Predicting urinary toxicity via 2D and 3D dose map analyses in prostate cancer radiotherapy

E. Mylona, A. Cicchetti, T. Rancati, F. Palorini, S. Supiot, N. Magne, G. Crehange, Oscar Acosta, R. de Crevoisier

OC-0615 Predicting urinary toxicity via 2D and 3D dose map analyses in prostate cancer radiotherapy

E. Mylona[1], A. Cicchetti[2], T. Rancati[2], F. Palorini[2], S. Supiot[3], N. Magné[4], G. Crehange[5], O. Acosta[1], R. De Crevoisier[1,6]

[1]INSERM U1099 - University of Rennes, Laboratoire Traitement du Signal et de l'Image, Rennes, France ; [2]IRCCS Istituto Nazionale dei Tumori, Prostate Cancer Program, Milan, Italy ; [3]Institut de Cancérologie de l'Ouest - René Gauducheau, Radiotherapy Department, Nantes, France; [4]Lucien Neuwirth Cancer Institute, Radiotherapy Department, St Priest en Jarez, France ; [5]Centre Georges François Leclerc, Radiotherapy Department, Dijon, France; [6]Centre Eugène Marquis, Radiotherapy Department, Rennes, France

Purpose or Objective

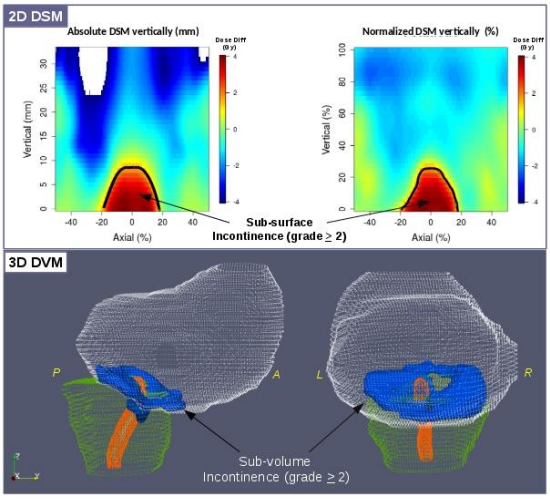
Risk estimation of urinary toxicity after prostate radiotherapy is generally based on bladder DVH, disregarding any spatial dose-distribution information. The objectives of the study were:
- To identify bladder subregions associated with urinary toxicity via pixel-wise and voxel-wise statistical analysis on 2D dose-surface maps (DSM) and 3D dose-volume maps (DVM), respectively.
- To evaluate their prediction capabilities with respect to the DVH of the whole bladder.

Material and Methods

In total 272 prostate cancer patients treated with IMRT/IGRT from two multicentric phase III trials (STIC-IGRT and PROFIT), were prospectively analyzed. Local relationships between dose and specific urinary endpoints were investigated via 2D DSMs and 3D DVMs, by analyzing the planning dose distribution at pixel and voxel scales, respectively. DSMs were generated by anteriorly cutting and virtually unfolding the bladder surface. Maps were laterally normalized and aligned at the most inferior-posterior point. Normalized DSMs (nDSM) both laterally and vertically were also computed. DVMs were produced by first non-rigidly registering the population to a common coordinate system and then propagating the 3D dose distribution according to the transformation beforehand obtained. Pixel and voxel-wise non parametric analyses were performed, for DSMs and DVMs respectively, to identify regions of statistically significant dose differences between patients with/without toxicities. The spatial correlation between the regions found with the nDSMs and DVMs for each symptom was evaluated with the Jaccard score (intersection surface divided by union surface). Prediction capability was estimated by the area under the ROC curve (AUC) from logistic regression, performed at each dose bin of the DVH of the sub-volumes, the dose-surface histogram (DSH) of the sub-surfaces, and the DVH of the whole bladder.

Results

A local dose-effect relationship was found for three late toxicity endpoints: incontinence (grade≥2), retention (grade≥1) and dysuria (grade≥1). The 5-year toxicity rates were 4%, 23% and 13%, respectively. The subregions found with the two methods are mostly located in the inferior and posterior bladder. The Jaccard scores were 0.3 (dysuria), 0.42 (retention) and 0.7 (incontinence). Figure 1 shows the identified sub-surface (top) and sub-volume (bottom) for urinary incontinence. Table 1 shows the prediction capabilities, for each endpoint, of the sub-volume's DVH, sub-surface's DSH and whole bladder's DVH. The dose bin with the highest significant AUC is reported.



Endpoint (late toxicity)	Method	Most predictive bin	AUC (p-value)	OR (95% CI)
Incontinence (grade≥2)	Sub-surface DSH	S78	77.5 (0.01)	1.03 (1.01-1.06)
	Sub-volume DVH	V79	79.7 (0.01)	1.04 (1.01-1.07)
	Whole bladder DVH	V80	70.2 (0.01)	1.21 (1.05-1.41)
Retention (grade≥1)	Sub-surface DSH	S62	62 (0.05)	1.01(1-1.02)
	Sub-volume DVH	V37, V62	68 (<0.01)	1.02 (1.01 -1.04)
	Whole bladder DVH	-	NS	-
Dysuria (grade≥1)	Sub-surface DSH	S77	70 (<0.01)	1.18 (1.07-1.3)
	Sub-volume DVH	V53	78.7 (<0.01)	1.06 (1.02-1.09)
	Whole bladder DVH	V63	70.1 (0.02)	1.04 (1.01-1.07)

Abbreviations: DVM= dose-volume map, DSM=dose-surface map, OR= odds ratio, AUC= area under the ROC curve, CI= confidence interval , NS = non significant

Conclusion

Specific bladder subregions were identified by the two methods as more predictive of urinary toxicity than the whole bladder. Particularly, the DVM method highlights the importance of volumes near the bladder surface, but inside bladder volume, underlining the influence of variable bladder filling and, thus, entailing the need of optimizing dose even in "non-obvious" regions (i.e. what appears to be urine at planning CT).