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FULL PAPER

Delineating the inner bladder surface using uniform contractions from the outer surface under variable bladder filling conditions

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Objective: To evaluate the methods to delineate the inner bladder (IB) surface using a uniform contraction from the outer bladder (OB) surface, assuming the bladder wall (BW) is either of constant thickness, constant volume or variable volume.

Methods: 14 prostate intensity-modulated radiotherapy patients with 2 planning CTs were identified. For both CTs, OB was delineated using model-based segmentation. IB was delineated manually. Then, using uniform contractions from OB, the position of IB was approximated using a: 2.5-mm contraction, patient-specific contraction, patient-specific constant wall volume method and variable wall volume method. The structures created using those strategies were compared against the manual IB contours using geometric and dosimetric indices.

Results: In the presence of variable bladder filling, use of a generic or patient-specific constant contraction

resulted in a significant overestimation of IB volume (+12 and +13 cm³, respectively; $p < 0.001$) that was inversely correlated with the difference in urine volume between the scans ($R^2 > 0.86$). Mean differences across 95% of IB surfaces were ≤ 2 mm for methods using either constant or variable wall volume. Mean dose-volume histogram (DVH) differences were < 1 cm³ across the whole BW DVH when using the method that assumed a variable wall volume.

Conclusion: The variable volume BW model provided the best approximation of the IB surface position under varying filling conditions, based on geometric and dosimetric indices.

Advances in knowledge: Use of the equation derived in this research provides a quick and accurate method to delineate the hollow BW on serial imaging for the purposes of dose reconstruction.

INTRODUCTION

Interfraction motion of the normal urinary bladder during external beam radiotherapy is large in magnitude, geometrically complex in nature, and varies significantly between patients.¹ This can result in substantial differences between the dose calculated on the planning CT (planCT) and the dose actually delivered to the bladder.² Dose reconstruction techniques hold the potential to accurately calculate the dose actually delivered to the bladder during radiotherapy using serial images acquired at the time of treatment delivery.³ However, for an accurate reconstruction of the dose delivered to the bladder functional tissue, it is necessary to delineate the outer bladder (OB) and inner bladder (IB) surfaces. This is because the use of solid volumes generated from OB surface contours will include the dose to the urine in the dose-volume histogram (DVH) obscuring the dose to the bladder

wall (BW) tissue,⁴ hollow BW DVHs have been more clearly linked to urinary toxicity⁵ and organ motion affects the reconstructed DVH differently when the structures of interest are modelled in a solid or wall form.⁶

The need to include only the functional tissue between the OB and IB surfaces in the dose reconstruction procedures poses a difficult technical challenge. It is not possible to visualize the IB surface on the most common types of in-room imaging systems. However, if the OB surface can be identified, several authors have suggested that, similar to rectal wall, the inner surface of the bladder can be delineated using a uniform contraction from the OB surface contours.^{4,7–11} There is, however, little information on the magnitude of uniform contraction that should be used. Rosewall et al⁴ suggested that a uniform contraction of

2.5 mm from the OB surface closely approximates the position of the IB surface for patients with a “comfortably full” bladder. However, large variations in BW thickness between patients have been noted,^{12,13} and wall thickness has also been inversely related to the volume of urine contained within the bladder.^{13–16} The specifics of that inverse relationship seem to vary for different filling volumes however,^{12,17,18} and it has been reported that the volume of the wall actually increases slightly with increasing urine volume owing to the increased blood perfusion in the detrusor muscle at larger urine volumes.^{9,19}

To facilitate dose reconstruction to the hollow BW, the objective of this study was to evaluate the use of a uniform contraction from the OB surface to delineate the IB surface under variable bladder filling conditions employing: a generic contraction (2.5 mm); a constant, patient-specific contraction; a variable contraction based on patient-specific constant wall volume; and a variable contraction based on patient-specific variable wall volume. Those experimental methods were compared geometrically and dosimetrically to manually delineate IB surfaces.

METHODS AND MATERIALS

A single-centre, experimental design was employed after research ethics board approval. 14 patients with intermediate-risk prostate cancer were identified as those who had received >1 planCT scan on the same day, prior to commencing radiotherapy during a 1-year period. The principle reason documented for the acquisition of multiple planCTs was that the patient did not achieve acceptable bladder and rectal preparation (*i.e.* “comfortably” full bladder and empty rectum). These patients were included in the “testing” cohort, and each patient met the following eligibility criteria:

- received 78 Gy in 39 fractions to prostate-only clinical target volume (CTV)
- intensity-modulated radiotherapy (IMRT) plan (seven-field coplanar, static field, step-and-shoot multileaf collimator) achieved departmental dose constraints
- received “comfortably full” bladder preparation instructions
- no positive or negative contrast agents in the pelvis
- no transurethral resection of the prostate and no metallic hip prostheses.

Image selection

Delivered dose reconstruction usually employs treatment verification images [such as kilovoltage cone beam CT (CBCT)]. However, to test the ability of the model to predict the position of the IB surface under variable bladder filling conditions, it was necessary to accurately delineate the IB surface on two sets of images with different bladder filling volumes. As the IB surface cannot yet be visualized on CBCT, the delineation methods were tested using two planCTs.

The planCT scans [2 mm slice thickness; 0 mm gap; 120 kVp; mAs regimen individualized per patient using ^{SURE}Exposure™ software (Toshiba Aquilion ONE™; Toshiba Medical Systems North America, Markham, ON)] and clinical plans were copied into a treatment planning system research directory (Pinnacle³ v. 9.0; Philips Medical Systems, Canada). Once imported, the planCT that was used to create the clinical treatment plan was considered the primary

image. All other planCTs were registered to the primary image in Pinnacle³ using an automated rigid registration algorithm (local correlation) to align the bony pelvis. For patients with two planCTs, both image sets were used. For those patients with >2 planCTs, the image set with the largest visual difference in urine volume from the primary image was selected for use. For the purposes of analysis, the primary (clinically used) planCT was labelled CTa and the secondary planCT was labelled CTb.

Benchmark delineation

For both planCTs from each eligible patient, the OB was delineated using model-based auto-adaptation procedures available in the Pinnacle³ treatment planning system v. 9.0 (Philips Medical Systems) with some small manual adjustments over the bladder/prostate interface.^{20,21} The IB surface was then delineated manually (IBm) using standard manual delineation tools. To quantify intraobserver variability of manually delineated contours, contouring was repeated three times on both CTs, by one observer. The observer was blinded to previous contours, with a minimum of 24 h between contouring sessions.

Experimental methods

Based on the assumption that a uniform contraction from OB is a reasonable method to create IB and in the absence of strong evidence regarding the thickness of BW under variable bladder filling conditions, four increasingly complex relationships between the bladder volume and the thickness of the wall were postulated.

Generic contraction (IB2.5)

It is possible that bladder thickness variations are minimal, and a uniform contraction of 2.5 mm from the outer surface is a good approximation of the position of the inner surface for any patient, at any bladder filling volume.

Contour generation A uniform 2.5-mm contraction was applied to the outer contour for CTb. This method ensured that the thickness of the BW was constant for all patients and at all urine volumes.

Patient-specific, constant contraction (IBcon)

It is possible that variations in BW thickness between patients are more important than the effect of urine volume variations within a patient; therefore, a patient-specific uniform contraction may be identified from one image and applied to subsequent images.

Contour generation On CTa, a uniform contraction was applied to OB. The magnitude of the contraction was varied iteratively (minimum change 0.1 mm) until the volume of the structure created by the contraction was equivalent to the median volume of IBm for the patient. The magnitude of the CTa contraction was noted, and a contraction of equivalent magnitude was applied to the OB on CTb. This method ensured that the thickness of the BW varied between patients but was constant for an individual patient, regardless of differences in urine volume.

Patient-specific, constant wall volume (IBvol)

It is possible that BW thickness does not remain constant for an individual patient. Rather, the volume of the BW could remain

constant for a patient, while the magnitude of the contraction required to create the wall volume varies based on urine volume.

Contour generation On CTa, the median IBm volume was subtracted from the median OB volume to calculate a BW volume. On CTb, the BW volume (from CTa) was subtracted from the OB volume to calculate an IB volume. A uniform contraction was then applied to CTb OB. The magnitude of the contraction was varied iteratively (minimum change 0.1 mm) until the volume of the structure created was equivalent to that of the calculated IB volume. This method would result in different BW thicknesses between patients and between scans, but a constant wall volume for an individual patient.

Patient-specific, variable wall volume (IBequ)

As suggested by Dale et al,⁹ it is possible that neither the wall thickness nor the wall volume remains constant while urine volume varies but that the BW volume (and the contraction to achieve it for a particular patient) varies in a predictable manner based on the change in urine volume. To test this hypothesis, a two-stage process was necessary. Firstly, the relationship between the absolute difference in OB volume and the absolute difference in IBm volume was quantified using the least squares method of linear regression in a separate cohort of patients (see Appendix A for details). The equation was then resolved to calculate an IB volume for the secondary image from the OB and IB volume of the primary image and OB volume of the secondary image:

$$V_{IBb} = V_{IBa} + \frac{V_{OBb} - V_{OBa} - 6.06}{1.109} \quad (1)$$

Contour generation The CTa IBm and OB volume were noted. On CTb, the OB volume was noted. These three values were then entered into the equation above, and the predicted CTb IB volume was noted. A uniform contraction was then applied to CTb OB. The magnitude of the contraction was varied iteratively (minimum changes 0.1 mm) until the volume of structure created by the contraction (IBequ) was equivalent to the IB volume predicted by Equation 1. This method ensured that the volume of the BW changed as urine volume changed, according to the independently derived relationship.

Data analysis

For each experimental volume on CTb, the volumes of each OB and IB pair were noted. The BW volume for each patient and each experimental method was calculated by subtracting the volume of each IB contour from the volume of the OB contour. Descriptive statistics were used to describe the IB and BW volumes for each experimental method. Analysis of variance or Student's *t*-test was used to identify any statistically significant volume differences between the study benchmark and the experimental methods ($p < 0.05$). The coefficient of determination (R^2) was used to identify any near-linear associations between the study volumes.

The volumetric concordance [three-dimensional (3D) overlap] between the median volume manual contour (IBm) and the contour from each of the experimental delineation methods (IBx) was quantified using the dice similarity coefficient (DSC).²² This

metric provided a value that simultaneously quantified differences in volume position, shape, size and orientation. Differences between the three IBm observations were also quantified in this manner. DSC was calculated as:

$$DSC = \frac{2x(IBm \cap IBx)}{IBm + IBx} \quad (2)$$

A value of zero indicates that the delineated volumes were completely disassociated, whereas a value of one indicates that the volumes were identical. Good agreement of the volumes is indicated by a DSC value > 0.7 .²²

Differences between the surfaces were described using approximately 3000 vectors (based on organ volume) spaced evenly across the 3D surface. These were projected perpendicularly from the median manual contour surface to each experimental method surface to measure the distance between them. Because this technique generated a range of surface displacements for approximately 3000 points, frequency line graphs were created to compare the percentage of the surface at vector differences between 1 and 15 mm. Differences between the three IBm observations were also quantified in this manner.

The dosimetric effect of IB contour differences was also evaluated. The clinically treated plans were recalculated using the collapsed cone convolution superposition algorithm and a 1.5-mm³ dose grid.²³ Dose interpolation was performed between the centres of the 1 mm³ voxels. To generate BW DVH for analysis, the IB DVH volume was subtracted from the OB DVH volume in 10 cGy dose bins. This was performed for the benchmark contours and all the experimental methods contours on CTb. The DVH from the median manual bladder wall (BWm) was then subtracted from the DVH created using the experimental methods and the other two manual observations. This was performed for each patient, individually to create a "subtraction DVH" to avoid the confounding effect of differences in BWm DVH between patients. The per-patient DVH differences between the delineation methods were then averaged for the 14-patient cohort and the mean subtraction DVH plotted for each method.

BW volumes at key dose levels were used as discrete comparison points between the methods. These key dose levels were those that have been previously associated with the risk of chronic urinary toxicity: BW volume receiving 30 Gy (V_{30Gy}),²⁴ 65 Gy (V_{65Gy})²⁵ and 78 Gy (V_{78Gy}).²⁶

RESULTS

For the 14 patients, the 3 OB volumes ranged from 114 to 495 cm³ in CTa and from 56 to 284 cm³ in CTb. The mean pairwise change in IBm volume between CTa and CTb was -109 cm³, but exhibited a large interpatient range (17 – 242 cm³). The magnitude of the uniform contraction used to generate the IB structures ranged from 1.7 to 3.0 mm for IBcon, from 2.4 to 6.5 mm for IBvol and from 2.5 to 5.0 mm for IBequ. The magnitude of the contraction from the OB surface to create the IBvol and IBequ surfaces (*i.e.* the bladder wall thickness) was inversely correlated with the volume of IBm (R^2 0.62 and 0.73, respectively).

Table 1. Raw volumes of outer bladder and inner bladder for the manual and experimental methods (14 patients). All volumes in cubic centimetres. IBm and BWm values indicate the range of the three manual observations

Patient number	PlanCTa			PlanCTb						
	OBm	BWm	IBm	OBm	BWm	IBm	IB2.5	IBcon	IBvol	IBequ
1	494	76–92	402–418	284	72–75	209–212	216	232	207	216
2	429	64–84	345–365	227	67–68	159–160	175	181	153	162
3	205	47–52	153–158	191	48–54	137–143	140	143	142	139
4	144	42–47	97–102	127	42–47	80–85	90	85	81	78
5	380	58–59	321–322	121	39–44	77–82	88	95	64	82
6	206	44–47	159–162	109	41–44	65–68	76	77	63	65
7	141	42–45	96–99	109	40–47	62–69	76	73	67	62
8	243	50–53	190–193	105	48–50	55–57	70	72	54	60
9	114	37–41	73–77	99	39–40	59–60	69	66	62	57
10	216	42–49	167–174	93	44–45	48–49	61	61	43	49
11	125	42–43	82–83	70	43–44	26–27	45	41	29	27
12	245	53–61	184–192	62	40–41	21–22	34	37	10	18
13	233	52–55	178–181	62	48–49	13–14	36	36	9	15
14	125	39–40	85–86	56	38–41	15–18	31	24	16	17

BWm, volume between OBm and IBm; IB2.5, inner bladder structure created using a 2.5mm contraction; IBcon, inner bladder structure created using a patient-specific constant contraction; IBequ, inner bladder structure created using a patient-specific variable volume; IBm, manually delineated inner bladder surface; IBvol, inner bladder structure created using a patient-specific constant volume; OBm, manually delineated outer bladder surface; planCTa, planning CT scan used clinically; planCTb, planning CT scan with different urine volume.

The volumes generated using the study methods are summarized in Table 1. Using a constant contraction of 2.5 mm, resulted in a significant overestimation of the IB volume [mean difference +12 cm³; standard deviation (SD) 6 cm³; $p < 0.001$]. The use of a patient-specific constant contraction also significantly overestimated the IB volume (mean difference +13 cm³; SD 7 cm³; $p < 0.001$). The volume differences between IBm and IBcon were significantly inversely correlated with the change in volume between CTa and CTb (R^2 0.86). IBvol created volumes that were significantly smaller than IBm volumes (mean difference -3 cm³; SD 5 cm³; $p = 0.04$). The differences between the IBm and IBvol volumes were significantly correlated with the change in volume between CTa and CTb (R^2 0.85). IBequ created volumes with small random and systematic differences from IBm (mean difference 0 cm³; SD 3 cm³) that were not significantly different from IBm ($p = 0.67$). Comparisons of the 3D overlap between the median volume IBm and the experimental methods using DSC revealed concordance >0.80 for all patients using IBvol and IBequ (Figure 1). Minimum DSC for IB2.5 was 0.55 and 0.53 for IBcon, but no significant differences between the experimental methods were found ($p = 0.17$). Minimum DSC for the three IBm observations was 0.81.

The mean 95th percentile surface differences between the median IBm and the experimental methods were 2.9 mm (IB2.5), 2.8 mm (IBcon), 2.0 mm (IBvol) and 1.9 mm (IBequ). IB2.5 and IBcon 95th percentile differences from IBm were significantly larger than IBvol and IBequ differences ($p = 0.001$). The mean 95th percentile differences between the three IBm observations were 1.8 mm, significantly smaller than IB2.5 and IBcon

($p < 0.001$). The frequency line graph of surface differences from the median volume IBm contour is presented in Figure 2. The mean percentage of surface with ≥ 2 mm difference from IBm was 38% (IB2.5), 37% (IBcon), 21% (IBvol) and 16% IBequ ($p = 0.01$). Intraobserver variation resulted in 15% of the surface with ≥ 2 mm differences, significantly smaller than the surface differences for IB2.5 and IBcon ($p > 0.003$).

The BW DVHs were calculated for each of the delineation methods and compared with the BWm using a subtraction DVH (Figure 3). BW2.5 and BWcon demonstrated substantial differences from BWm across the whole DVH curve. Mean pairwise differences between BWm and BWequ were <1 cm³ across the full dose range. Mean pairwise volume differences between BWm and BWvol were <1 cm³ at doses >70 Gy and >2 cm³ at doses <35 Gy. When considering each patient individually, at doses >40 Gy, only two patients exhibited per-patient DVH volume differences of 2 cm³ with BWequ, whereas with BWvol, four patients had DVH volume differences >2 cm³, and three patients had differences >3 cm³.

The effects of the experimental delineation methods on the key dose levels for the BW DVH are summarized in Table 2. BW2.5 significantly underreported the volumes at all three of the key dose levels, compared with BWm ($p < 0.0002$). BWvol overreported the $V_{30\text{Gy}}$ volumes ($p = 0.04$), and only BWequ did not result in any significant volume differences from BWm. When each patient was considered individually (Figure 4), pairwise differences between BWm and the experimental methods at $V_{30\text{Gy}}$, $V_{65\text{Gy}}$ and $V_{78\text{Gy}}$ were the smallest for BWequ and the largest for BW2.5 and BWcon.

Figure 1. Box and whisker plot of dice similarity coefficient (DSC) quantifying the three-dimensional overlap between the median manual contour (IBm) and the contours from a 2.5 mm contraction (IB2.5), a patient-specific constant contraction (IBcon), a patient-specific constant volume (IBvol) and a patient-specific variable volume (IBequ) for 14 patients. Plot for IBm indicates DSC for observer-based variation of IBm contours (three observations).

DISCUSSION

In this research, various magnitudes of uniform contraction were applied to the outer surface contours to create a BW of constant thickness, and constant or variable volume. For the fixed contraction methods (generic or patient-specific), the magnitude of the differences from IBm increased as volume differences between the scans increased. For the variable contraction methods, the magnitude of the contractions showed variation between patients but for a given patient was always smaller at large filling volumes. This is consistent with the literature evaluating BW thickness at urine volumes up to 250 cm³,^{12,17} where wall thickness was inversely correlated with urine volume and intravesical pressure.^{13,15} This suggests that, for the purposes of generating a BW structure for DVH calculations and dose reconstruction, it would be inaccurate to apply a generic uniform contraction (such as 2.5 mm) to a group of patients. Furthermore, it would also be inaccurate to apply a constant, but patient-specific contraction in multiple images when bladder filling is variable. Variation of BW thickness with variations in urine volume is a well-recognized phenomenon in the urodynamic and ultrasound literature, but it has been largely unexplored in the radiotherapy setting. This phenomenon is, however, gaining new importance in the era of dose reconstruction, adding a new level of complexity to bladder functional tissue changes during fractionated radiotherapy.

This research found that under variable urine filling conditions, changes in IB volume do not have a one-to-one relationship with simultaneous changes in OB volume. Rather, the volume of the BW itself increased predictably with increasing urine volume. The relationship was well described using Equation 1 postulated in this research, which was derived in an independent cohort. Dale et al⁹ also attempted to quantify the relationship between BW volume and OB volume. Consistent with our

Figure 2. Frequency histogram of the mean per-patient surface differences between the median volume manual contour surfaces (IBm) and the surfaces from a 2.5 mm contraction (IB2.5), a patient-specific constant contraction (IBcon), a patient-specific constant volume (IBvol) and a patient-specific variable volume (IBequ) for 14 patients. IBm [three observations (obs)] demonstrates the surface differences between the median volume IBm and the other two IBm observations.

Figure 3. Subtraction bladder wall dose-volume histogram (DVH) for 14 patients. The DVH volumes from median volume manually delineated structures were subtracted from the DVH volumes (in each 10 cGy dose bin) created using a 2.5 mm contraction (BW2.5), a patient-specific constant contraction (BWcon), a patient-specific constant volume (BWvol) and a patient-specific variable volume (BWequ) and the other two manual contours (BWm). Bold lines indicate mean of per-patient differences. Dashed lines indicate mean ± 1 standard deviation.

findings, they reported that wall volume increased by approximately 10% for each 100 cm³ increase in OB volume. These findings are somewhat supported by the literature which found that the wall thickness remained constant at filling volumes beyond 250 cm³.^{12,17} The specific inference being, if bladder surface area is increasing and wall thickness remains constant, then the BW volume is increasing. All other evaluations of this subject have either not attempted to quantify the relationship between filling volume and wall volume¹⁹ or have attempted to quantify the relationship across a group of patients,²⁷ which suffered from the confounding effect of inpatient variations in initial BW volume.

The equation derived in this research (Equation 1) was used to create a BW structure that produced a DVH curve closely approximating one for manually delineated BW. This has important ramifications for delivered dose reconstruction in pelvic radiotherapy. It is necessary to delineate both the outer and inner surfaces of the bladder to accurately calculate the dose delivered to the functional bladder tissue.^{4,6} This poses a significant challenge

for dose reconstruction procedures, as it is often not possible to visualize the IB surface using in-room images. The methods described in this research suggest that delineation of the outer surface on in-room images, and then application of the formula (based on the BW volumes from the planCT) will result in a geometrically and dosimetrically accurate delineation of the inner surface despite large changes in urine volume. Therefore, until biomechanical modelling is able to accurately predict the motion of the inner surface from deformations of the outer surface, this method can provide an accurate and logistically viable method to delineate the bladder functional tissue on serial imaging, even when it cannot be directly visualized.

The results of this research should be interpreted in context with its limitations. Although multiple manual observations were made for each image and each patient, all manual contours were performed by a single observer. It is possible that the inclusion of other observers may increase the variability of both the manual and the experimental methods. Although Equation 1 was derived

Table 2. Summary of the volume variation for key dose levels using the experimental inner bladder delineation methods to create a bladder wall dose-volume histogram (14 patients)

Dose level	BWm	BW2.5	BWcon	BWvol	BWequ
V _{30Gy}	24 (9)	17 (4) ^a	17 (4) ^a	26 (10) ^a	24 (9)
V _{65Gy}	13 (5)	9 (2) ^a	9 (2) ^a	14 (7)	13 (6)
V _{78Gy}	4 (2)	3 (1) ^a	3 (1) ^a	4 (2)	4 (2)

Bladder wall volumes: between manually delineated outer bladder surface and manually delineated inner bladder surface (BWm); between manually delineated outer bladder surface and inner surface created using a 2.5 mm contraction (BW2.5), a patient-specific constant contraction (BWcon), a patient-specific constant volume (BWvol) and a patient-specific variable volume (BWequ). Volumes reported as those receiving 30 Gy (V_{30Gy}), 65 Gy (V_{65Gy}) and 78 Gy (V_{78Gy}).

Volumes presented as mean (standard deviation) in cubic centimetres.

^aStatistically significant differences from BWm, $p < 0.05$.

Figure 4. Box and whisker plot of per-patient volume differences between manual contours (BWm) and the contours created using a 2.5 mm contraction (BW2.5, white), a patient-specific constant contraction (BWcon, light grey), a patient-specific constant volume (BWvol, dark grey) and a patient-specific variable volume (BWequ, black). Volumes reported as those receiving 30 Gy ($V_{30\text{Gy}}$), 65 Gy ($V_{65\text{Gy}}$) and 78 Gy ($V_{78\text{Gy}}$). Box indicates interquartile range, whiskers indicate maximum and minimum volumes and circles indicate outliers. Dashed horizontal line indicates zero differences from BWm and negative values indicate that experimental methods report volumes smaller than BWm.

and tested across a wide range of clinically relevant initial filling volumes and volume changes, it is possible that the equation may not hold for volumes or volume changes beyond those ranges. The dosimetric comparison of the model was performed using prostate IMRT distributions. Although this is a limitation in the generalizability of the findings from this study, the sharp dose fall-off across the BW should make the DVH very sensitive to small changes in the BW contours when absolute volume DVHs are considered (as they are herein). Thus, if the model can generate DVHs which hold up to scrutiny with IMRT dosimetry, it is likely to be applicable in other less sharp dose gradient scenarios.

CONCLUSION

This study evaluated the efficacy of various methods to predict the position of the IB surface using uniform contractions from

the OB surface, based on the assumption that the BW was either of constant thickness, constant volume or volume that varies predictably based on urine filling. The volumetric and dosimetric results from this study suggest that the use of the equation derived in this research more accurately predicted the position of the IB surface under varying bladder filling conditions, compared with the other methods tested, particularly when filling changes were large. This technique can provide a quick and accurate method to delineate the bladder functional tissue on serial imaging for the purposes of dose reconstruction.

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APPENDIX A METHODS

The “derivation” cohort consisted of 20 consecutive patients with prostate cancer who had undergone planning CT scan (planCT) during the same time period as the “testing” cohort and who also had a diagnostic staging pelvic CT scan suitable for electronic import into the treatment planning system. Additional inclusion criteria were:

- received 78 Gy in 39 fractions to prostate-only clinical target volume
- intensity-modulated radiotherapy plan (seven-field coplanar, static field, step-and-shoot multileaf collimator) achieved departmental dose constraints
- no transurethral resection of the prostate and no metallic hip prostheses
- no positive or negative contrast agents in either CT scan

- staging CT scan acquired with slice thickness of ≤ 2 mm and included the whole bladder.

All CTs were acquired using 120 kVp; mAs regimen individualized per patient using ^{SURE}Exposure™ software (Toshiba Aquilion or Toshiba Aquilion ONE™; Toshiba Medical Systems North America). PlanCTs were acquired with “comfortably full” bladder filling instruction, but the staging CTs used no bladder filling instructions. The staging CTs were exported electronically from the hospital electronic archiving system and registered to the planCT using local correlation rigid registration algorithm in Pinnacle³ (Philips Medical Systems). For both images, the outer bladder (OB) and inner bladder (IB) surfaces were delineated as noted in the benchmark delineation section.

Figure A1. Scatter plot of the association between changes in inner bladder volume and changes in outer bladder volume for the 20-patient derivation cohort. Absolute volume differences for inner bladder volume were calculated by subtracting the staging CT volumes (V_{IBb}) from the planning CT volumes (V_{IBa}). Similarly, volume differences for outer bladder volume were calculated by subtracting the staging CT volumes (V_{OBb}) from the planning CT volumes (V_{OBa}). Dashed line indicates unity.

For each patient, the absolute difference in OB volume and the absolute difference in IBm volume between the two CTs was quantified. A linear relationship between the absolute difference in OB volume and the absolute difference in IBm volume was quantified using the least squares method of linear regression. Linear regression was applied to the whole organ volume, not on a slice-by-slice basis. The linear equation was then resolved to provide a model to predict the IB volume for the secondary image, when only the inner and outer volumes of the primary image, and the outer volume of the secondary image, are known.

EQUATION DERIVATION

In the 20-patient derivation cohort, planCT OB reference volumes ranged from 89 to 546 cm³ and from 53 to 746 cm³ for the staging CT. The mean pairwise change in the IBm reference volume between the two CTs was 146 cm³ but exhibited a large inpatient range (13–457 cm³). The absolute change in IBm volume (ΔV_{IB}) and the absolute change in OB volume (ΔV_{OB}) between the CTs was plotted (Figure A1). The following linear equation was found to closely describe the relationship between changes in OB volume (ΔV_{OB}) and changes in IB volume (ΔV_{IB}) between the two scans for the same patient (R^2 0.995):

$$\Delta V_{OB} = (1.109 \times \Delta V_{IB}) - 6.06 \text{ cm}^3 \quad (\text{A1})$$

The equation was then resolved to provide a method to predict the IB volume for the secondary image, when the inner and outer surface volumes of the primary image and the outer surface volume of the secondary image are known.

$$\text{Specifically if : } \Delta V_{OB} = V_{OBa} - V_{OBb} \text{ and } \Delta V_{IB} = V_{IBa} - V_{IBb} \quad (\text{A2})$$

$$\text{then : } (V_{OBa} - V_{OBb}) = [1.109 \times (V_{IBa} - V_{IBb})] - 6.06 \quad (\text{A3})$$

$$\text{or : } V_{IBb} = V_{IBa} + \frac{V_{OBb} - V_{OBa} - 6.06}{1.109} \quad (\text{A4})$$

where V_{IBb} is the volume contained within the IB contour of the secondary image; V_{IBa} is the volume contained within the IB contour of the primary image; V_{OBb} is the volume contained within the OB contour of the secondary image; V_{OBa} is the volume contained within the OB contour of the primary image.

This equation (Equation A1) was used to calculate the IBequ volume on CTb for the “testing” cohort and create the IBequ structure.