(E, z_{WET}) \times \int_0^{r-a_4(E, z_{WET})} \exp(-a_1(E, z_{WET}) \times r^2)\, dr$$

Calculate LET in patients using the hybrid 3D model



Analytical

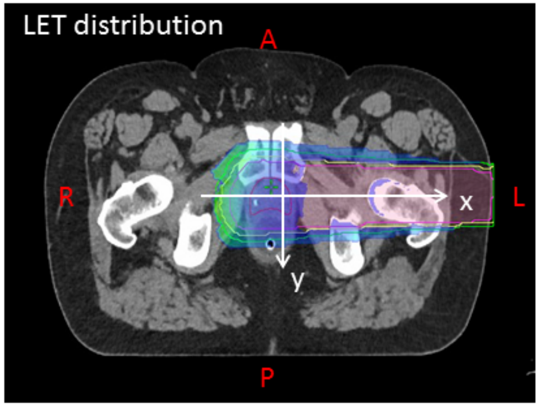
Monte Carlos

$$LET_{d,w}(x,y,z) = \frac{\sum_{j=1}^{n_s} (LET_d)_j(x,y,z) \cdot D_j(x,y,z)}{D(x,y,z)}$$

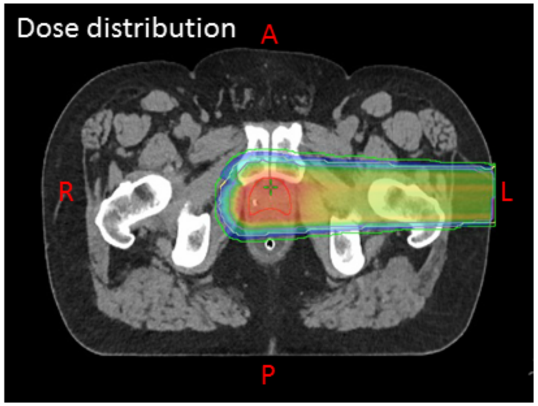
$$LET_{d,m}(x,y,z) = LET_{d,w}(x,y,z) \times S_{rel}(x,y,z)$$

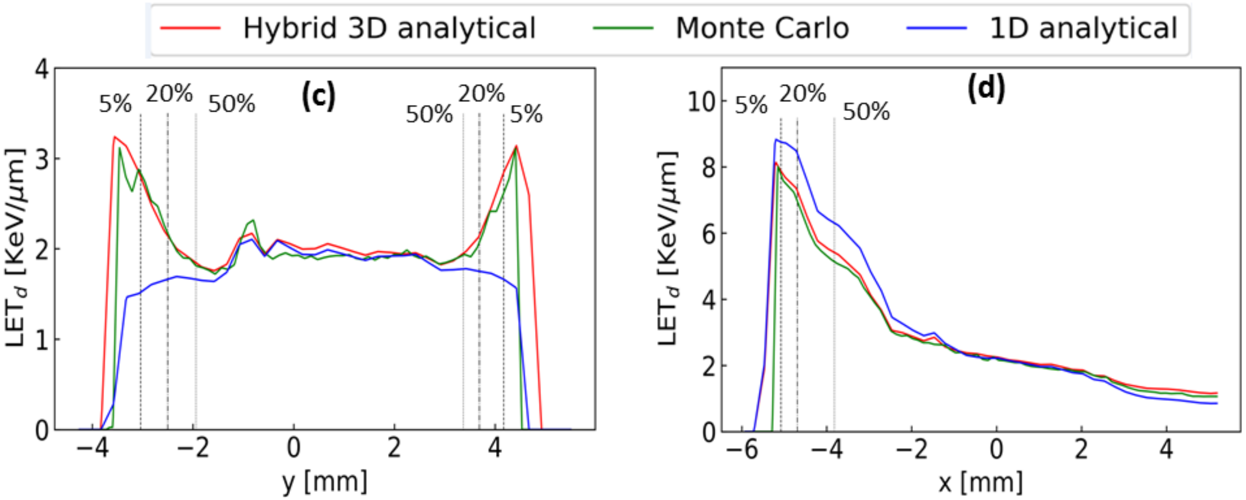
Comparison between Hybrid 3D analytical, 1D analytical, and Monte Carlo LET calculation: (1) Prostate

(a)



(b)





(e)

	5% dose level	20% dose level	50% dose level
Diff-1 (new method and MC)	3%	1%	1%
Diff-2 (old method and MC)	-52%	-22%	-8%

Performance comparison between hybrid 3D and 1D LET calculation in 12 patients across various disease sites

3D-3D Gamma Analysis (3mm/2%/10%) and Calculation Time

Patient	Hybrid 3D method passing rate	1D method passing rate	hybrid 3D method calculation time [s]	gMC calculation time [s]
Prostate	97.8%	89.5%	76	405
Prostate	97.6%	91.9%	50	366
Prostate	98.8%	90.8%	38	325
Prostate	97.6%	93.5%	86	469
Head & neck	96.4%	93.3%	29	361
Head & neck	98.0%	93.8%	93	422
Head & neck	97.6%	96.8%	110	1011
Lung	98.6%	95.5%	96	182
Lung	98.2%	95.7%	190	363
Brain	99.2%	97.8%	88	483
Breast	96.1%	93.0%	232	301
Craniospinal	99.7%	96.5%	655	722
Average ± standard deviation	98.0±1.0%	94.0±2.5%	145±171	451±218
P value	0.0003			

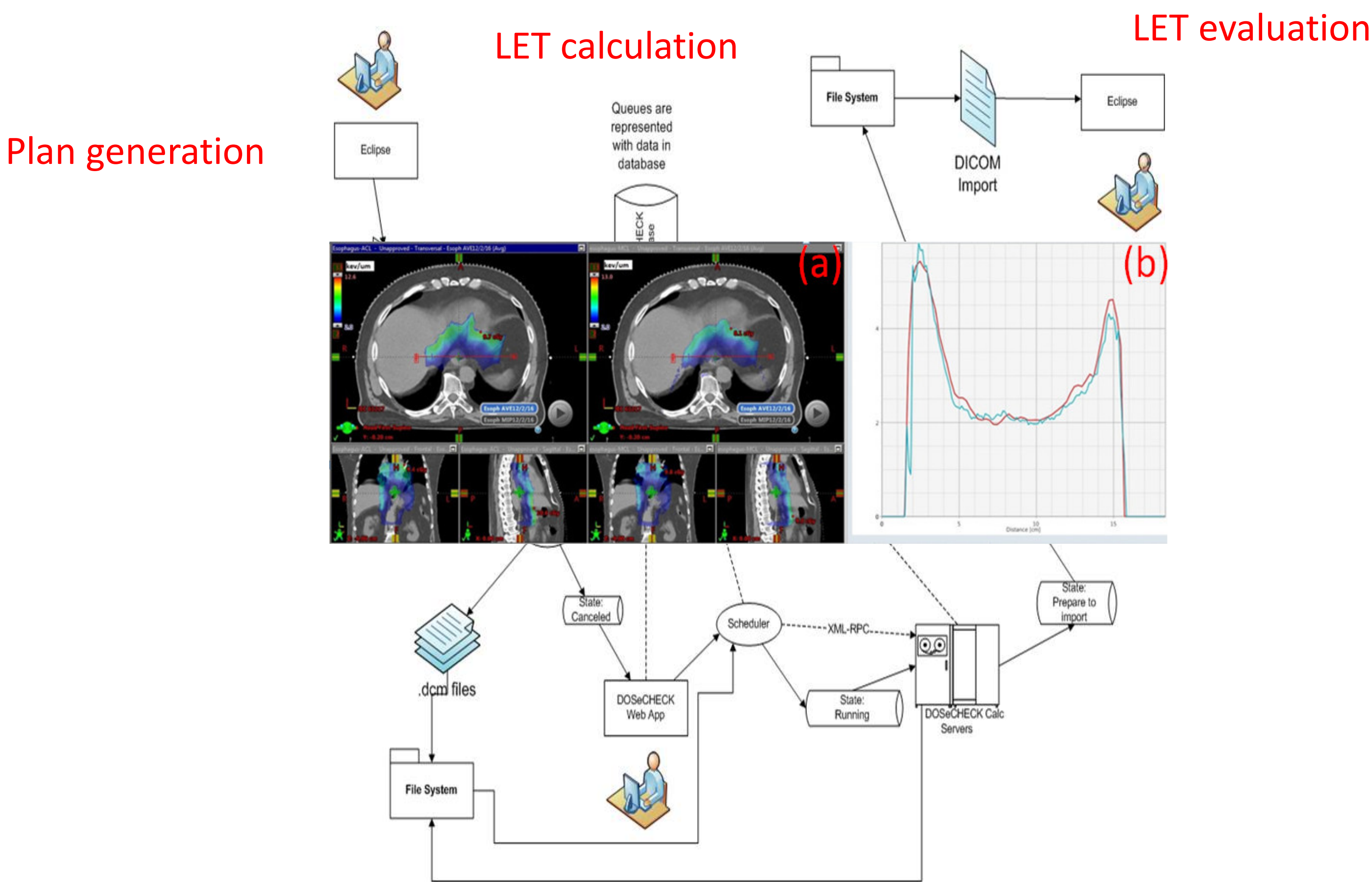
Dual ES 2680-v3 CPUs and 64GB (2133MHz) RAM

HOW TO USE LET IN PLAN QUALITY EVALUATION IN IMPT

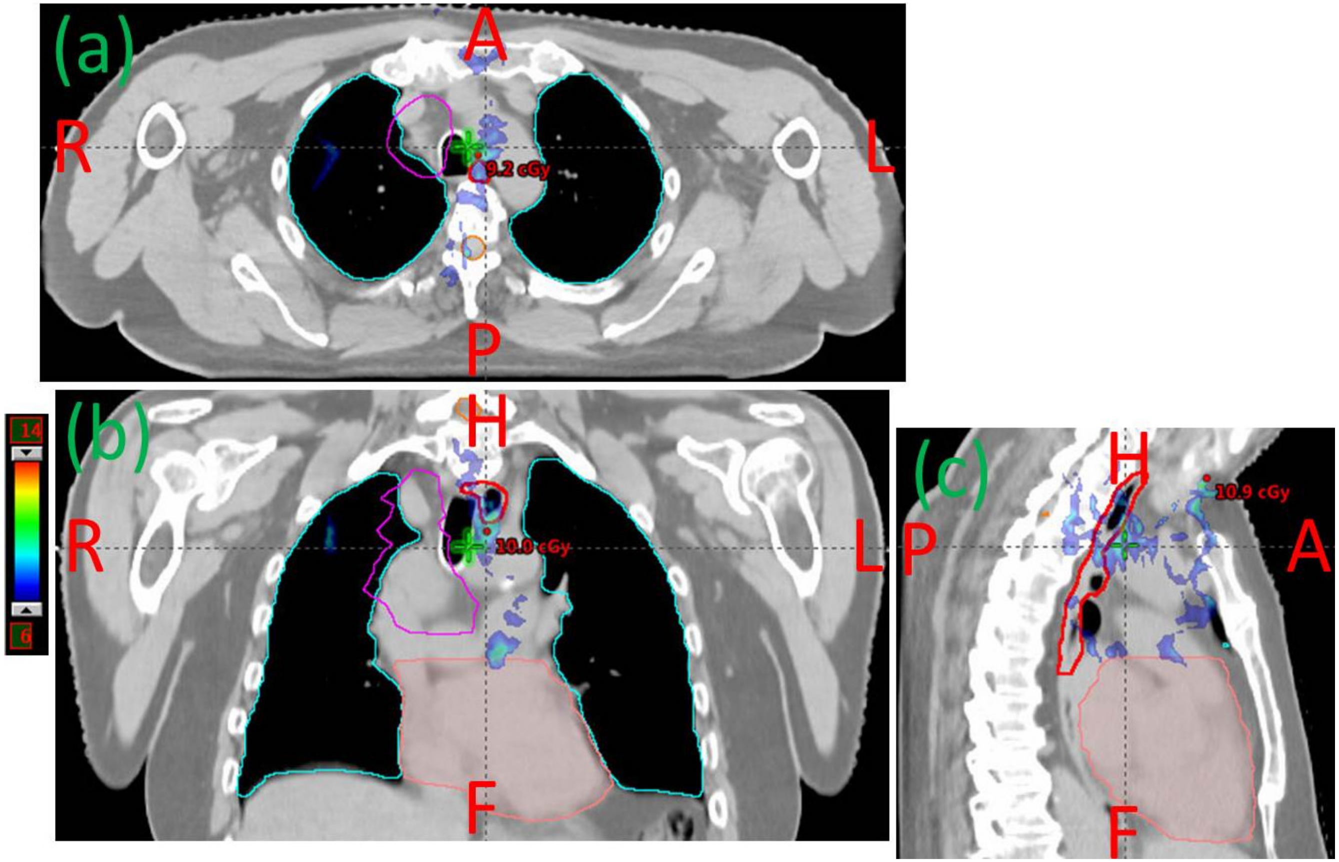
Use of LET at Mayo Clinic in Arizona

- Every patient receives an LET calculation
- LET distribution are imported into Varian Eclipse TPS for display purposes.
- A planning goal is to keep LET below 6 keV/μm within the high dose region of nearby critical organs.

Computational Environment



High LET distribution (greater than 6 keV/μm) overlaps within the high dose region

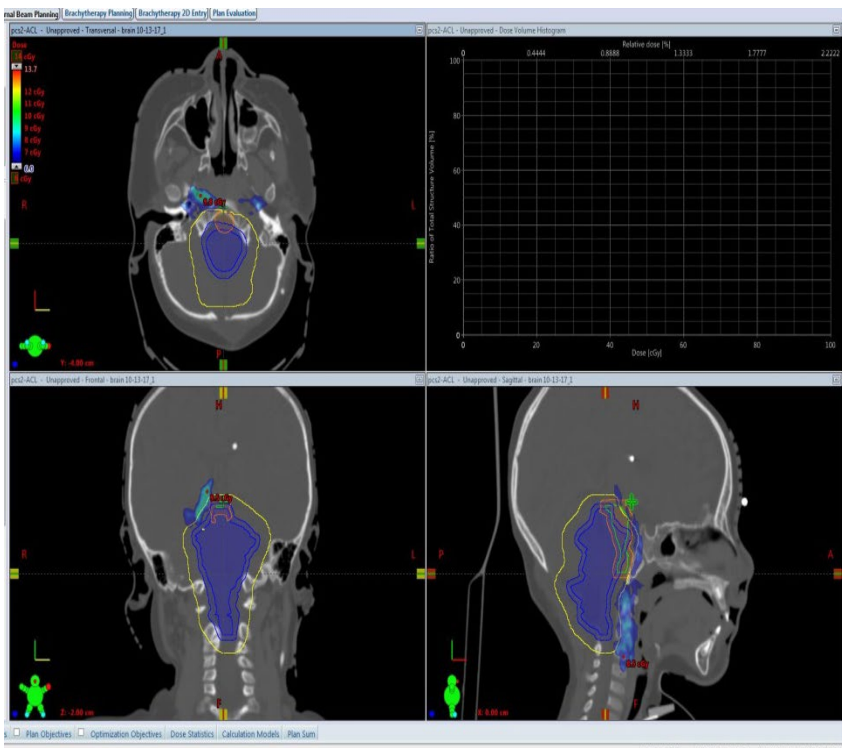


ITV: Magenta Esophagus: Red Cord: Orange Heart: Pink Total Lung: Cyan

High LET distributions are observed in critical organs.

Beam angle change was performed due to LET-guided plan evaluation in IMPT to minimize the overlap region of high dose and high LET in critical OARs

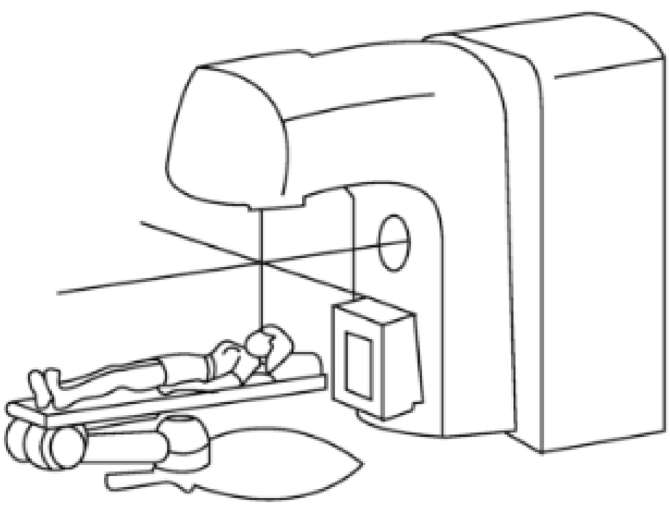
Initial plan LET distribution



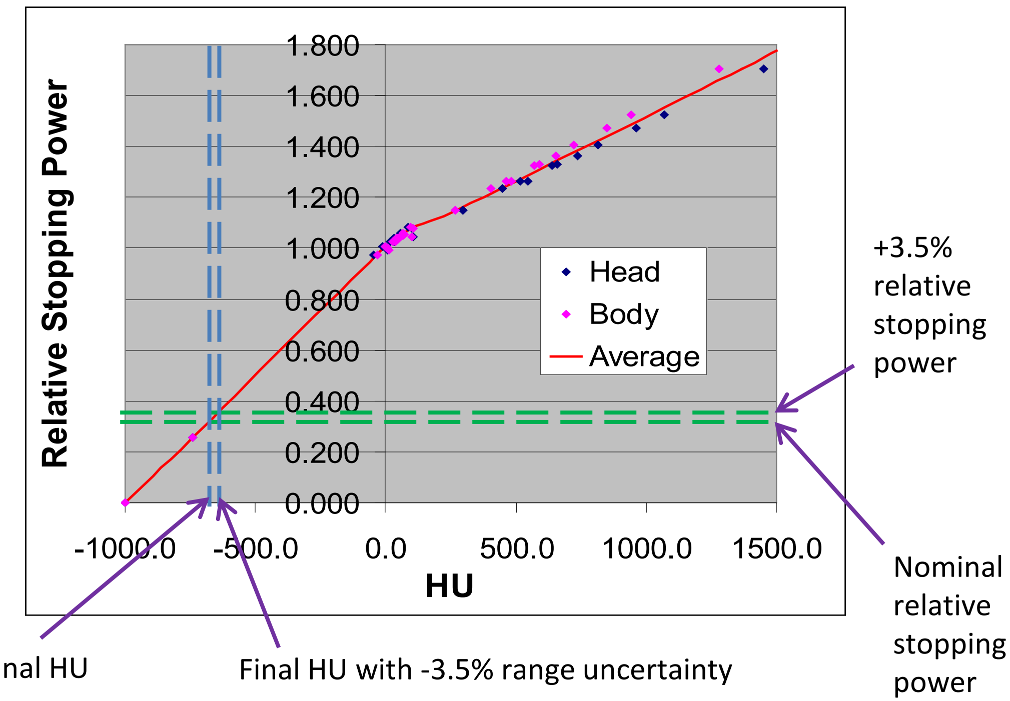
Final plan LET distribution

HOW TO USE LET TO IMPLEMENT LET-GUIDED ROBUST OPTIMIZATION IN IMPT

Accounting for setup and range uncertainties: robust optimization

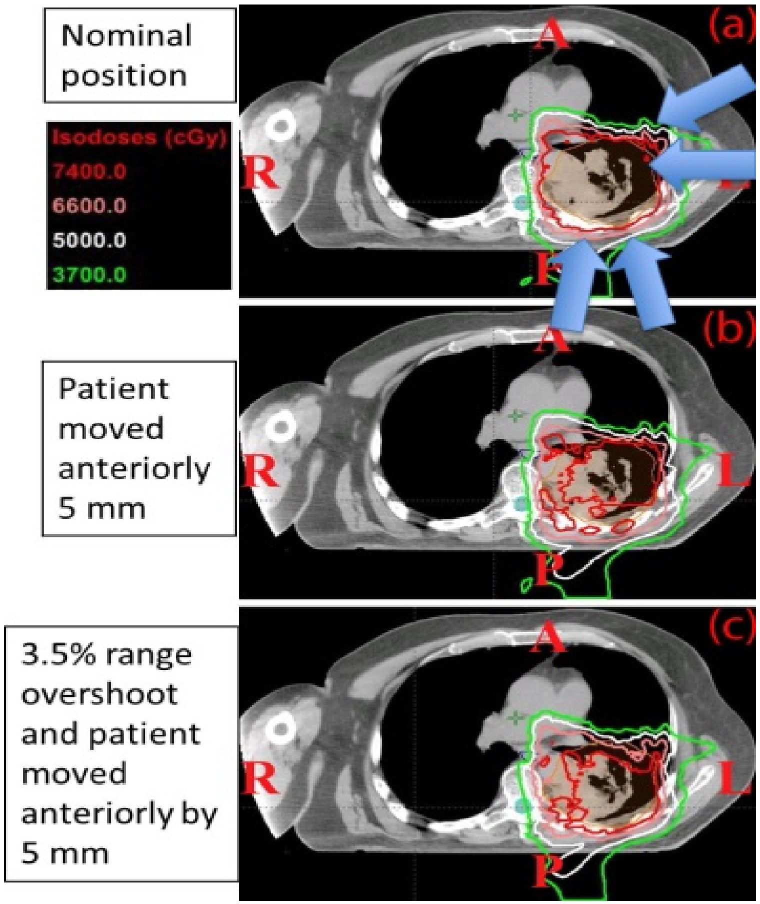


Setup Uncertainties



Range Uncertainties

LET and uncertainties combined



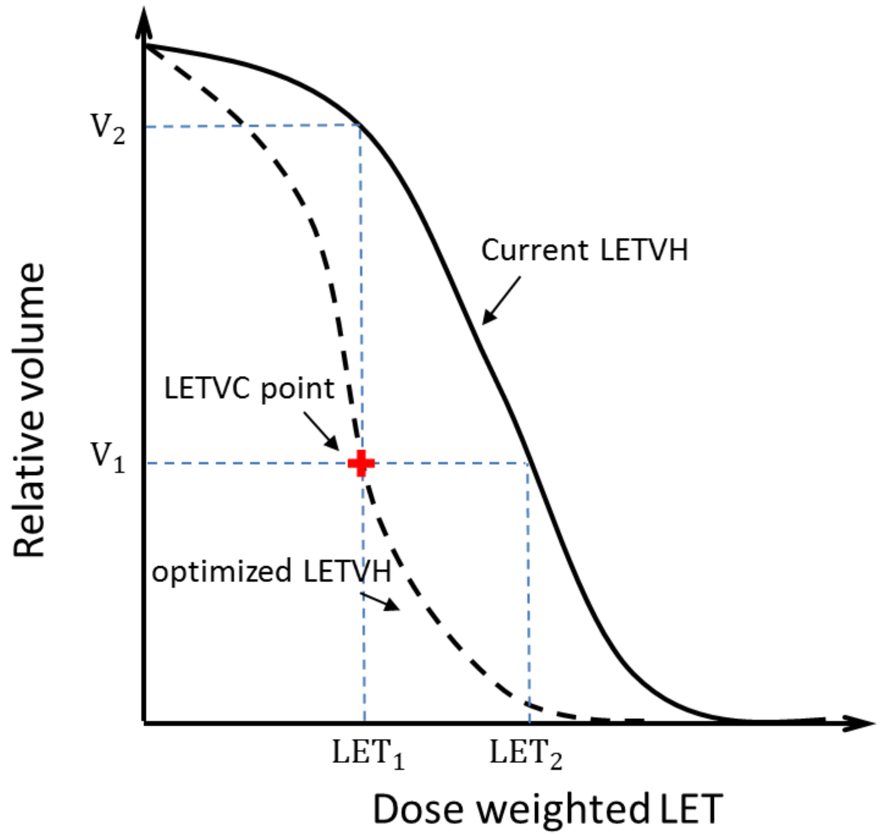
- **LET will also change under different uncertainty scenarios**

More Challenging Problem

Question

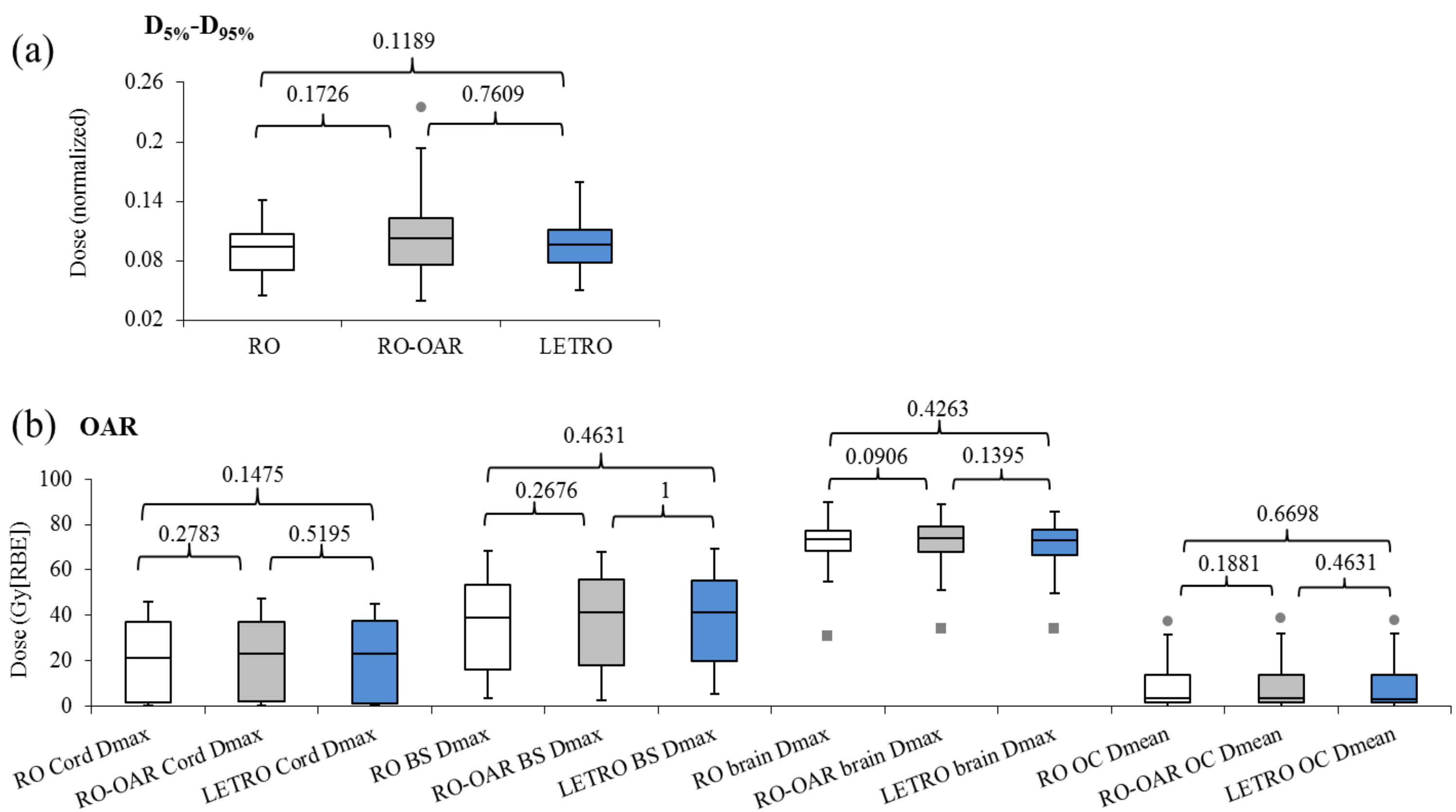
Can we find a robust treatment plan, which also redistribute high LET from organs at risk to tumors?

LET volume histograms and LET volume constraints in LET guided robust optimization

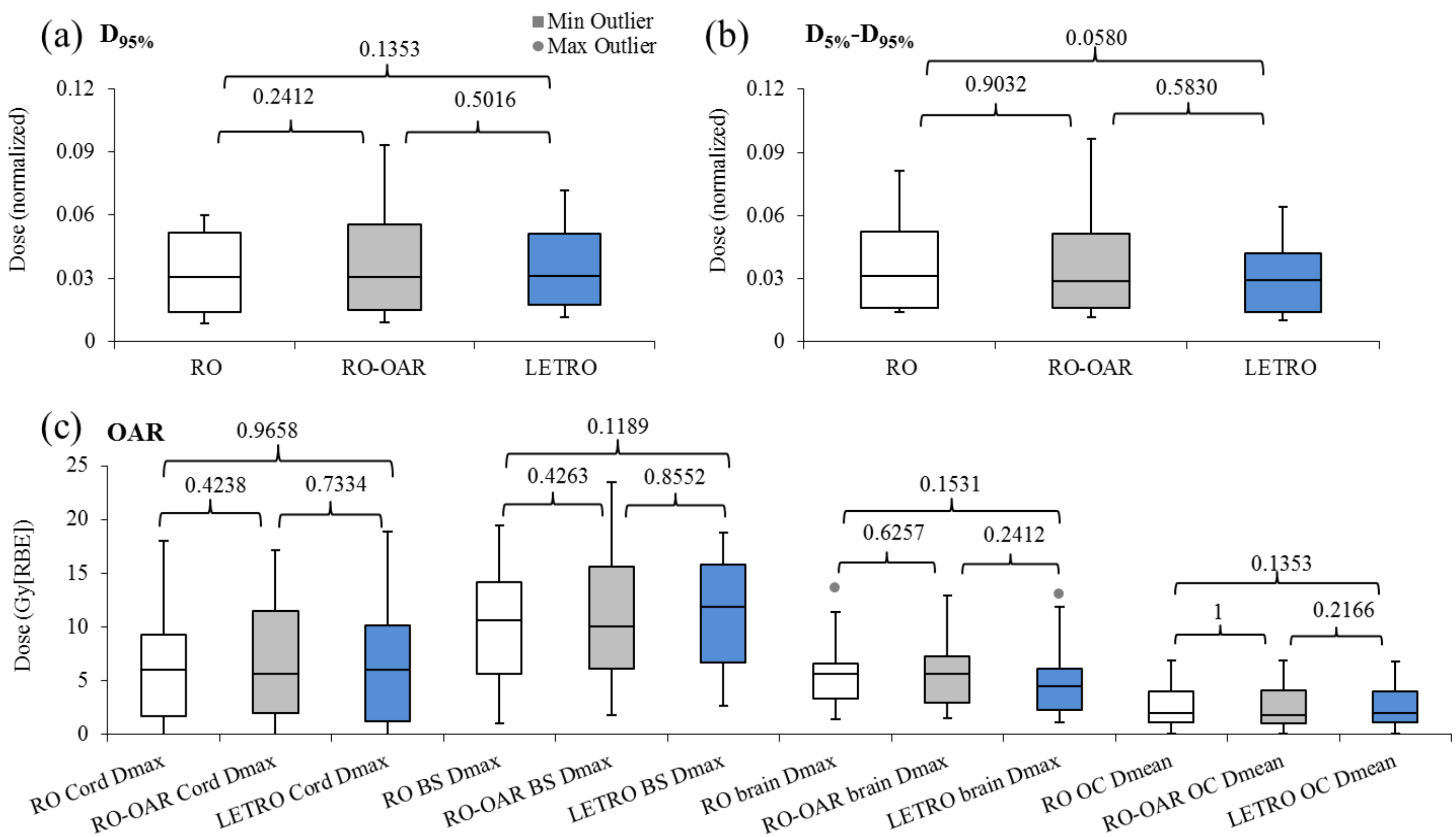


Only the voxels with LET between LET_1 and LET_2 are penalized in the LET-guided robust optimization.

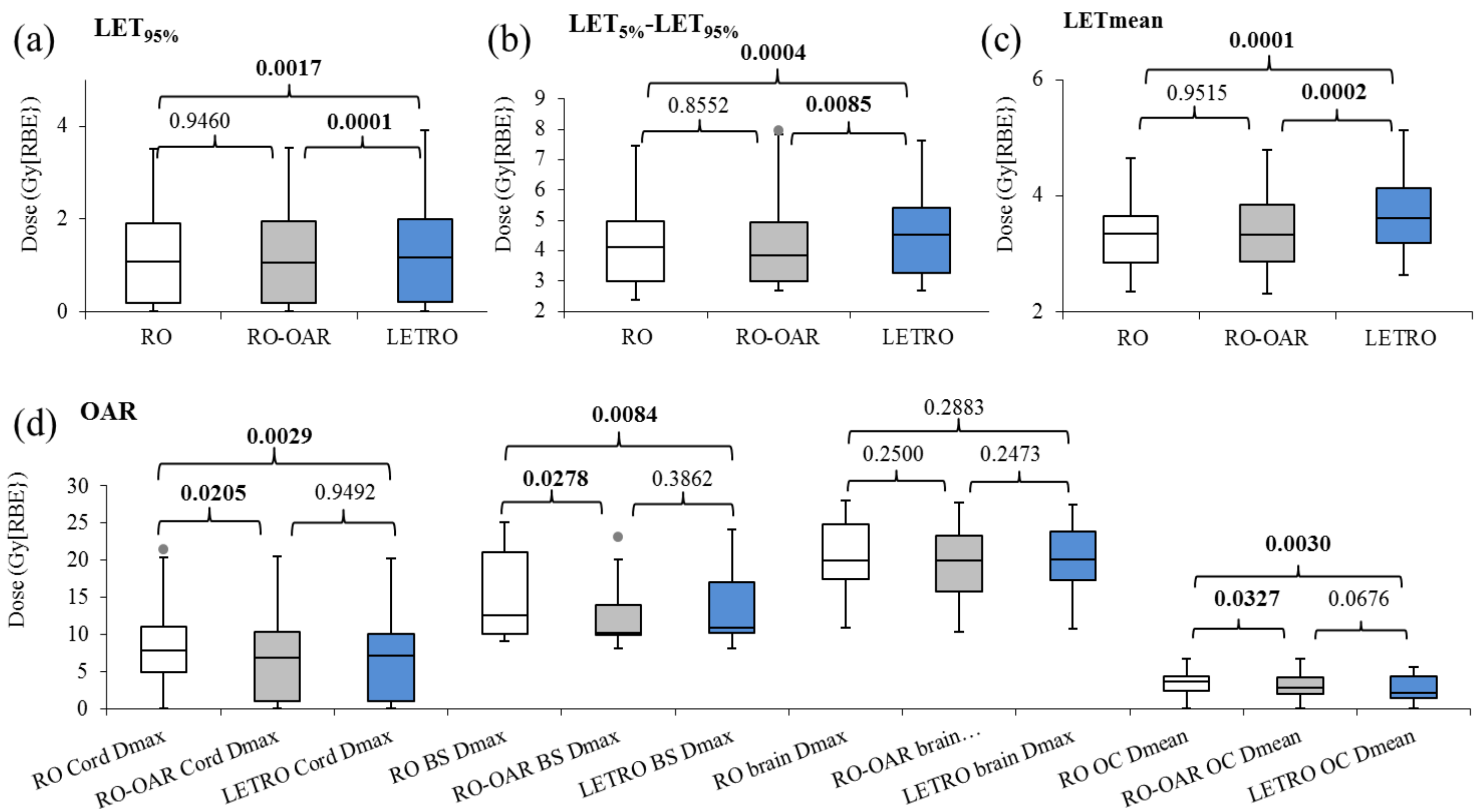
Comparison of the DVH indices of the treatment plans generated by RO, RO-OAR, and LETRO

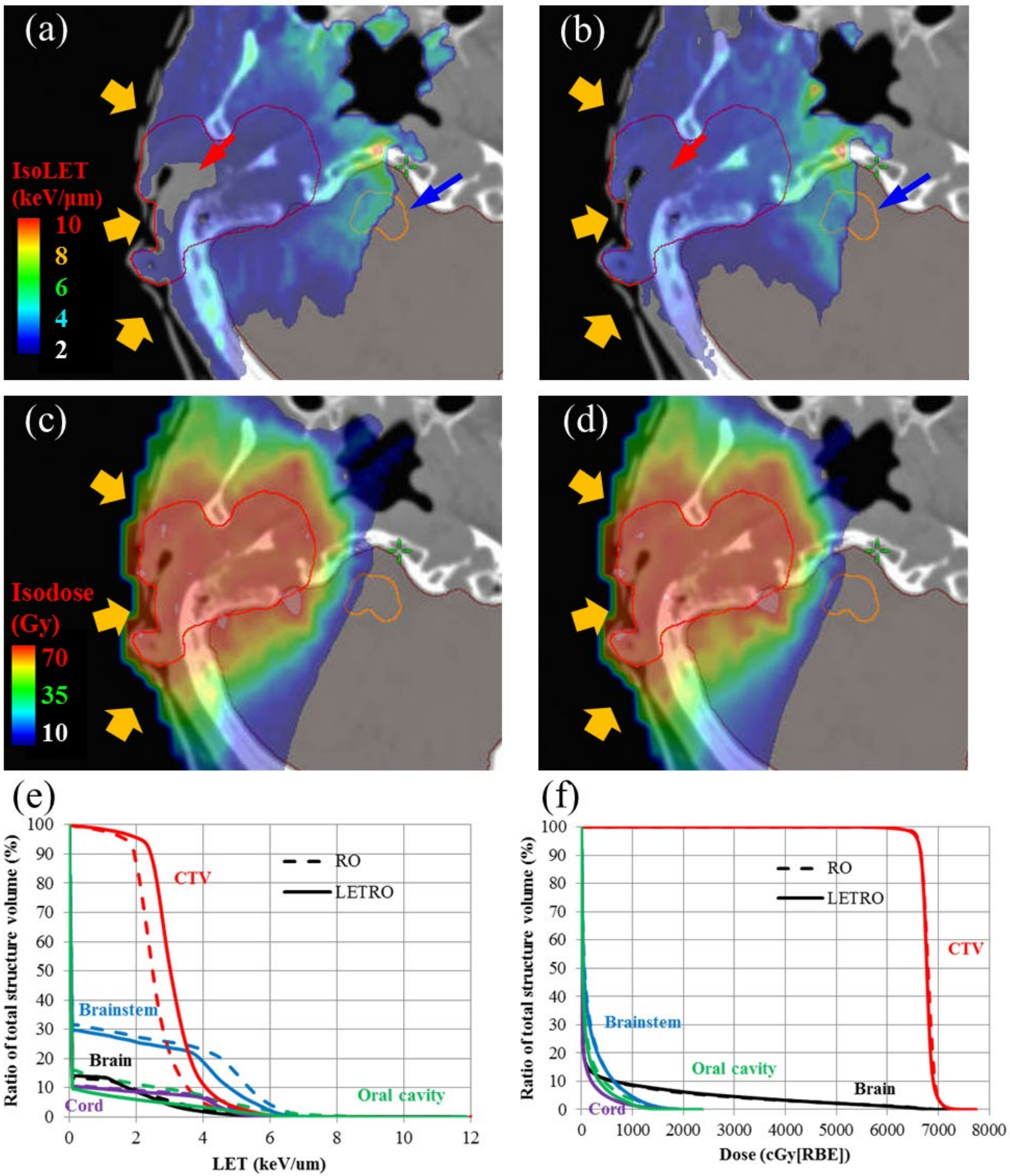


Comparison of plan robustness of the treatment plans generated by RO, RO-OAR, and LETRO



Comparison of LET dosimetric indices of the treatment plans generated by RO, RO-OAR, and LETRO



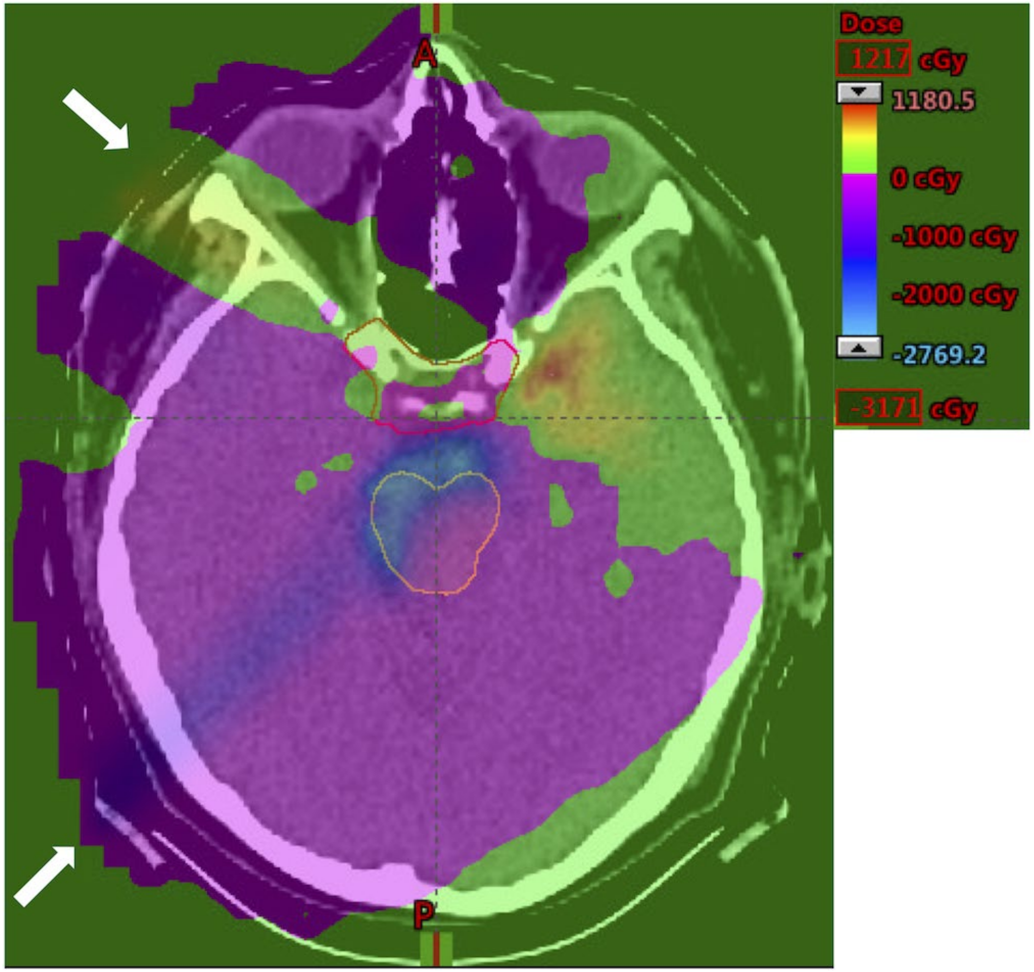


LET distribution

Dose distribution

LETVH and DVH

Why can LET-guided robust optimization redistribute LET distribution without sacrificing the physical dose distributions and plan robustness?



Medical Physics
The International Journal of Medical Physics Research and Practice

Explore this journal >

Research Article

Robust intensity-modulated proton therapy to reduce high linear energy transfer in organs at risk

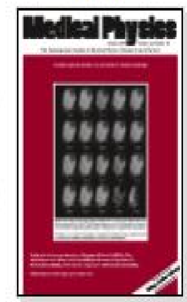
Yu An, Jie Shan, Samir H. Patel, William Wong, Steven E. Schild, Xiaoning Ding,
Martin Bues, Wei Liu

First published: 26 October 2017 Full publication history

DOI: 10.1002/mp.12610 View/save citation

Funding Information

Early View



Browse Early View Articles
Online Version of Record published before inclusion in an issue

Editor's Choice in *Med. Phys.* in 2017

Conclusion

- Hybrid 3D model can calculate the LET accurately and efficiently in IMPT
- LET-guided plan evaluation is important to minimize the overlap between high dose and high LET in IMPT
- LET-guided robust optimization redistributes high LET from OARs to tumors, thus it potentially improves tumor control without sacrificing the physical dose distributions quality and plan robustness

Acknowledgement

Physicians:

Dr. Steven E. Schild
Dr. Samir Patel
Dr. Terence T. Sio
Dr. William Wong
Dr. Carlos Vargas
Dr. Sujay Vora

Physicists and Staffs:

Dr. Martin Bues
Dr. Xiaoning Ding
Dr. Jason Shen
Dr. Yanle Hu
Dr. Yixiu Kang
Mr. Kurt Augustine
Dr. Mirek Fatyga

PostDocs and Graduate Students:

Mr. Jie Shan
Dr. Yu An
Dr. Wei Deng
Dr. Chenbin Liu