Multivariable Dosimetric Models for Urinary and Rectal Toxicity Prediction Assessed from Patient Reported Outcome after Prostate Stereotactic Body Radiotherapy

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INTRODUCTION

Machine learning techniques have shown advantages in identifying complex mathematical relationships from observational data, and are rapidly emerging in multiple areas within radiation oncology, including treatment planning and plan evaluation. We hypothesize that assessment of a patient's full DVH profile, rather than a few pre-selected DVH metrics, may provide more comprehensive information in predicting patient-reported toxicities. The aims of this study were three-fold: first, to interrogate the full DVH profiles of the rectum and bladder organs at risk (OARs) to evaluate the strength of dose-volume associations with patient-reported subacute toxicities after prostate SBRT; second, to identify plausible dosimetric quantities that are most associated with patient reported quality of life (QOL) changes to inform future treatment planning practices; lastly, multivariable linear logistic regression models were constructed using the selected top dosimetric features. To this end, we performed a retrospective study using a cohort of 116 patients who underwent prostate SBRT and investigated the applicability of machine learning methods to address these two aims.

AIM

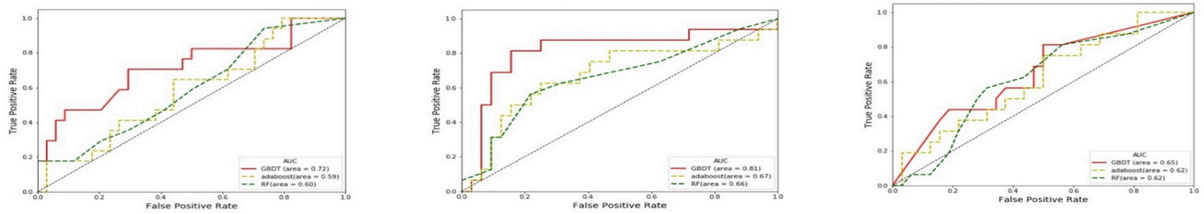
Better understanding of the relationships between treatment planning parameters and treatment-related toxicities may further inform planning objectives. We assessed dosimetric quantities and their associations with patient-reported quality of life urinary and rectal toxicities using advanced machine learning and multivariable modeling.

METHOD

116 prostate SBRT patients treated on a Brainlab Novalis Tx linear accelerator using RapidArc delivery technique (40 Gy in 5 fractions) were pooled and analyzed. Patient-specific differential dose-volume histograms (dDVHs, in 1 Gy dose bins from 0 to maximum doses) for the rectum and bladder were extracted from Eclipse. Other dosimetric quantities including planning target volume (PTV) /rectal/bladder volumes and maximum doses, conformality index, etc were also considered as potential predictors. Patient-reported QOL (EPIC-26) scores were collected and fed into eML algorithms to identify most plausible dosimetric predictors. Performance of the classifiers was evaluated via area under the curve (AUC) using 5-fold cross-validation for the subset of 86 patients. The Pearson's R tests were performed on the top selected dosimetric features, which were used to construct multivariable linear logistic regression predictive models. An independent cohort of 30 patients was used to validate the models.

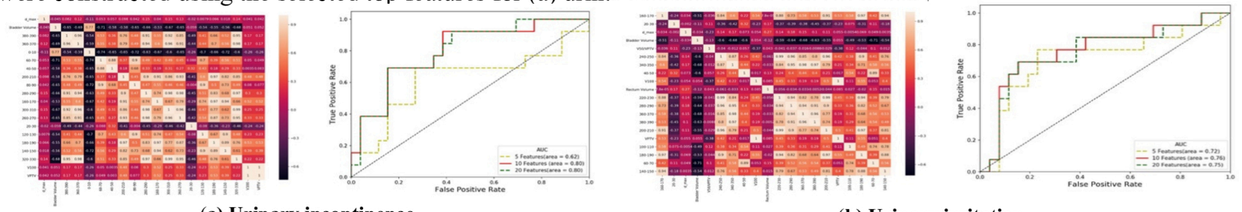
RESULTS

Figure 1: Receive Operating Characteristic curves calculated from the differential dose-volume histograms using three machine learning methods for urinary irritation (a), urinary incontinence (b), and rectal toxicity (c) at 12 months.



(a) (b) (c)

Figure 2: Heatmaps of the selected top 5, 10, and 20 dosimetric features. Multivariable linear logistic regression models were constructed using the selected top features for (a) urinary incontinence and (b) urinary irritation



(a) Urinary incontinence (b) Urinary irritation

Table 1: AUCs for the predictive models based on identified 20, 10 and 5 plausible dosimetric parameters.

	Area under the curve (AUC)		
	# Features 5	# Features 10	# Features 20
Urinary irritation	0.72	0.76	0.75
Urinary incontinence	0.62	0.80	0.80
Rectal toxicity	0.73	0.76	0.73

Linear multivariable predictive models constructed with top 10 identified dosimetric features for urinary incontinence QOL score changes :

$f_0(change\ within\ 6)$
$= 0.000956948508919328 3x_1 - 0.002853150675127234x_2$
$- 0.000768738301982542 3x_3 0.001292292803552564 8x_4 - 0.000968392964076689 2x_5$
$- 0.014483344187060598x_6 - 0.000465928009910554 26x_7 - 0.001027344016620618x_8$
$+ 0.000855926681322129x_9 - 0.001166585039028945 8x_{10} + 1.88607691$

$f_1(increase\ more\ than\ 6)$
$= -0.004951989346092322x_1 + 0.002375556267658281x_2 + 0.000618605245591160 4x_3$
$- 0.017661638026131959x_4 + 0.000129122868081571 24x_5 + 0.003514270051700946x_6$
$- 0.001405878677680737x_7 + 0.000200718552739730 92x_8 + 0.001487081941219481 4x_9$
$- 0.000717130142689419 2x_{10} - 1.28527283$

$f_2(decrease\ more\ than\ 6)$
$= 0.003703404744471224 7x_1 + 0.001275623394802829x_2 + 0.000213469577653693 2x_3$
$+ 0.016463706994073717 + 0.000867308614451433 6x_5 + 0.009282925640882367x_6$
$+ 0.001486268261493899x_7 + 0.000846649932039611 1x_8 - 0.002203545229487704x_9$
$+ 0.001580787059800295 3x_{10} - 2.83732862$

Linear multivariable predictive model constructed with top 10 identified dosimetric features for urinary irritation QOL score changes:

$f_0(change\ within\ 5)$
$= 0.001001067533011912 6x_1 + 0.000470815023164653 9x_2$
$+ 0.002268139168791708 7x_3 + 0.003822195112179099 4x_4$
$- 0.001427856483140808 3x_5 - 0.008206890819355061x_6 - 0.000492113800519647 8x_7$
$- 0.000143024334038201 03x_8 + 0.009304815461443546x_9$
$- 0.000222258431260145 6x_{10} - 1.77299104$

$f_1(increase\ more\ than\ 5)$
$= -0.006143183509641554x_1 - 0.000691369844672045 9x_2 - 0.005120476234958585x_3$
$- 0.002004358717593732x_4 + 0.000486584982574577 45x_5 + 0.004708351320238266x_6$
$+ 0.000059928476249481 88x_7 - 0.000203987493285531 38x_8 + 0.003759033400552347 5x_9$
$- 0.000181834784802752 9x_{10} + 0.29329707$

$f_2(decrease\ more\ than\ 5)$
$= 0.004559294871297409x_1 + 0.000135618443773560 33x_2$
$+ 0.002445348715612059 6x_3 - 0.000948133844232159 3x_4$
$+ 0.000821079700800036 17x_5 + 0.001011625651081792 6x_6$
$+ 0.000352015917434782x_7 + 0.000298340878448396x_8 - 0.014655047923870354x_9$
$+ 0.000360654924034621 73x_{10} - 0.39769307$

CONCLUSIONS

Dosimetric correlations were found for patient-reported bladder toxicities at 12 months after prostate SBRT. The linear models utilizing the top 10 dosimetric parameters achieved great predictive ability. The identified dosimetric features and the multivariable predictive models can be used to refine planning guidelines and potentially reduce toxicity.

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