Dose-Linear Energy Transfer (LET) Volume Histogram (DLVH) for Adverse Events Study in Intensity-Modulated Proton Therapy (IMPT)

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*Yang Y, Vargas CE, Bhangoo RS, Wong WW, Schild SE, Daniels TB, Keole SR, Rwigema JCM, Glass JL, Shen J, DeWees TA, Liu T, Bues M, Fatyga M, Liu W. Exploratory Investigation of Dose-Linear Energy Transfer (LET) Volume Histogram (DLVH) for Adverse Events Study in Intensity-Modulated Proton Therapy, *accepted by Int J Radiat Oncol Biol Phys*. 2021.

Disclosures

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- I am a PI on a grant funded by Arizona Department of Health Sciences (ADHS) (R01 type)
- The LET calculation software reported in this presentation has been licensed to .decimal LLC by Mayo Clinic

Outline

- Introduction of LET and RBE
  - Motivation of our study
- Dose-LET Volume Histogram (DLVH) for adverse events study in rectal bleeding
  - Study Design
  - Introduction of the tool of DLVH
  - Results
  - Clinical use of the proposed tool
- Summary

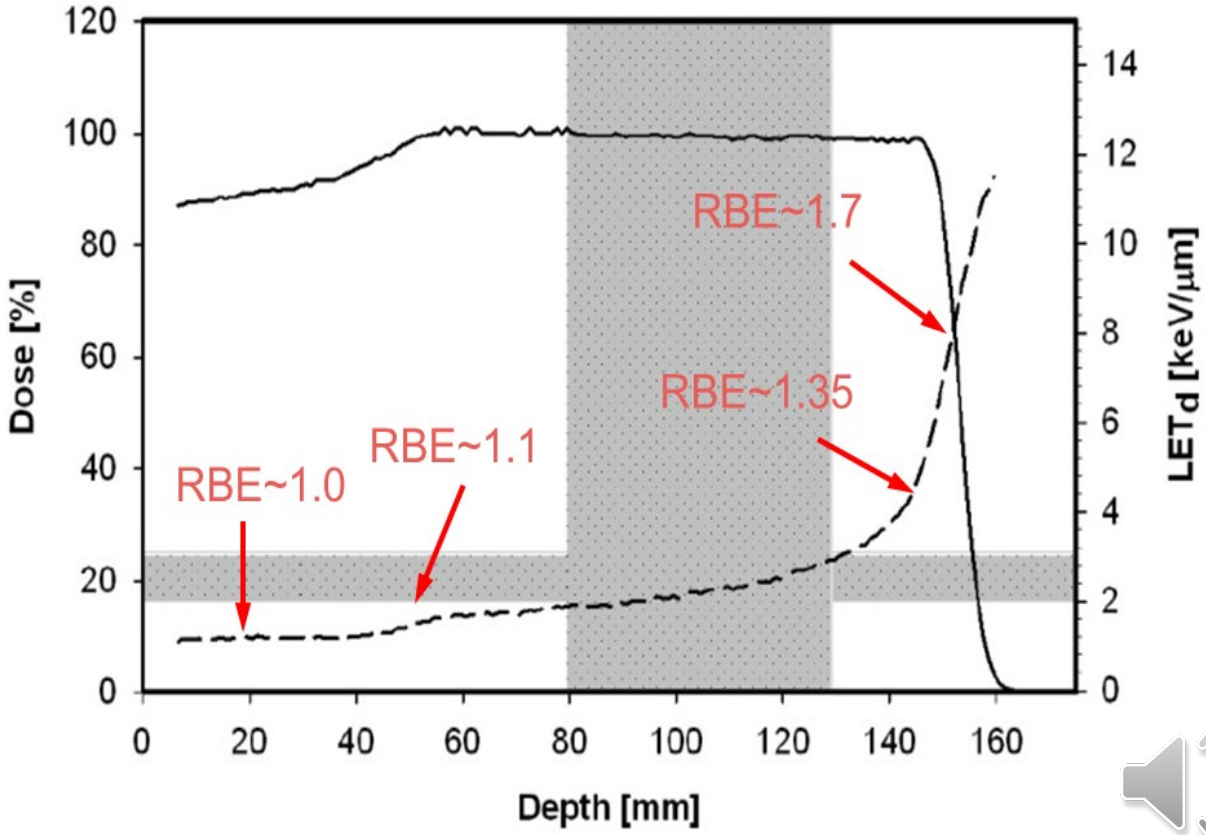
Linear Energy Transfer (LET)

- Average energy loss in a short distance (locally imparted)

$$LET = \frac{dE}{dx}$$

For protons

- Increases dramatically with the deceleration of the particles
- High at the end of the proton ranges
- Highly related to the relative biological effectiveness (RBE) of protons



However,……

- The LET effect to patient outcome is unclear
- The parameters of the current RBE models have lots of uncertainties
- Different RBE models give very different results
- Current IMPT planning ignores LET information and exclusively relies on physical dose
- The ignorance of LET distribution may result in severe AEs and undesirable patient outcome

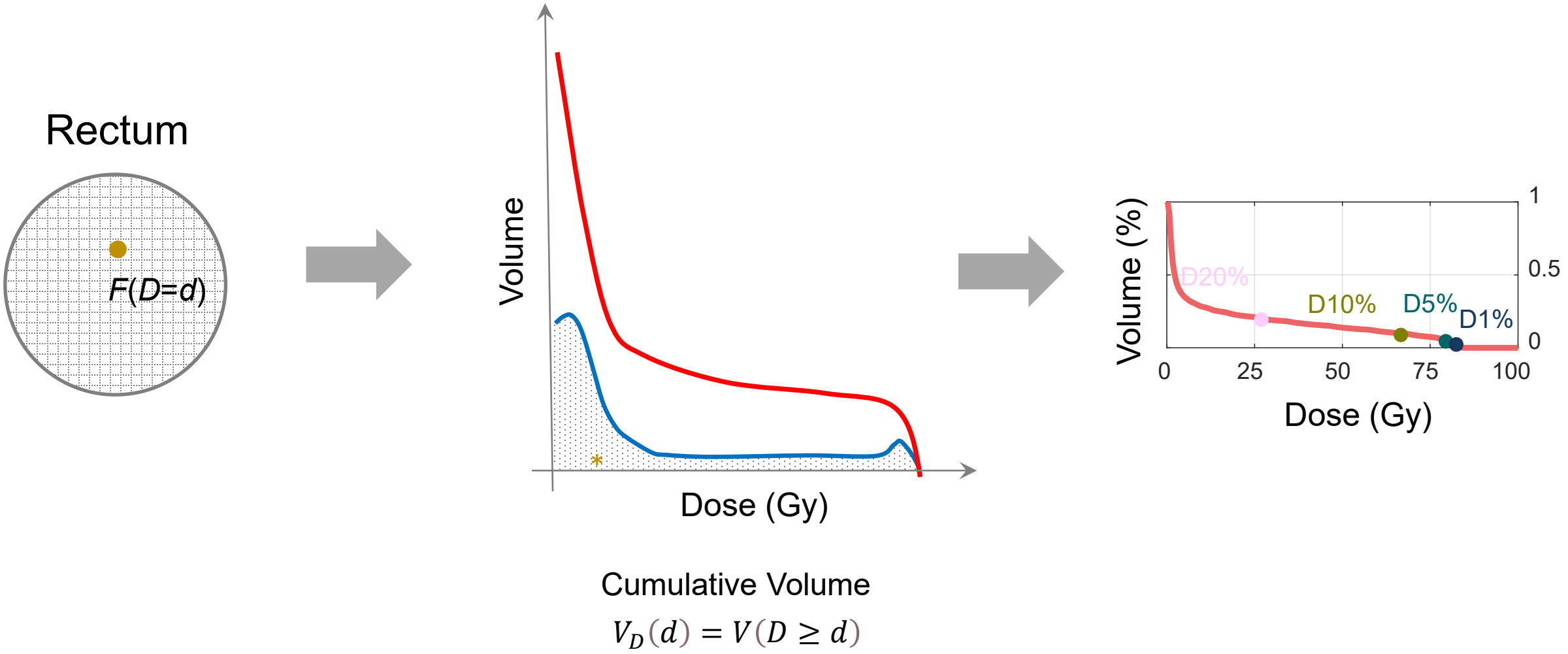
- It is important to bypass the uncertainties in the current RBE models, use accurate physics quantities like dose and LET to correlate patient outcomes data, and combine dose and LET for IMPT evaluation and treatment planning

Patient Cohort

Patient cohort: 57
Rectal bleeding: 9
Control: 48

- Aug 2016 – Sep 2017
- Conventional fractionations
- Alternating plans
- Bilateral fields
- Prostate only

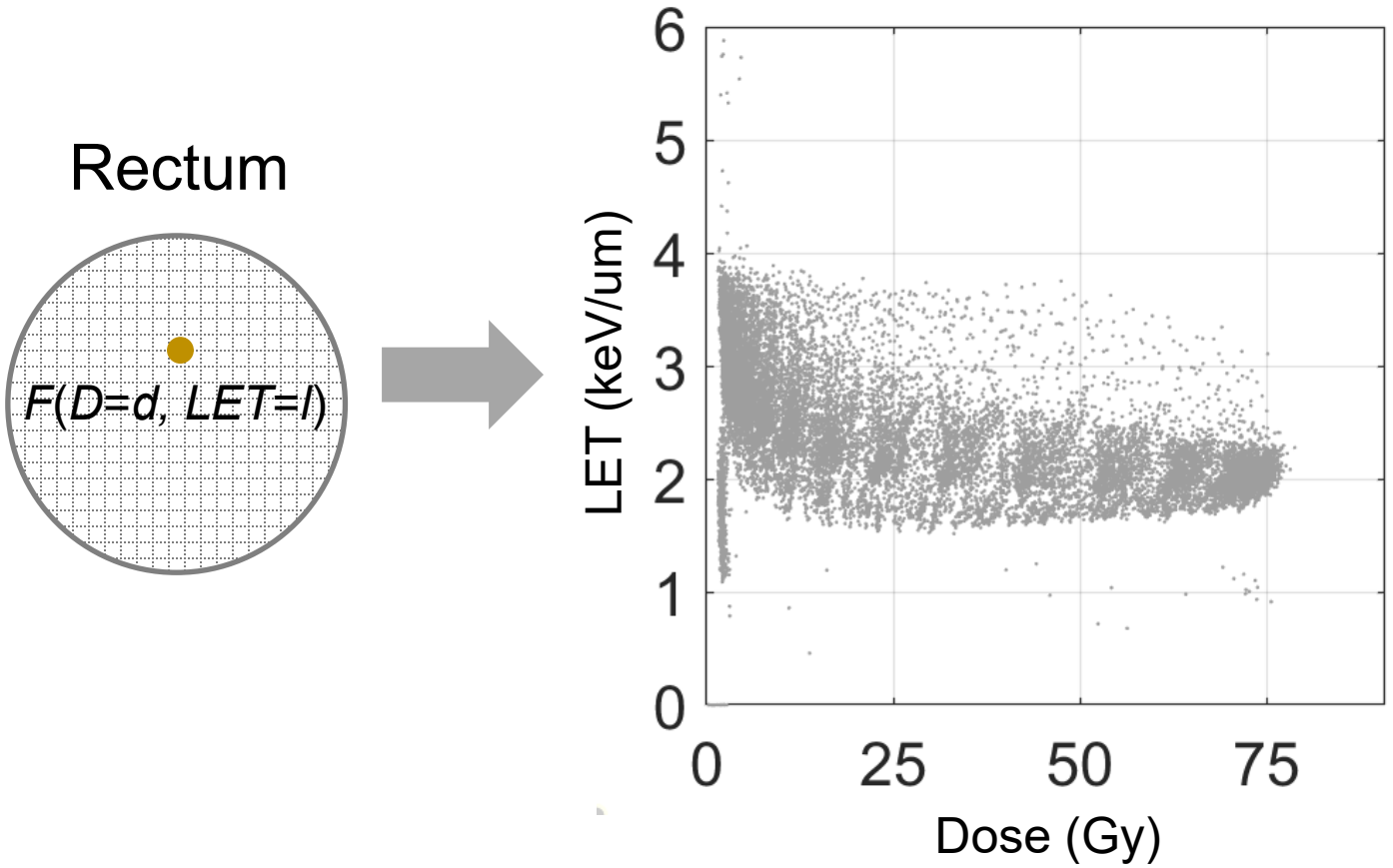
Dose Volume Histogram (DVH)



Cumulative Volume

$$V_D(d) = V(D \geq d)$$

Dose LET Volume Histogram (DLVH)



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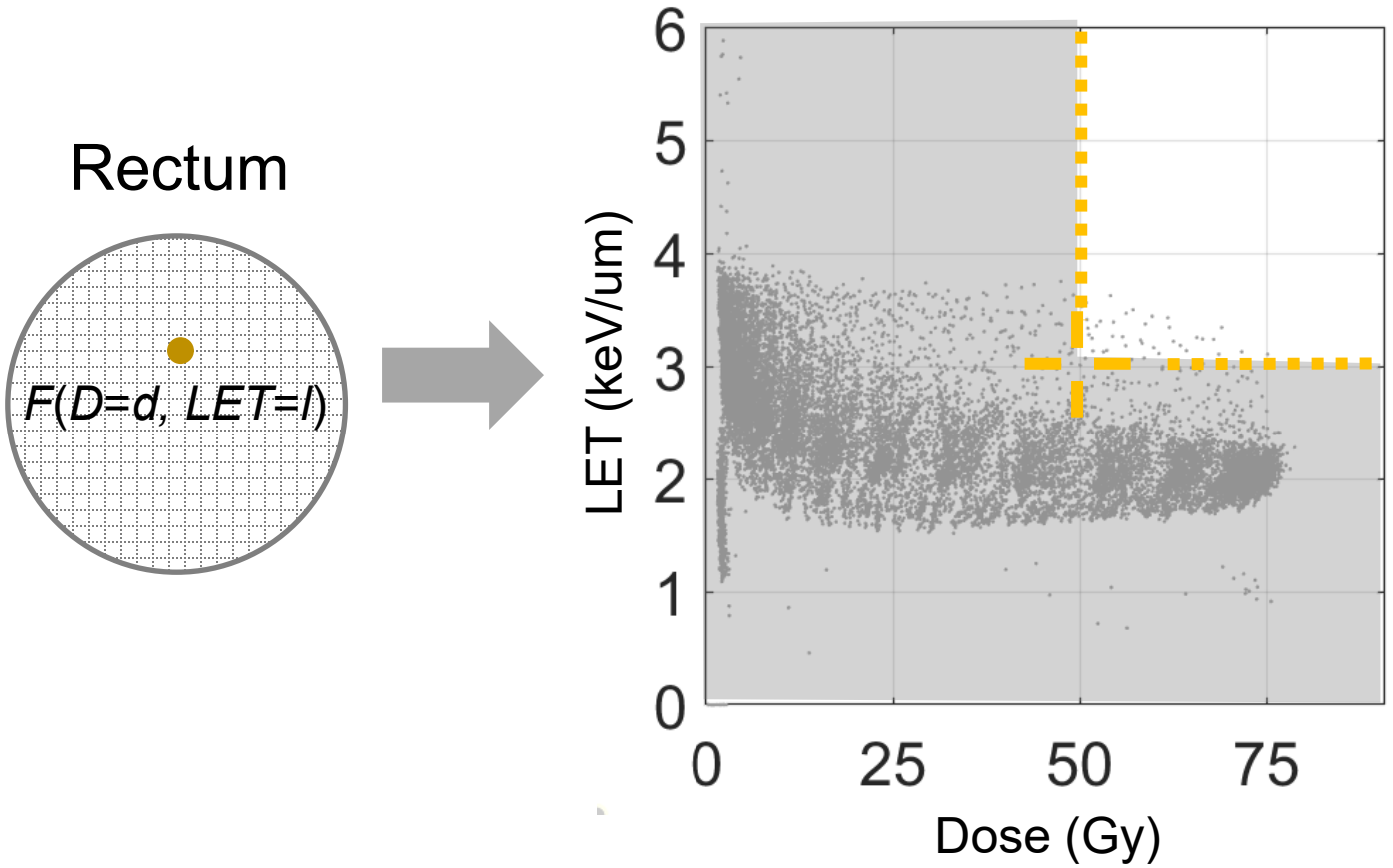
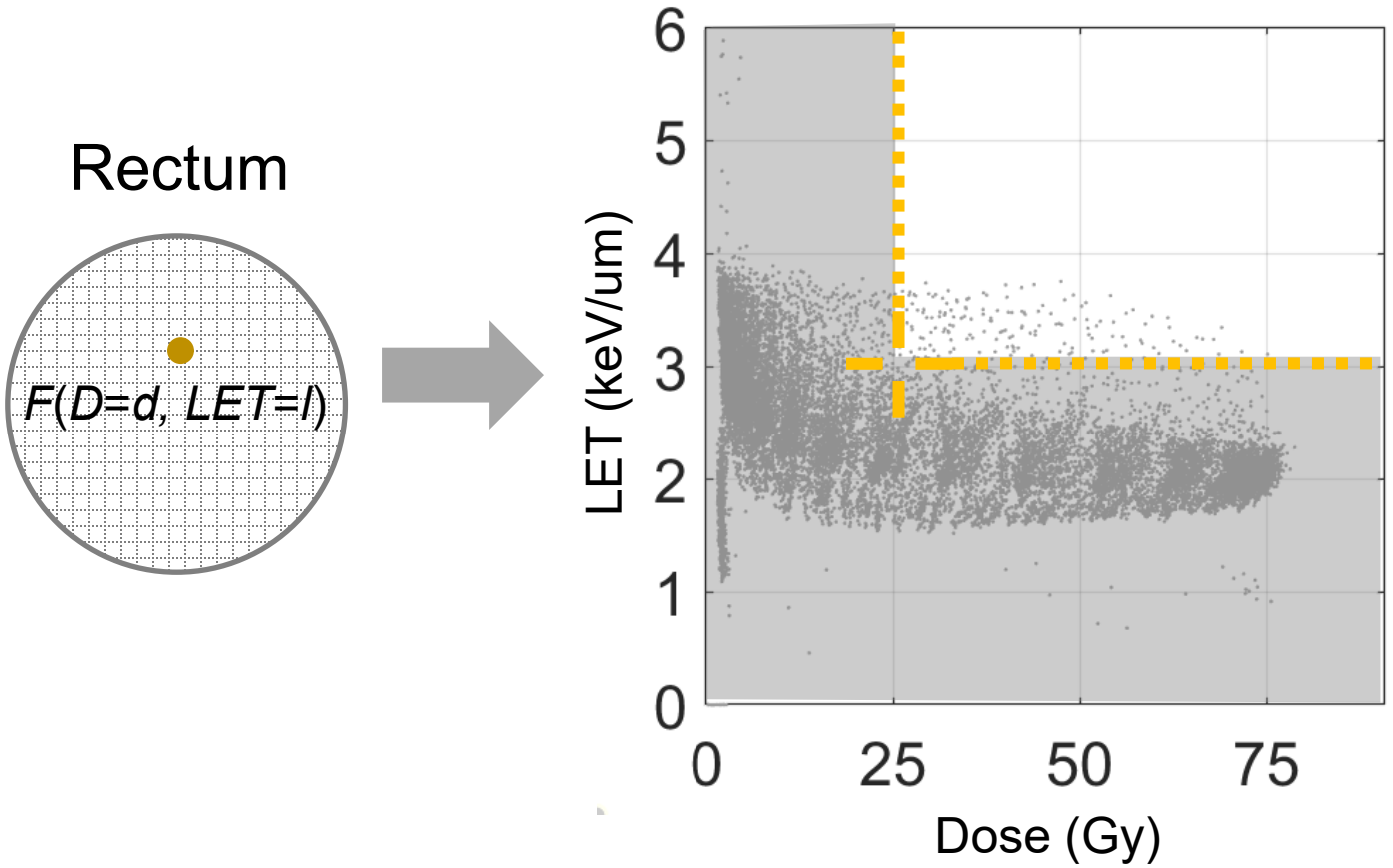


$$V_{D,LET}(d,l) = V(D \geq d, L \geq l)$$

Dose LET Volume Histogram (DLVH)



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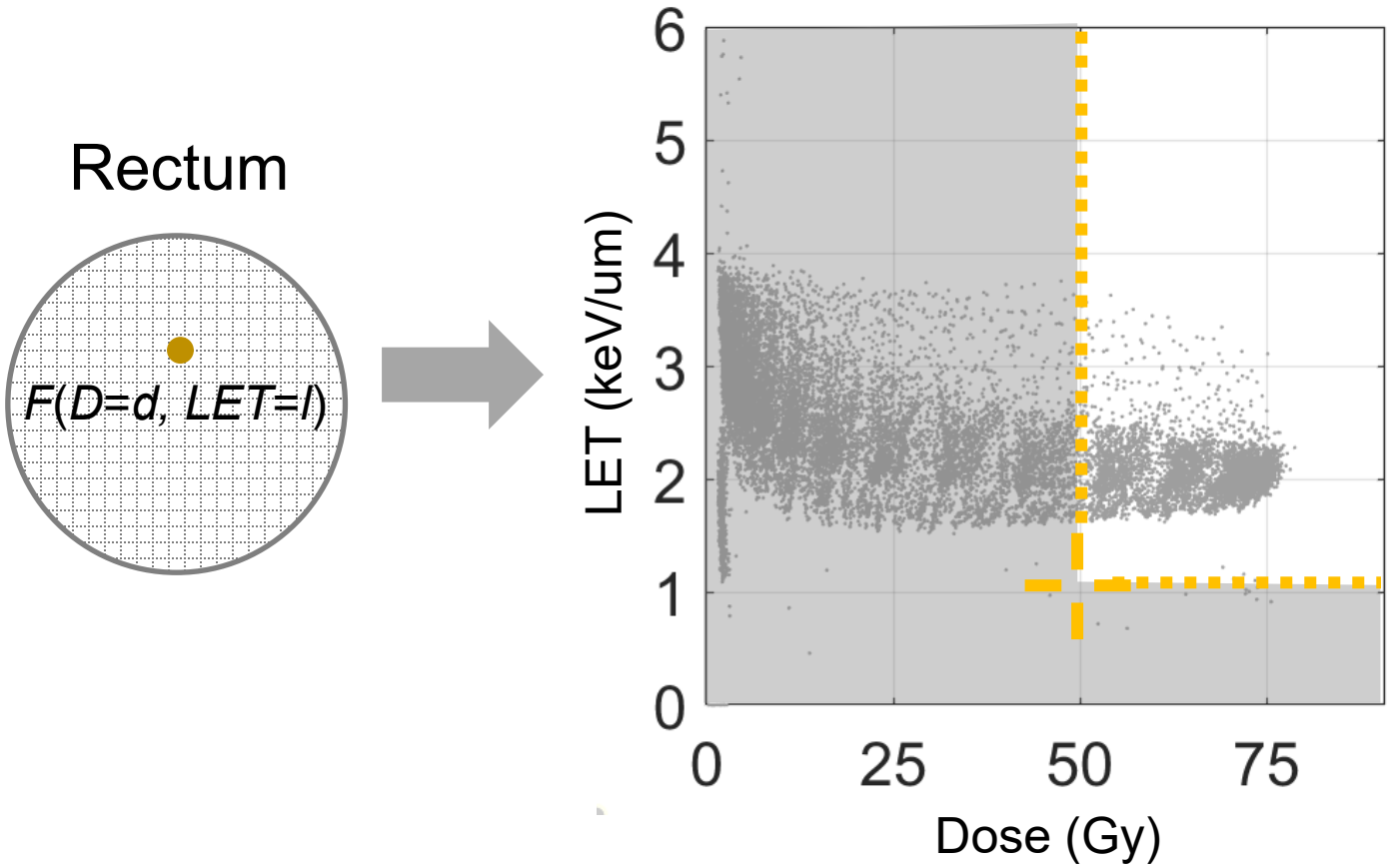
Dose LET Volume Histogram (DLVH)



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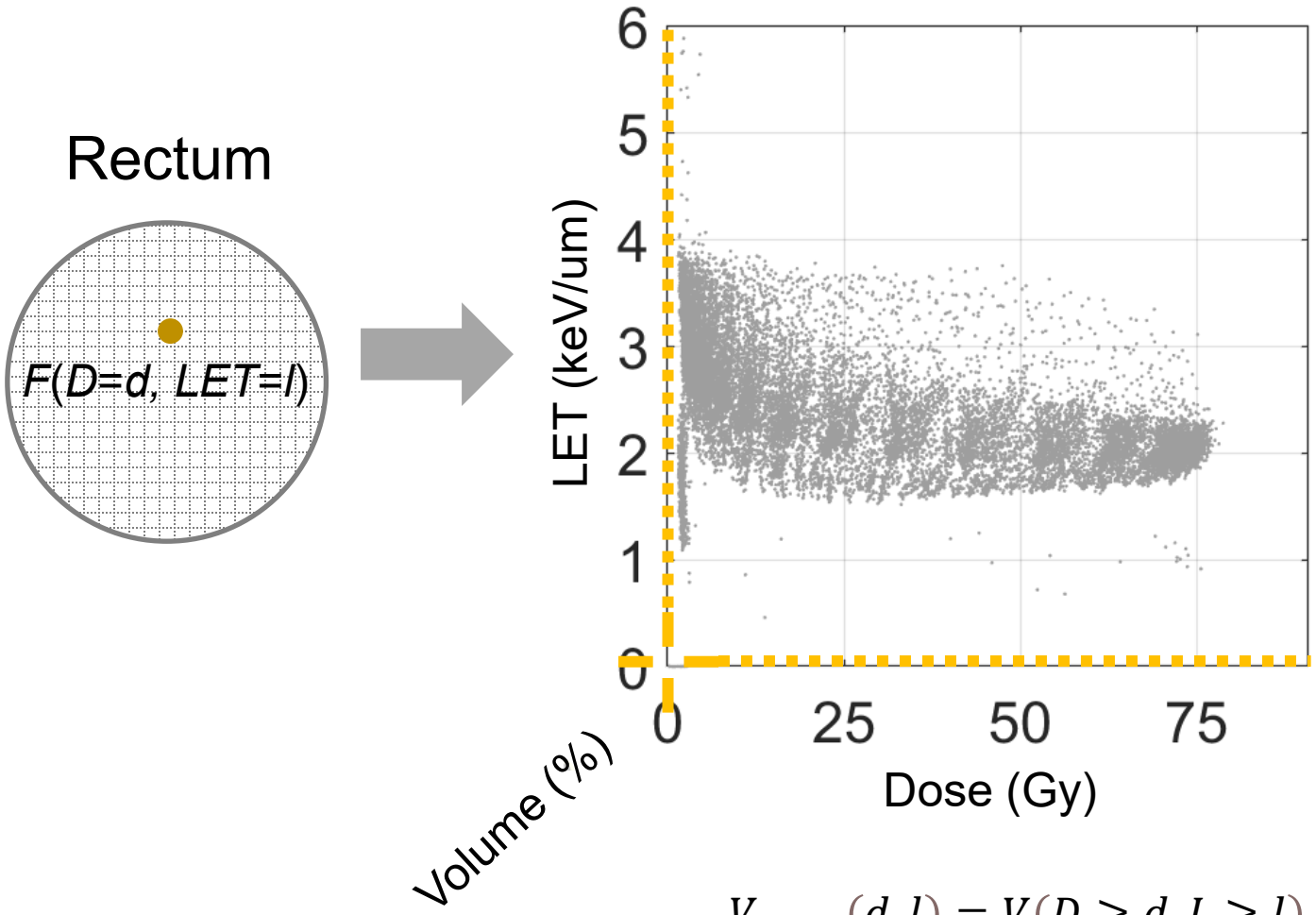

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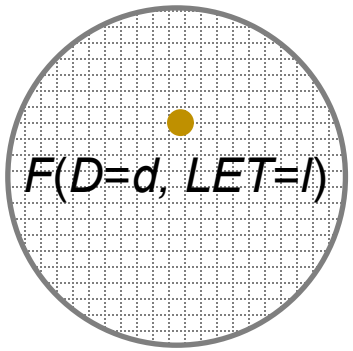

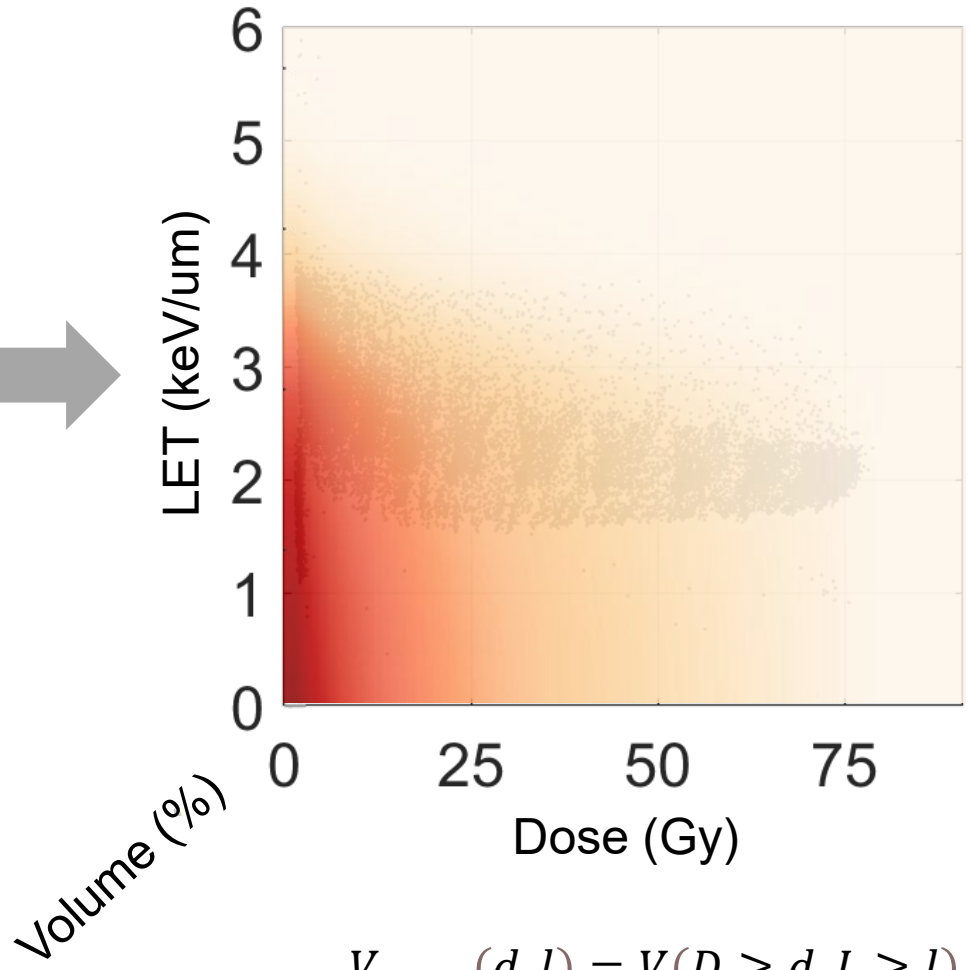

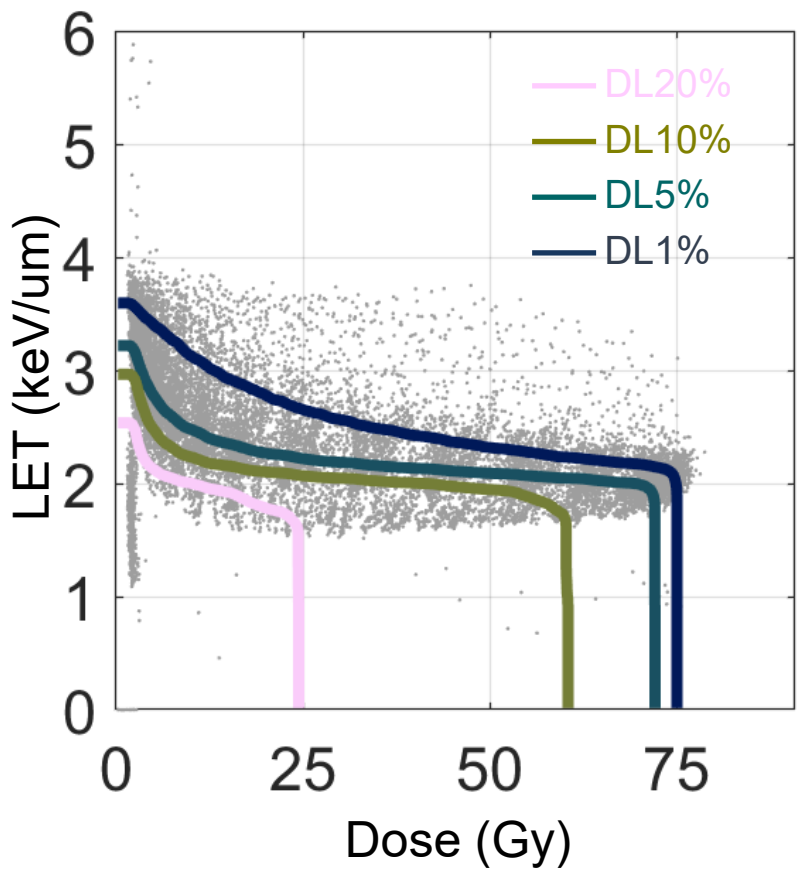

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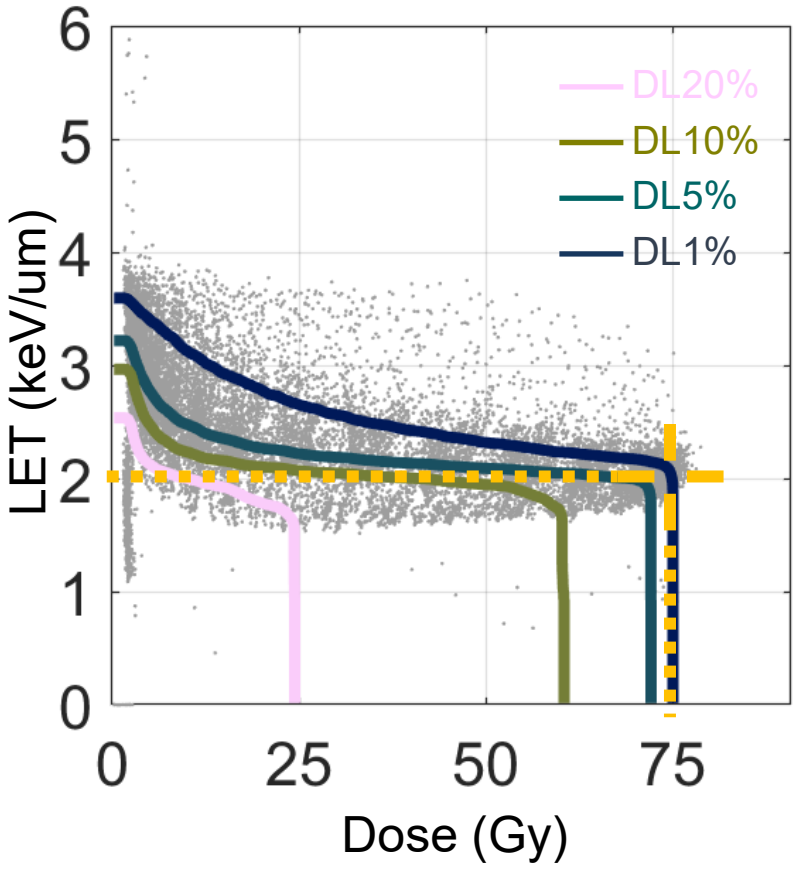
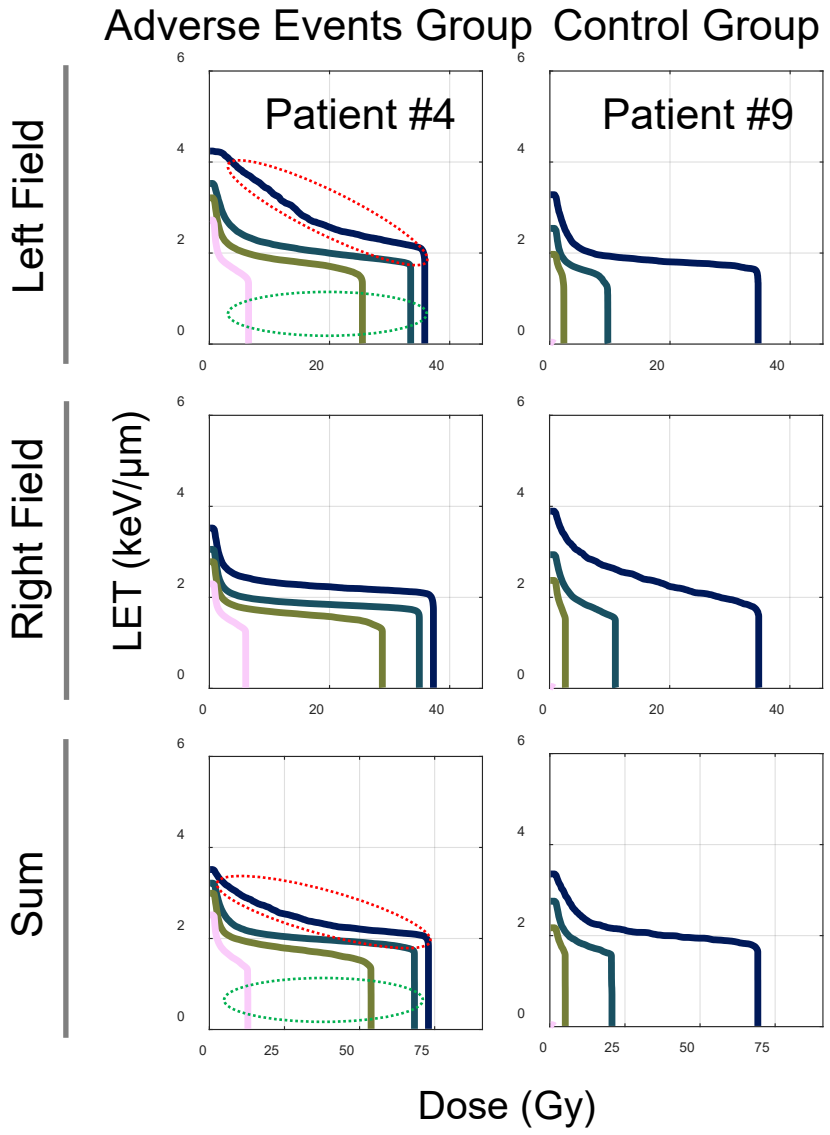
Dose LET Volume Histogram (DLVH)

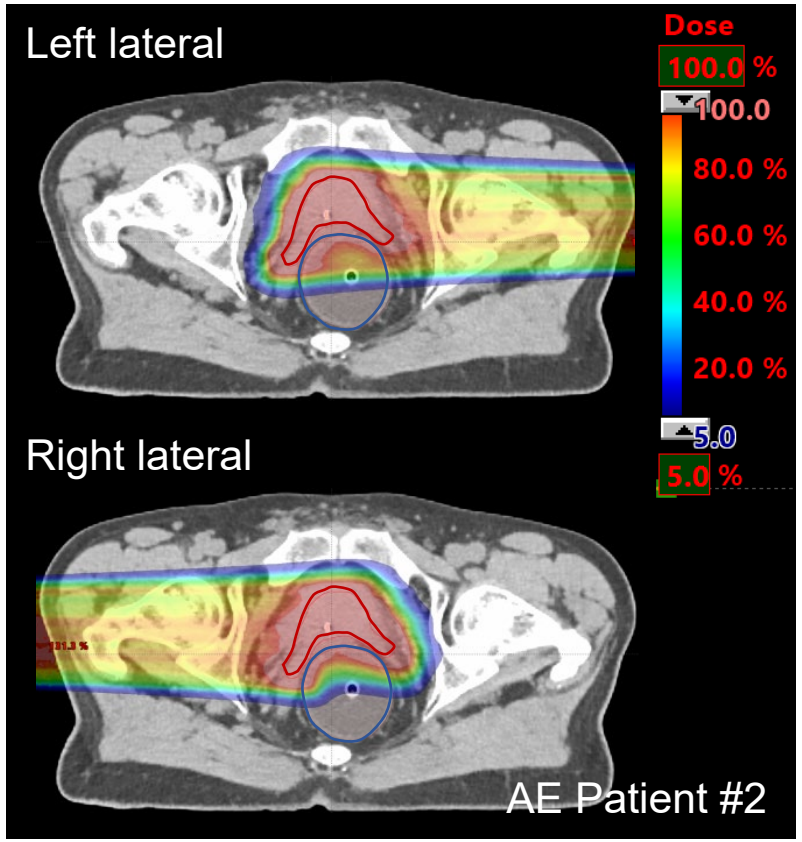


- DLv%, represent the percentage volume of a structure that has a dose (D) of at least d Gy and an LET of at least l keV/µm
- Present dose and LET in one plot and their interplay

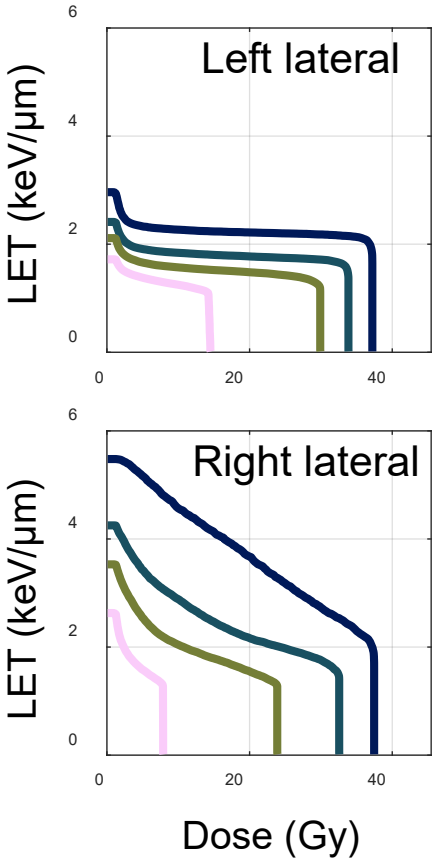
Prostate patients



Dose distributions for individual fields



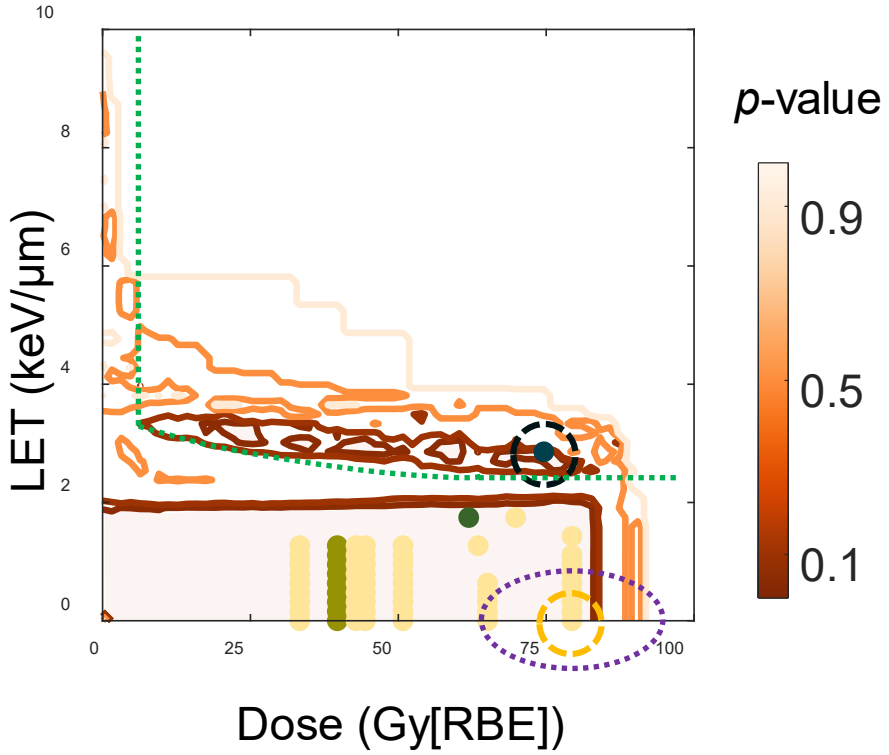
DLVHs for individual fields



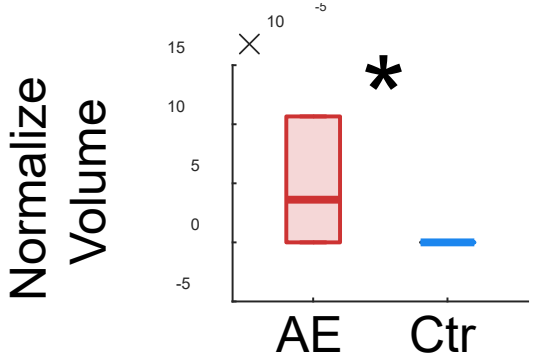
Rectum Prostate

DL1% DL5% DL10% DL20%

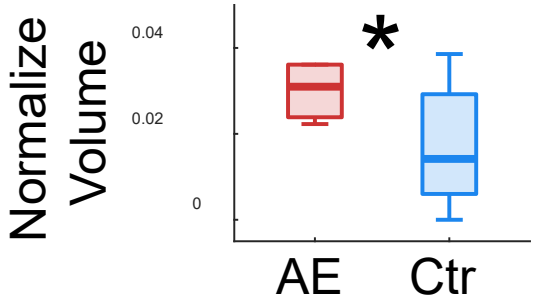
Dose LET Volume Constraints (DLVC)



V(74.6 Gy[RBE], 2.86 keV/μm)



V(79.4 Gy[RBE], 0 keV/μm)



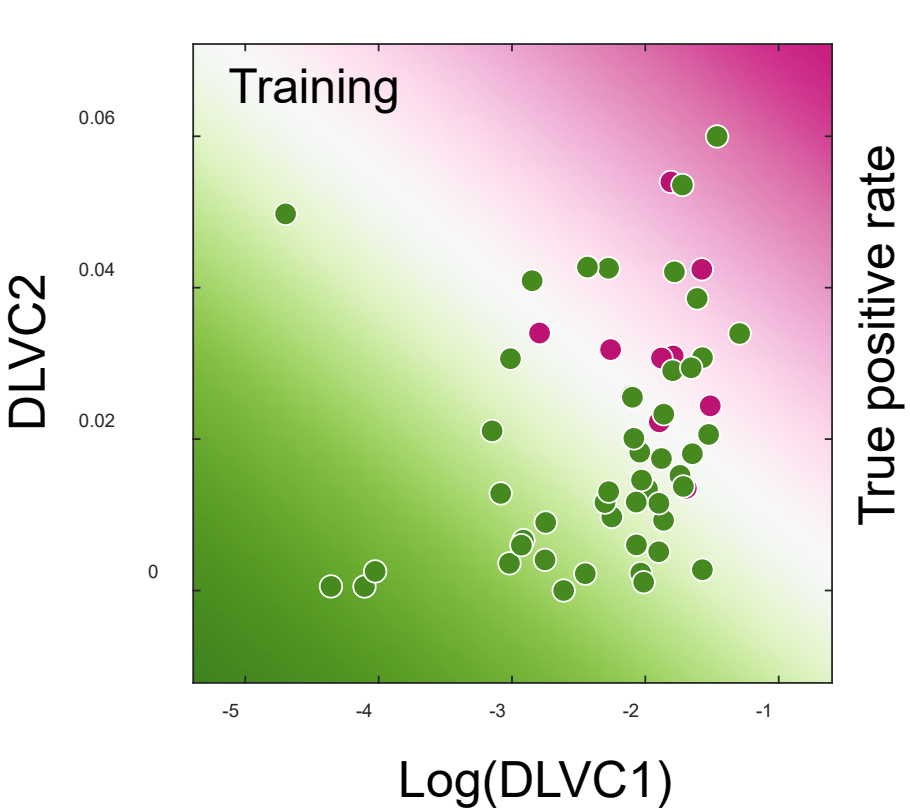
DLVC1: high LET constraint

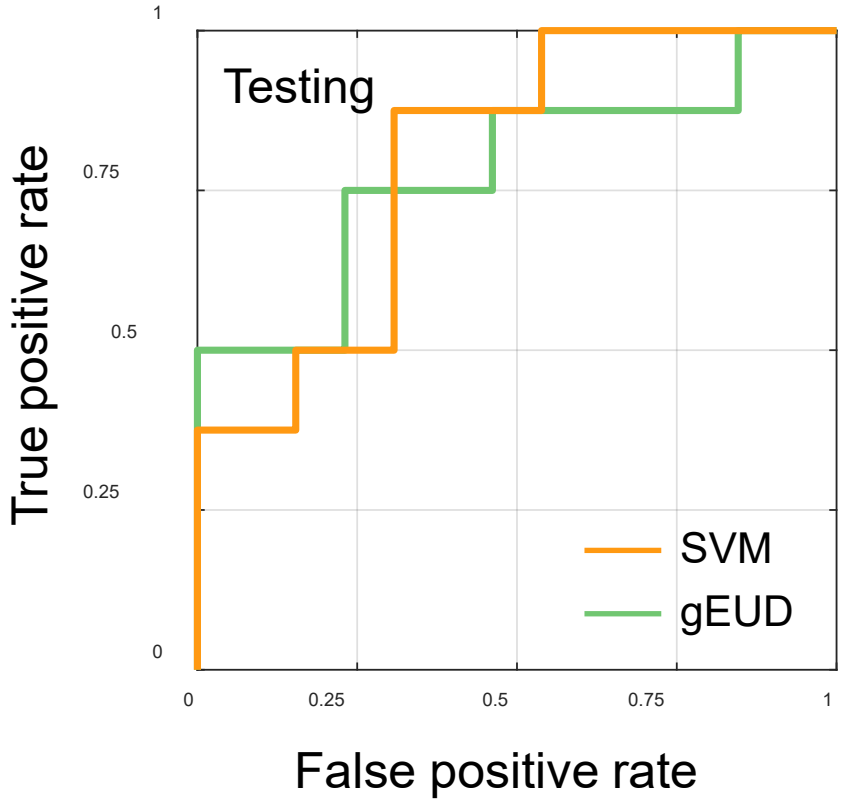
$V_{2.5\ \mathrm{keV/\mu m}\ \mathrm{at}\ 79\ \mathrm{Gy[RBE]}\ \mathrm{to}\ 3.2\ \mathrm{keV/\mu m}\ \mathrm{at}\ 9.52\ \mathrm{Gy[RBE]}}$
$< 1.27\%$ or $1.71\mathrm{cc}$

DLVC2: high dose constraint

$V_{79.4\ Gy[RBE],0\ keV/\mu m}$
$< 2.23\%$ or $2.68\mathrm{cc}$

DLVC based NTCP model



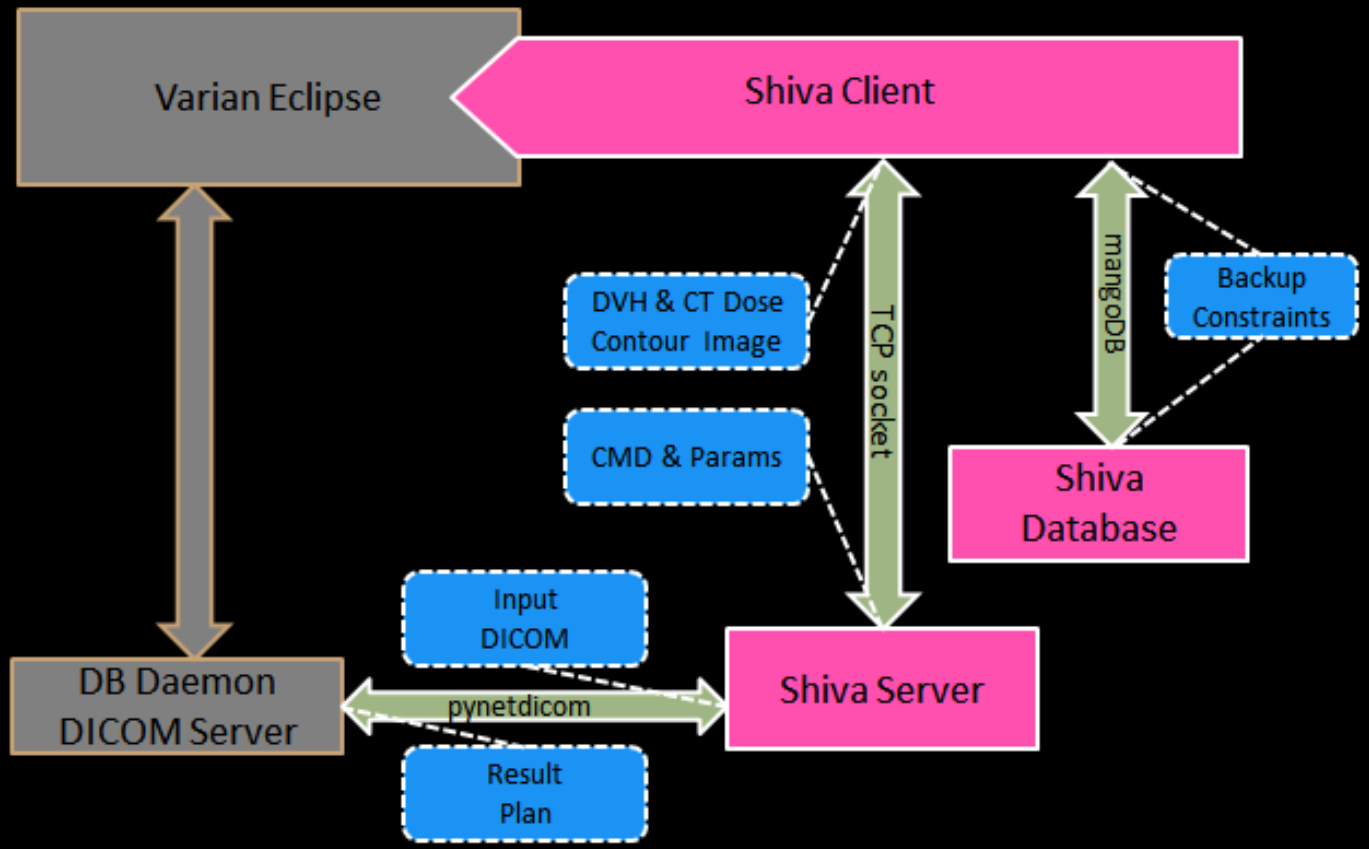


Testing

Patient cohort: 21
Rectal bleeding: 8,
hyperfractionation
Control: 13

Model*	Training	Validation (Loocv)	Testing
	AUC(95%CI)	AUC(95%CI)	AUC(95%CI)
SVM	0.785(0.633-0.887)	0.720(0.501-0.866)	0.798(0.537-0.942)
gEUD	0.762(0.614-0.875)	0.704(0.480-0.822)	0.779(0.441-0.950)

Shiva: System Diagram



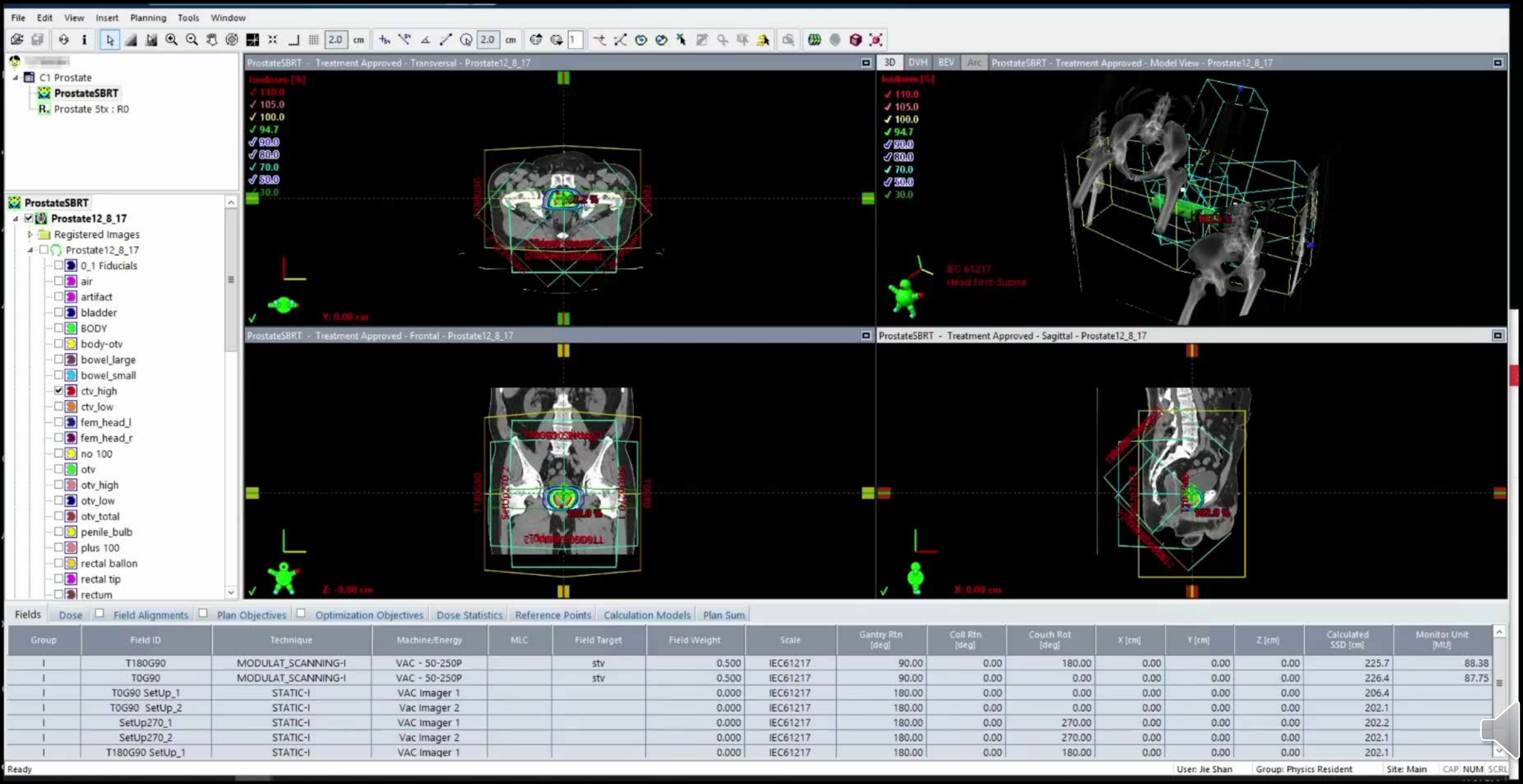
Shiva provide functions:

- Dose, LET, and Biological dose second check
- Interplay evaluation
- 3D/4D robust optimization
- Robust evaluation
- LET guided optimization
- SFO, MFO and IFSO
- Real-time user interaction
- Real-time on-the-fly DVH band, dose, LET, Biological dose map rendering
- Real-time point dose/LET constraint
- Dose LET Volume Histogram
- Rectum bleeding prediction
- Dose/LET engine type choice: analytical, MC2 Monte-Carlo or VPMC

In the future:

- Spot position opt

Demo: Rectum bleeding predicting



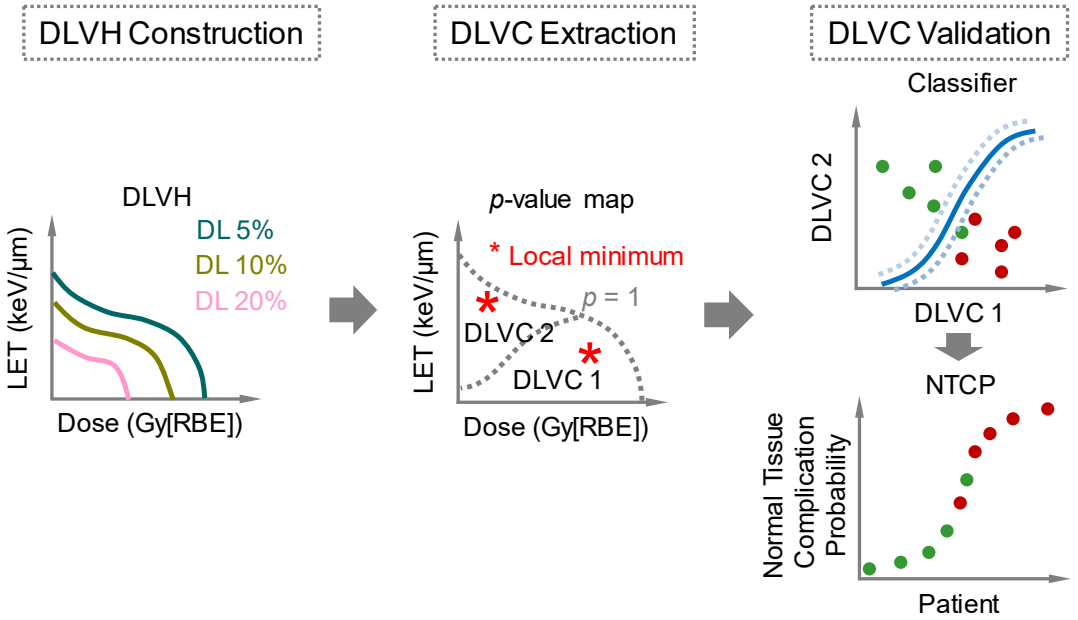
Group	Field ID	Technique	Machine/Energy	MLC	Field Target	Field Weight	Scale	Gantry Rtn [deg]	Coll Rtn [deg]	Couch Rot [deg]	X [cm]	Y [cm]	Z [cm]	Calculated SSD [cm]	Monitor Unit [MU]
I	T180G90	MODULAT_SCANNING-I	VAC - 50-250P		stv	0.500	IEC61217	90.00	0.00	180.00	0.00	0.00	0.00	225.7	88.38
I	T0G90	MODULAT_SCANNING-I	VAC - 50-250P		stv	0.500	IEC61217	90.00	0.00	0.00	0.00	0.00	0.00	226.4	87.75
I	T0G90 SetUp_1	STATIC-I	VAC Imager 1			0.000	IEC61217	180.00	0.00	0.00	0.00	0.00	0.00	206.4	
I	T0G90 SetUp_2	STATIC-I	Vac Imager 2			0.000	IEC61217	180.00	0.00	0.00	0.00	0.00	0.00	202.1	
I	SetUp270_1	STATIC-I	VAC Imager 1			0.000	IEC61217	180.00	0.00	270.00	0.00	0.00	0.00	202.2	
I	SetUp270_2	STATIC-I	Vac Imager 2			0.000	IEC61217	180.00	0.00	270.00	0.00	0.00	0.00	202.1	
I	T180G90 SetUp_1	STATIC-I	VAC Imager 1			0.000	IEC61217	180.00	0.00	180.00	0.00	0.00	0.00	202.1	

Seed Spots Analysis to Characterize Linear-Energy-Transfer (LET) Effect in the Adverse Event Regions of Head and Neck Cancer Patients Treated by Intensity-Modulated Proton Therapy (IMPT)

ORAL PRESENTATION *(TU-A-TRACK 6-6)* by Yang et al. on Tuesday (7/27) at 11:05AM in the session of "Outcome Modelling and Assessment" for the AAPM Virtual 63rd Annual Meeting

Summary

- Developed DLVH for LET study
- Derived DLVCs based on patient outcomes
- Established NTCP models for patient outcome prediction based on DLVCs
- Revealed both high dose and high LET effects on rectal bleeding



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