



A Prospective Study of the Impact of PTV Margin Reduction for Patients with Localized Prostate Cancer: Delivered Dose and Quality of Life

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Introduction and Objectives

- For localized prostate cancer patients, reduced CTV-to-PTV margins have been linked to reduced toxicity^{1,2}
- However, with reduced margins, loss of target coverage may become more prominent, particularly over the course of radiation therapy
- This work uses deformable image registration (DIR) based cumulative dose to track actual (delivered) dose to targets and organs at risk (OAR) to determine the impact of reduced margins on:
 - ✓ Dosimetric endpoints
 - ✓ Prospectively acquired quality of life (QOL)

Methods: Dose Accumulation

- Under an IRB-approved protocol, 20 prostate cancer patients were evaluated
 - ✓ 11 control patients with standard margins (10 mm uniform with 6 mm at prostate/rectum interface)
 - ✓ 9 patients with reduced planning margins (5 mm uniform with 4 mm at prostate/rectum interface)
- To mitigate known limitations associated with CBCT images, Planning CT of each patient was deformably resampled to each daily CBCT using a parameter optimized^{3,4} Elastix B-spline DIR algorithm for *dose of the day* calculations
- Dose of the day* was then accumulated on the planning CT for all fractions, using energy-mass mapping based on the Elastix transformation. Full adaptive radiotherapy (ART) workflow is shown in Figure 1.

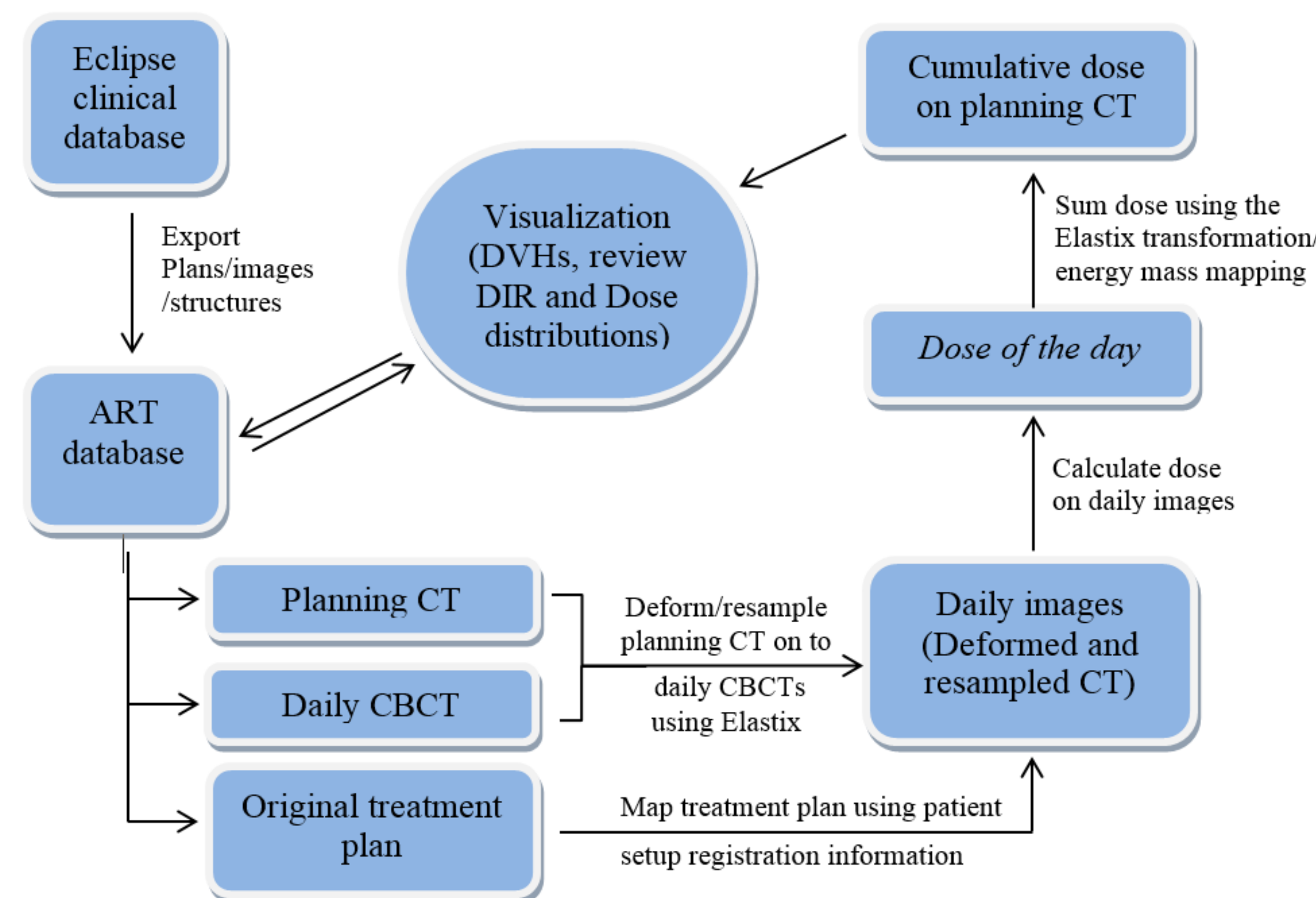
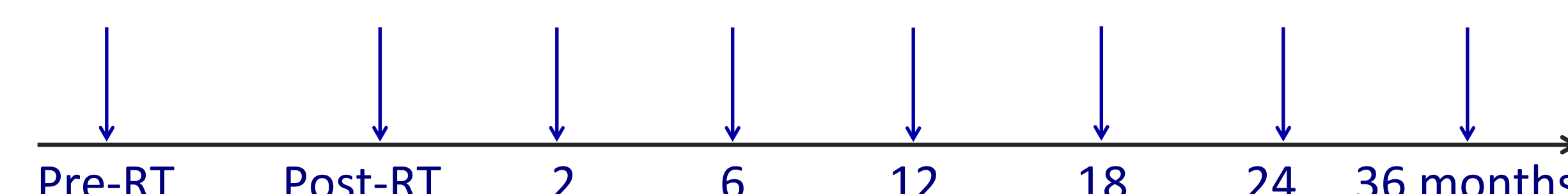


Figure 1: DIR based dose accumulation workflow

Methods: Quality of Life

- Abbreviated Expanded Prostate cancer Index Composite (EPIC-26)⁵ forms were used to collect patient reported QOL data
- QOL collection time points:



- Standardized QOL scores [range: 0-100] were determined for the 5 following EPIC domains, and baseline-corrected by subtracting pre-treatment QOL data
 - ✓ Urinary Incontinence
 - ✓ Urinary Irritative/Obstructive
 - ✓ Bowel
 - ✓ Sexual
 - ✓ Hormonal
- Mean QOL differences between the margin reduced group and control group ($QOL_{\text{Margin-reduced}} - QOL_{\text{control}}$) were calculated
- We also investigated the correlations of the dose distributions to QOL by evaluating the dose to PTV/bladder, and PTV/rectum intersection volumes (hot spot volumes in OAR), and correlating them to relevant EPIC domains

Results: Dose Accumulation

Target /OAR	Reduced Margin (5/4 mm, N=9)			Standard Margin (10/6 mm, N=11)		
	D _{mean} Delivered	D _{mean} Planned	Deviation in Gy (and as a %)	D _{mean} Delivered	D _{mean} Planned	Deviation in Gy (and as a %)
PTV	78.00±1.32	80.25±0.61	-2.2±1.0 (-2.8±1.3%)	76.93±2.98	77.78±2.93	-0.8±2.0 (-1.0±2.6%)
Prostate	80.98±0.42	80.68±0.44	0.3±0.5 (0.4±0.6%)	79.85±1.87	79.98±1.65	0.9±1.4 (1.1±1.8%)
Bladder	33.37±9.50	34.11±10.2	-0.7±2.6 (-1.5±6.7%)	31.91±12.09	32.55±17.89	-0.7±3.1 (-1.2±10.4%)
Rectum	33.02±4.39	35.15±3.61	-2.1±1.3 (-6.2±3.9%)	38.72±5.92	39.72±5.12	-1.0±2.4 (-2.6±6.2%)
SV	74.54±9.09	78.18±5.63	-3.6±3.6 (-5.0±5.5%)	75.21±4.41	76.63±3.07	-1.4±2.2 (-1.9±2.9%)

Table 1: D_{mean} delivered (i.e. cumulative) and planned in Gy, for reduced margin patients (N=9) and standard margin patients (N=11). The deviation is shown in Gy and as a % (within parentheses)

- Analysis of the deviation of delivered dose from planned dose for D_{mean} (Table 1) and D_{max}, D_{min} (not shown) shows only minimal differences between the margin-reduced and control groups. Differences are not statistically significant (p>0.1)
- This suggests that lowering the margin to 5/4 mm does not affect the clinical deliverability of the plan

Results: QOL

Time Point	EPIC Domains				
	Urinary Incontinence	Urinary Irritative/ Obstructive	Bowel	Sexual	Hormonal
Baseline (pre-RT)	2.6	-9.4	-5.0	-6.9	6.1
End of RT (N=20)	-6.4	13.4	6.3	8.4	-2.6
2-month post RT (N=20)	3.1	8.2	6.6	10.1	-3.2
6-month post RT (N=19)	-2.0	8.5	19.0	16.7	4.4
12-month post RT (N=18)	5.5	10.3	8.0	21.9	7.1
18-month post RT (N=15)	-0.3	13.2	4.2	10.5	-3.0
24-month post RT (N=14)	-3.8	3.4	13.9	16.4	-1.1
36-month post RT (N=6)	-14.6	-10.9	-13.5	7.0	-1.3
Mean QOL _{Margin-reduced} - QOL _{control}	2.2	12.5	10.4	13.5	-1.1
Minimally important difference range ⁶	6-9	5-7	4-6	10-12	4-6

Table 2: QOL_{Margin-reduced} - QOL_{control} for different time points and mean baseline-corrected values for each domain. Follow up time: mean 23.5 months, median 24 months.

- Difference in mean QOL scores for the [end of RT - 36 months] period for domains *Urinary Irritative/Obstructive*, *Bowel* and *Sexual* are above the “*minimally important difference*”, suggesting that QOL increase in margin-reduced patients are clinically meaningful for these 3 domains.
- Urinary Incontinence is usually associated with prostatectomy, and the patients were not under hormonal treatments, so we do not expect to see any changes in the other two EPIC domains.

Results: QOL Correlations to Hot Spots in OAR

Target /OAR	Reduced Margin (5/4 mm, N=9)				Standard Margin (10/6 mm, N=11)			
	Volume (cc)	D _{min}	D _{max}	D _{mean}	Volume (cc)	D _{min}	D _{max}	D _{mean}
PTV/Bladder Intersection	12.5±8.3	70.7±9.9	83.8±1.5	79.4±2.6	18.2±8.1	70.3±8.3	83.9±1.2	80.4±1.7
PTV/Rectum Intersection	2.6±1.8	70.1±11.9	83.5±2.2	79.3±1.6	7.2±5.8	70.4±8.1	83.1±2.3	79.7±3.2

Table 3: Mean ± Std. Dev. intersection volumes and dose metrics for the two groups

- D_{max}, D_{mean}, and D_{min} values were not statistically different between the groups (p>0.1). However, the standard margin group has larger PTV/bladder and PTV/rectum intersection volumes (Table 3).
- This suggests that the hot spots in the bladder and rectum are significantly smaller for the margin-reduced group, which may contribute to the improvement in QOL scores. A typical patient from each group is shown in Figure 2.
- The PTV/rectum intersection volume shows a moderate correlation to the *bowel* EPIC domain (Pearson's coefficient R = -0.51).

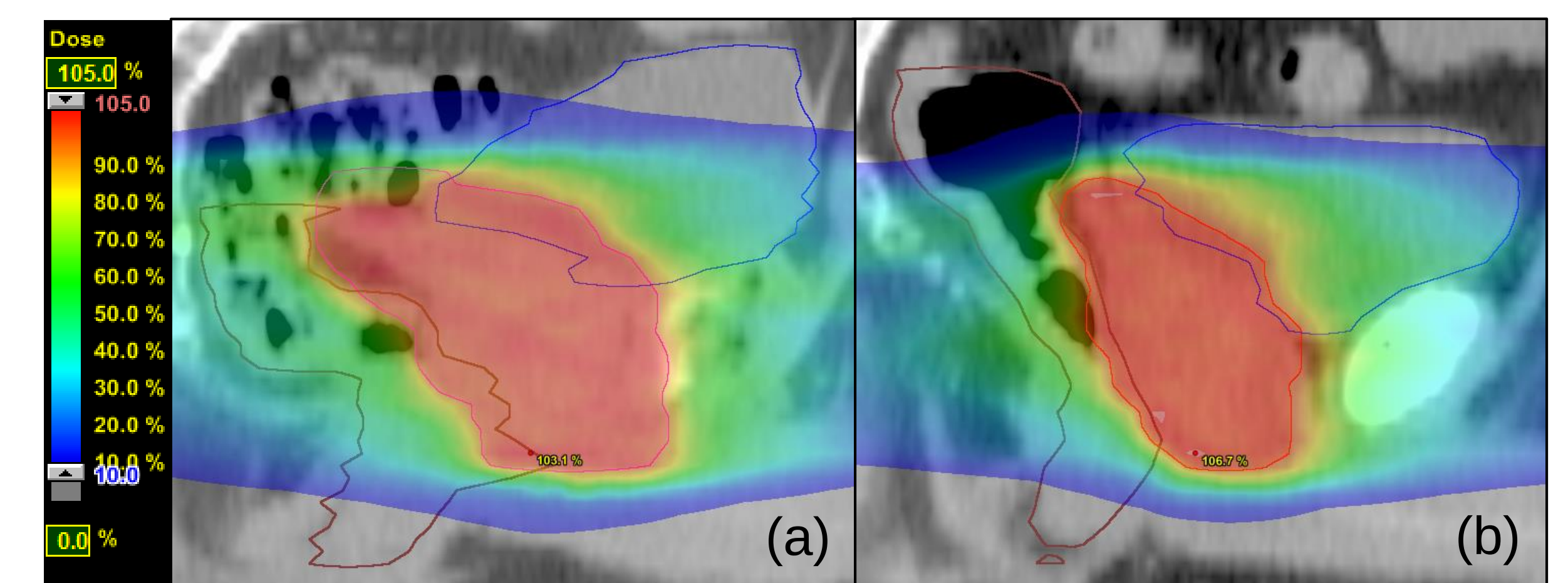


Figure 2: Sagittal view of PTV (red), rectum (brown) and bladder (blue) of a typical patient from (a) standard margin group (b) reduced margin group

Conclusions

- Daily deformable dose accumulation shows that deviation of the cumulative (delivered) dose from planned dose is minimal. Lowering the margin to 5/4 mm does not affect the clinical deliverability of the plan at the treatment unit.
- Early QOL results from the first 20 patients (9 margin reduced and 11 control) shows that there is a clinically meaningful difference in QOL for the margin reduced group
- A larger number of patients and greater follow-up is needed to draw unequivocal conclusions.

Limitations and Future Directions

- More patients and longer follow ups needed. Trial will continue until protocol goals (30 patients in each arm, 60 total) are met. Currently median QOL follow up time is 24 months for the 20 patients studied. Follow ups will continue for 5 years post-RT for each patient.
- Better correlations between QOL and dosimetric parameters are expected with more patients and longer follow-ups.

References

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