Accumulating delivered dose to the rectum using finite element analysis improves toxicity prediction

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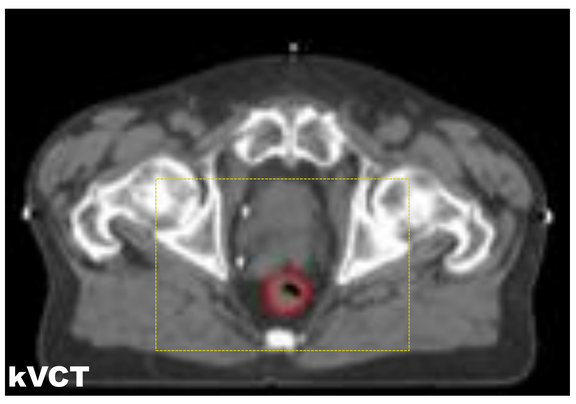
Introduction

- In prostate cancer radiotherapy, the rectum is a dose-limiting organ
- Delivered dose to the rectal wall in prostate radiotherapy differs from planned dose due to interfraction motion and deformation [1]
- The hypothesis of the VoxTox research programme [2, 3] is that delivered dose is a better predictor of toxicity than planned dose

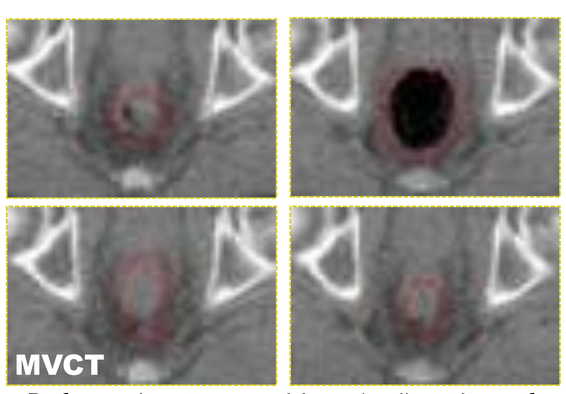
Objectives

- Use biomechanical finite element analysis (FEA) to accumulate motion-inclusive daily delivered dose to the rectum
- Statistical analysis of voxel-level dose differences between patients with and without toxicity
- Develop multivariable normal tissue complication probability (NTCP) models based on spatial delivered dose features

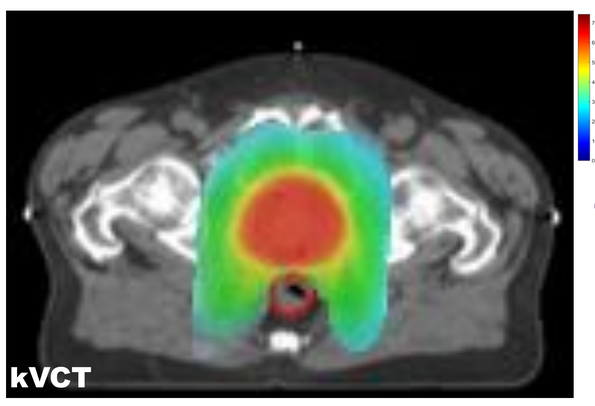
Why is delivered dose to rectum different to planned?



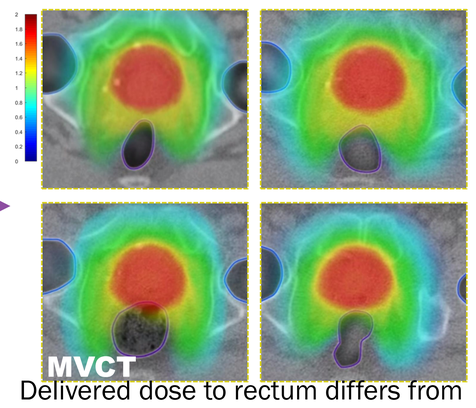
Rectum position (red) at treatment planning



Deformed rectum positions (red) at time of treatment (4 of typically 37 treatments shown)

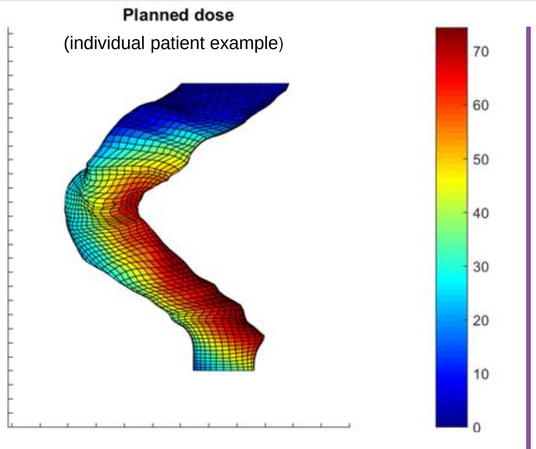


Planned dose distribution (avoiding rectum)

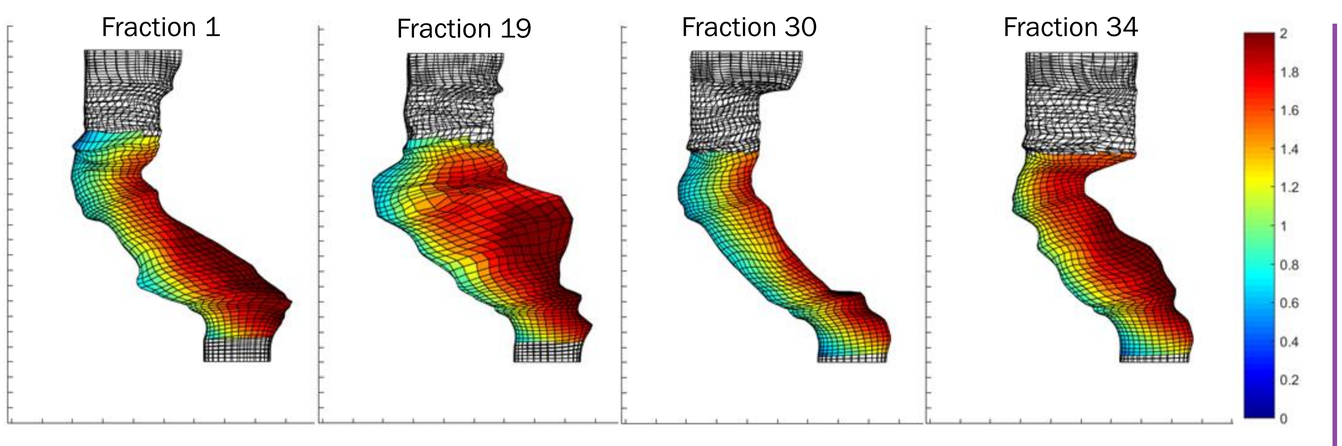


Delivered dose to rectum differs from planned due to daily deformation

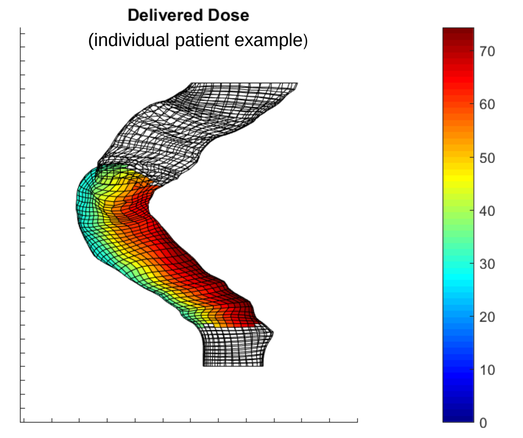
Biomechanical finite element accumulation of dose to rectal wall



Planned dose displayed on rectal contour from planning CT scan (prescribed 74 Gy)



Daily delivered dose accounting for rectal deformation (4 of 37×2 Gy daily fractions shown). Rectal contours autosegmented from MVCT IGRT scan (data limited by imaging field of view)

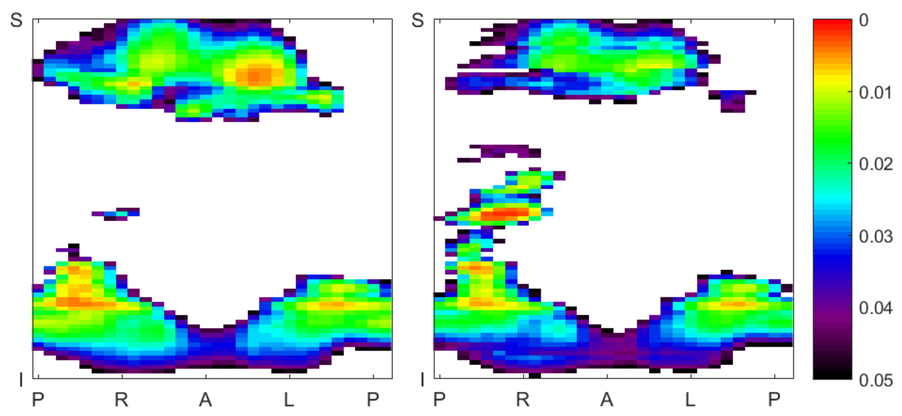


Accumulated delivered dose displayed on planning CT rectal contour

Material/Methods

- 185 prostate cancer patients treated with TomoTherapy helical image guided radiotherapy (IGRT), prescribed 74 Gy/37 fx or 60 Gy/20 fx, converted to equivalent dose in 37 fractions (α/β = 2.149 [4]), split into training (n = 139) and validation sets (n = 46).
- Rectum autosegmented on daily MVCT IGRT scans [5]. Dose calculated using CheckTomo [6].
- FEA performed using Abaqus (Dassault Systèmes®) biomechanical hyperelastic neo-Hookean model, deformed to planned and daily contours.
- Cumulative incidence of rectal bleeding (RB) ≥ Grade 2 (CTCAEv4.03) at 2 years (11 %) was prospectively assessed, and maintained as closely as possible in training and validation sets.
- 3D voxel-wise t-test of dose differences between patients with and without RB used to identify spatial subregions at risk (SRR) where p<0.05 ($SRR_{0.05}$) and p<0.01 ($SRR_{0.01}$). Equivalent uniform dose (EUD) was calculated for each SRR, as well as the full rectal wall (RW).
- Univariate analysis was performed for clinical prognostic factors.
- *NTCP = 1/(1+exp(-S)),* where *S* is dependent on output of logistic regression [7].

Voxel-wise statistical analysis



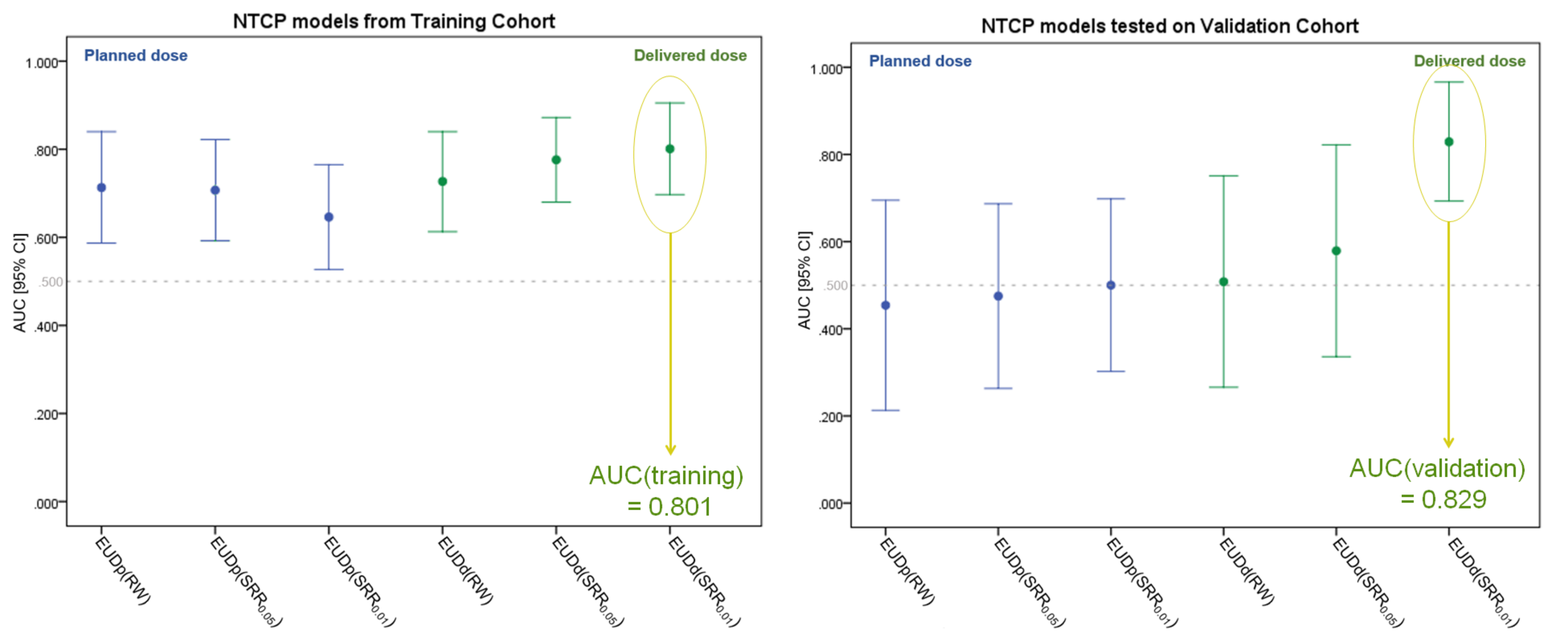
p-value maps showing areas of significant dose difference between patients with and without rectal bleeding. Regions where p<0.05 and p<0.01 determined subregions at risk, $SRR_{0.05}$ & $SRR_{0.01}$, respectively.

Results

Univariate analysis	Planned dose AUC [95% CI]	Accumulated dose AUC [95% CI]
EUD of RW	0.629 [0.515, 0.742]	0.690 [0.568, 0.812]
EUD of $SRR_{0.05}$	0.583 [0.445, 0.721]	0.692 [0.567, 0.817]
EUD of $SRR_{0.01}$	0.478 [0.336, 0.621]	0.765 [0.646, 0.884]
Hypertension (HTN)	Odd's ratio 3.565[1.076, 11.814]	

- NTCP models developed on the training set data were predictive of RB for both planned and delivered dose metrics, the strongest being delivered dose model EUDd($SRR_{0.01}$)+HTN, where $S = 1.317(HTN) + 1.433(SRR_{0.01}) - 3.003$, with AUC 0.801 [95%CI: 0.697, 0.905].
- The only model predictive of RB upon testing of the validation cohort was the same delivered dose model, with AUC 0.829 [95%CI: 0.693, 0.966].

NTCP Model Performance



Conclusions

- Rectal simulation using FEA enables dose accumulation at the voxel-level.
- NTCP models based on delivered dose to rectal wall were more discriminative of rectal bleeding than planned dose.
- Delivered dose to spatial SRRs were more predictive than dose to the full rectal wall.
- Improved toxicity prediction based on delivered dose could be useful for decision making in adaptive radiotherapy.

Acknowledgements & References

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[1] Shelley et al, 2017, , Radiother Oncol 123(3), [2] www.comprt.org/voxtox, [3] Burnet et al, 2017, CERN IdeaSquare 1(1), [4] Shelley et al., Radiother Oncol 123:S481-S482, [5] Shelley & Sutcliffe et al, 2019, Biomed. Phys. Eng. Express 5 025006, [6] Thomas et al., 2016, Br J Radiol.89:20150770, [7] Schakke et al, 2016, Radiother Oncol 119

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Physics track: Adaptive radiotherapy and inter-fraction motion management

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