Daily CBCT-Guided Online Adaptive Radiotherapy for Enhanced Personalization and Precision in the Treatment of Muscle Invasive Bladder Cancer

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INTRODUCTION

Standard image-guided radiotherapy **(IGRT)** approaches for muscle invasive bladder cancer **(MIBC)** require large target margins (1.5-2.0cm) due to bladder fill variability, inevitably resulting in increased organ-at-risk **(OAR)** doses and toxicity risk. CBCT-guided online adaptive radiotherapy **(oART)** mitigates this by improving precision with daily delineation of patient anatomy followed by personalization of target coverage and OAR sparing via dose optimized to the anatomy of the day.

METHODS AND MATERIALS

- Retrospective analysis of CBCT-guided oART treatments for n=32 MIBC patients
- Target definitions and prescriptions are shown in **Table 1**
  - Bladder dose varied from 5100-5500cGy to respect OARs
  - Bladder PTV margins were patient specific and determined based on 2 CT scans separated by 15 minutes at simulation.
  - Nodal boost implemented for n=3 patients

RESULTS

Figure 2 shows the dose distributions from two consecutive oART treatments for the same patient with and without plan adaptation compared to the initial reference plan. This highlights daily variability and both target coverage and organ sparing benefits.

Average oART session time(CBCT acquisition to treatment completion) was 31±8min.

Average patient-specific bladder PTV margin was 1.0cm(range:0.5-1.5).

Daily oART revealed appreciable variability in bladder fill and proximity of bowel to high-dose region (quantified as overlap volume between bowel and PTV), with average daily changes of 26±22% and 34±31%, respectively. However, the magnitude of this variability is patient dependent **(Figure 1)**.

The adaptive plan was selected over non-adapted("scheduled") plan in 99.8% of fractions due to improved target coverage and/or OAR sparing.

The primary bladder PTV coverage goal(D95%>100%) was achieved for 19%/70% of scheduled/adapted plans. These increased to 50%/99%, respectively, for the secondary goal(D95%>95%) **(Table 3/Figure 3)**.

Plan adaptation also increased the percentage of plans satisfying OAR goals: bowel, sigmoid, and rectum D0.03cc goals achieved for scheduled/adapted plans were 89/99%, 91/96%, and 64/97%, respectively **(Table 2/Figure 4)**.

CONCLUSION

Daily oART for treatment of MIBC is a powerful tool that enhances personalization and precision by ensuring optimal dose distributions in the face of appreciable daily bladder fill and OAR variability. This facilitates use of smaller target margins and generally improves target coverage and OAR sparing compared to non-adaptive approaches.

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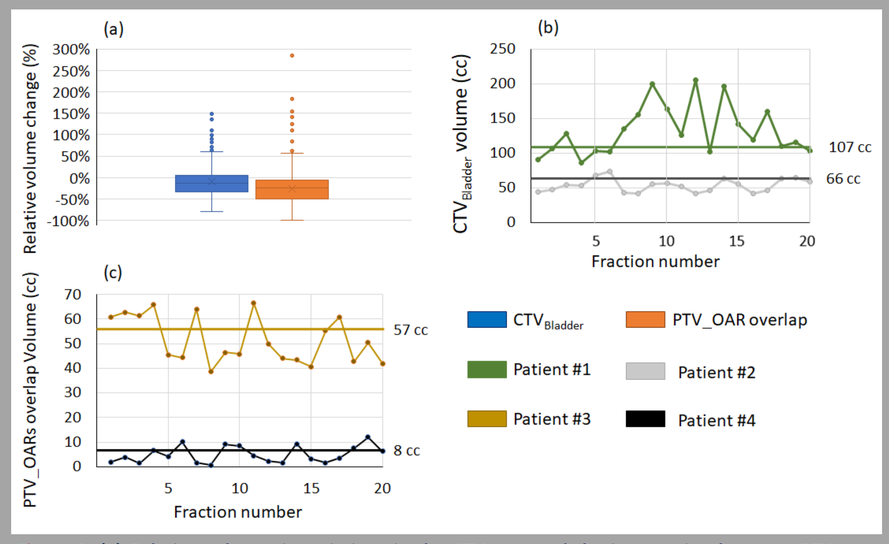

Figure 1: (a) Relative volumetric variations in the $CTV_{Bladder}$ and the intersection between $PTV_{Bladder}$ and critical OAR ("PTV_OARs overlap") between the reference and adapted treatment plans. A value of 0% represents no change and a positive/negative value represents an increase/decrease in volume from reference to adaptive fractions. (b) Interfraction variation in $CTV_{Bladder}$ volumes (cc) for two representative patients. Patients #1 (green) and #2 (gray) had major (σ = 37cc, 34% of reference volume) and minor (σ = 10cc, 14% of reference volume) bladder volume variation, respectively. Horizontal lines show $CTV_{Bladder}$ reference volumes (107cc for Patient #1 and 66cc for Patient #2). (c) Interfraction variation in volumetric overlap (cc) between $PTV_{Bladder}$ and critical OARs (bowel and sigmoid) for two representative patients. Patient #3 (yellow) and #4 (black) demonstrated relatively large and small overlaps between target and critical OARs in the reference plans (horizontal lines; 57cc and 8cc, respectively). The variations in this volume throughout the adaptive fractions were also comparatively large (σ = 10cc) and small (σ = 3cc), respectively.

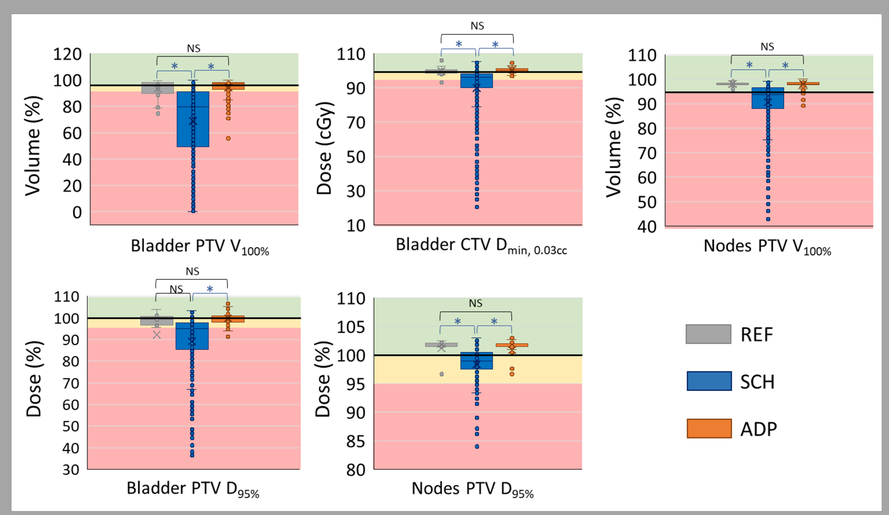

Figure 3: Dosimetric evaluation of achieved target coverage in reference(REF), scheduled(SCH) and adapted(ADP) plans. Black horizontal bar indicates associated goals. The shaded green, yellow, and red areas indicate the areas where clinical goals were met, met within the acceptable variation, and not met, respectively. *Statistically significant difference ($p < 0.05$) and NS (statistically non-significant) difference.

Structure	Clinical Goal	Percentage of Plans Achieving Goal			Average Achieved Value		
		REF	SCH	ADP	REF	SCH	ADP
Bowel	$D_{0.03cc} \leq 290$ *(cGy)*	100 %	89 %	99 %	274 ± 18	268 ± 32	269 ± 26
	$V_{55Gy} \leq 3$ *(cc)*	88 %	68 %	86 %	2 ± 4	5 ± 16	2 ± 3
Sigmoid	$D_{0.03cc} \leq 290$ *(cGy)*	87 %	91 %	96 %	262 ± 32	265 ± 30	263 ± 33
	$V_{57Gy} \leq 3$ *(cc)*	100%	97 %	99 %	0 ± 0	0 ± 2	0 ± 1
Rectum	$D_{0.03cc} \leq 280$ *(cGy)*	100 %	64 %	97 %	255 ± 33	259 ± 39	245 ± 38
$CTV_{Bladder}$	$D_{0.03cc} \leq 290$ *(cGy)*	99%	87%	91%	287 ± 2	284 ± 6	287 ± 5

Table 2: Comparison of OAR sparing metrics between reference(REF), scheduled(SCH), and adapted(ADP) plans. Note, $CTV_{Bladder}$ $D_{0.03cc}$ is included as an organ sparing objective. Percentages of plans achieving OARs goals and average (± σ) achieved values for these clinical goals are presented.

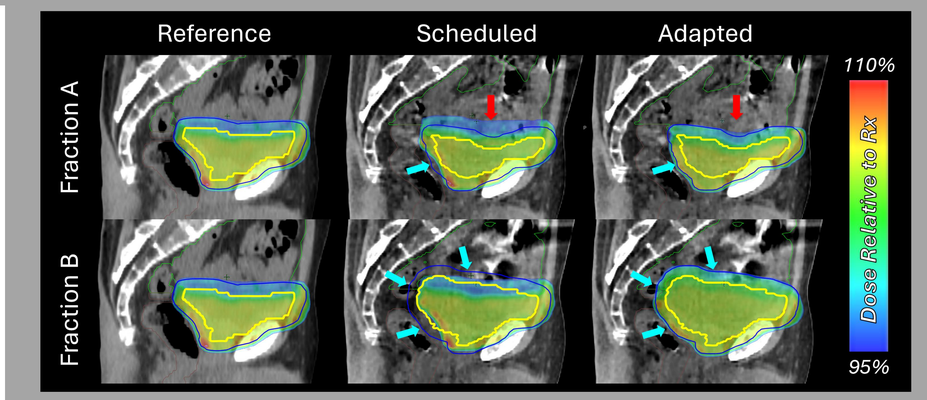

Figure 2: Target dose distributions in reference, scheduled, and adapted plans for 2 consecutive oART fractions in a representative patient. Targets: $CTV_{Bladder}$(yellow), $PTV_{Bladder}$(dark blue); OARs: combined bowel and sigmoid(green), rectum(brown). $CTV_{Bladder}$ volumes were 145cc, 100cc, and 245cc for reference, Fraction A, and Fraction B, respectively. Red arrows indicate regions where scheduled plan would over-dose OARs and blue arrows indicate regions where scheduled plan would under-dose targets, whereas the adapted plans fix these issues.

Structure name	Derivation	Dose
$PTV_{Bladder}$	$CTV_{Bladder}$ + Margin*	51-55 Gy
$CTV_{Bladder}$	Bladder	
CTV_{Nodes}	NA	40-42 Gy
PTV_{Nodes}	CTV_{Nodes} + 0.3cm	
†PTV_{Nodes_Boost}	GTV_{Nodes_Boost} + 0.3cm **	54-55 Gy
†$PTV_{Tumor\_Priority}$	$GTV_{Tumor\ priority}$ + 0.5cm	
†$GTV_{Tumor\_Priority}$	NA	

Table 1: Targets and optimization structures with derivation and doses created in the planning directive.
*Margins are anisotropic based on patient-specific bladder fill.
†Optional target structures

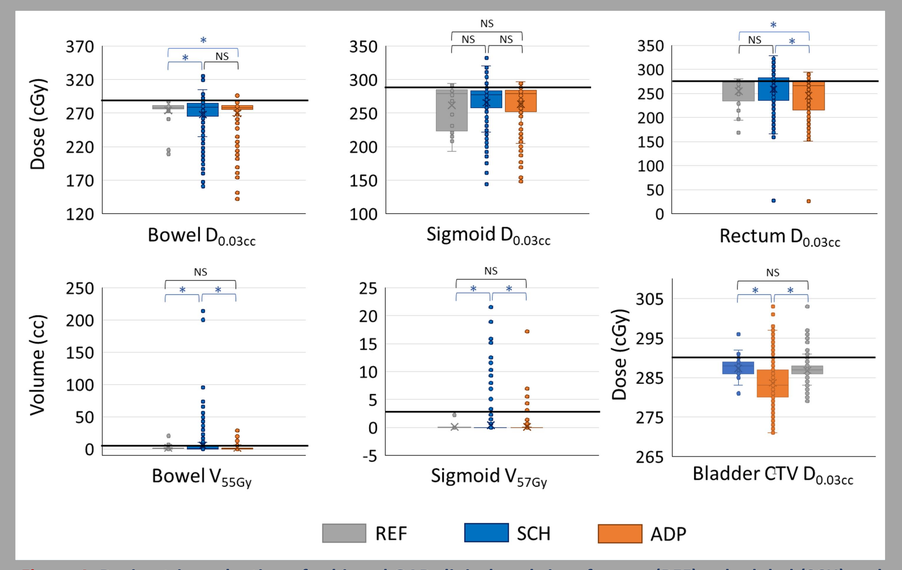

Figure 4: Dosimetric evaluation of achieved OAR clinical goals in reference (REF), scheduled (SCH) and adapted (ADP) plans. Black horizontal bar indicates the clinical goals. *Statistically significant difference ($p < 0.05$) and NS (statistically non-significant) difference.

Structure	Clinical Goal (acceptable variation)	Percentage of Plans Achieving Goal (acceptable variation)			Average Achieved Value			Relative Difference	
		REF	SCH	ADP	REF	SCH	ADP	SCH - REF	ADP - REF
$PTV_{Bladder}$	$V_{100\%}$	NA	NA	NA	93 ± 7	69 ± 28	94 ± 6	-26 ± 30%	3 ± 7%
	$D_{95\%} \geq 100$ *% (>95%)*	52 % (100%)	19 % (50%)	70 % (99%)	95 ± 21	89 ± 14	100 ± 3	-10 ± 14 %	1 ± 1 %
$CTV_{Bladder}$	$D_{min,\ 0.03cc} \geq 100$ *% (>95%)*	52% (97 %)	10 % (59%)	61 % (100%)	100 ± 2	90 ± 16	101 ± 4	-10 ± 16 %	1 ± 4 %
PTV_{Nodes}	$V_{100\%} \geq 95$ *%*	100%	40 %	99 %	98 ± 1	91 ± 9	98 ± 1	-8 ± 9 %	0 ± 1 %
	$D_{95\%} \geq 100$ *% (>95%)*	88 % (100%)	34 % (84%)	93 % (99%)	101 ± 2	98 ± 3	101 ± 5	-3 ± 2 %	0 ± 5 %

Table 3: Comparison of target coverage metrics between reference(REF), scheduled(SCH), and adapted(ADP) plans. Note, there was no quantitative goal for $PTV_{Bladder}$ $V_{100\%}$, but plans sought to maximize this metric. The percentage of plans achieving clinical goals (with acceptable variation), Average (± σ) of achieved clinical goals for targets, as well as average change (± σ) in dose between SCH-REF and ADP-REF (negative/positive values represent a decrease/increase, respectively, in target coverage metric when compared to REF) are all shown.