ORIGINAL ARTICLE

Retrospective evaluation of planning margins for patients undergoing radical radiation therapy treatment for bladder cancer using volumetric modulated arc therapy and cone beam computed tomography

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Abstract

Introduction: Current contouring guidelines for curative radiation therapy for muscle-invasive bladder cancer (MIBC) recommend margins of 1.5–2.0 cm, applied to the clinical target volume (CTV). This study assessed whether the use of volumetric modulated arc therapy (VMAT), cone beam computed tomography (CBCT) and strict bladder preparation allowed for a reduced planning target volume (PTV) expansion, resulting in lower doses to surrounding organs at risk (OARs). **Methods:** Daily CBCT images for 12 patients (382 scans total) were retrospectively reviewed against four potential PTV margins created on and exported with the reference CT scan. To form the PTVs, three isotropic expansions of 0.5, 1.0 and 1.5 cm were applied to the CTV, as well as an anisotropic expansion of 1.5 cm superiorly and 1.0 cm in all other dimensions. Following treatment completion, the CBCTs were visually assessed to determine the margins encapsulating the bladder. For retrospective planning purposes, the 1.0-cm and anisotropic margins were compared with the previously recommended margins to determine differences in OAR doses. **Results:** The 0.5-, 1.0- and 1.5-cm isotropic margins (IM) and the anisotropic margin (ANIM) covered the CTV in 46.1, 96.8, 100 and 100% of CBCTs retrospectively. Doses to OARs were significantly lower for the reduced margin plans for the small bowel, rectum and sigmoid. **Conclusion:** Bladder planning target volumes may be safely reduced. We endorse a PTV margin of 1.0cm anteriorly, posteriorly and inferiorly with 1.0–1.5 cm superiorly for radical whole bladder cases using strict bladder preparation, VMAT and pretreatment CBCTs.

Introduction

Radiation therapy has an established role as a curative treatment in muscle invasive bladder cancer (MIBC).[1] The potential changes in the size and shape of the bladder, depending on the degree of bladder filling, pose a challenge in accurate treatment delivery.[2–4] Historically, this was overcome by the use of generous margins expanded from the clinical target volume (CTV).[5,6] Generally, bladders fill anisotropically – that is, with the greatest magnitude in the superior aspect followed by anterior then in all other dimensions.[5] To accommodate

the anisotropic filling of the bladder, margin expansions of 2.0–2.5 cm superiorly; 1.5–2.0 cm anteriorly, posteriorly, and laterally; and 1.0–1.5 cm inferiorly from the clinical target volume are recommended by eviQ, an Australian government online resource of cancer treatment protocols, to ensure adequate bladder coverage for radiation treatment.[7] These margins are valid for 3D conformal radiation therapy (3D-CRT) with bony image matching for treatment,[8] however, may not be best practice in the presence of volumetric modulated arc therapy (VMAT) and soft tissue image verification.[9,10] Due to the relative dearth of studies on appropriate margins for cases treated with VMAT and soft tissue matching, the recommendations from eviQ were adopted within our organisational protocol, which served three geographical sites – the North Coast Cancer Institute, Lismore, and Mid-North Coast Cancer Institutes at Coffs Harbour and Port Macquarie – at the implementation of VMAT for radical bladder cases.

Reductions in margins for the treatment of radical bladder cancer with VMAT and soft tissue matching are clearly desirable. Direct patient benefits from a reduction in margins would likely include a decrease in dose to surrounding organs at risk (OARs), that is, small bowel, rectum and sigmoid, with a possible subsequent reduction in side effects.[11,12] Another benefit of decreased margins is likely to be a reduction in integral dose. As described by Foroudi et al., increasing CTV to PTV margins progressively beyond 0.5 cm results in modest improvement in CTV coverage but a large increase in integral dose.[13]

Bladder margins are also a consideration in partial bladder treatments. A reduction in margins, supported by robust imaging protocols, may provide an appropriate basis for a transition from whole bladder to partial bladder treatments in selected patients. Partial bladder treatments deliver a higher dose to the gross tumour volume with a lower dose to the lower risk portion of the bladder.[14] Although the doses to OARs may be lower with partial bladder than whole bladder treatments, partial bladder treatment may also be more dependent on the minimisation of bladder filling and retention for safe and appropriate treatment.

A caveat within the current eviQ treatment protocol for bladder urothelial carcinoma is that 'Smaller margins may be used if departmental set up error has been appropriately quantified'.[7] To ascertain if a reduction to the PTV margins was possible, and if so, to what degree, we sought to assess whether the use of rigid bladder emptying instructions, VMAT and cone beam CT (CBCT) would consistently allow for a smaller PTV expansion.

Methods

Twelve patients (7 male and 5 female patients) were included in this retrospective analysis of CBCTs which was approved by the Northern NSW Local Health District Ethics Committee with site-specific approval for the Mid-North Coast Cancer Institutes. The study period was from January 2017 to January 2018. Patient ages ranged from 56 to 84 (median 74.3) years. All patients had a diagnosis of MIBC (C67) and were staged at T2N0M0 with localised disease only (with no direct invasion into adjacent organs). Four patients were ECOG status 0 (33.3%) and 8 were EGOG 1 (66.7%). All patients were treated with curative intent; eleven patients were prescribed 64 Gy in 32 fractions, although one received 60 Gy in 30 fractions. Patients received concurrent chemotherapy.

As per the organisational protocol for our curative bladder cases, a stringent fluid intake protocol was used for the simulation CT and all treatment sessions. Patients were instructed to remain nil fluid by mouth for at least an hour preceding their appointment and to double void their bladder, that is, to void upon arrival to the department and again immediately prior to their simulation and treatment.

Written information was given to the patient and confirmed verbally prior to their CT appointment. All patients were scanned with a bladder ultrasound scanner (Verathon BVI 9400) to gauge their bladder volume prior to their CT simulation appointment.[15] As Verathon BVI 9400 has a bladder volume accuracy of $\pm(15\%+15$ mL), the patient was asked to repeat their bladder emptying if the bladder scanner recorded any volume.

For simulation, all patients were scanned supine and immobilised with a fixed headrest, knee fix and foot fix indexed at suitable positions dependent on the patient habitus. The CT dataset was transferred to our Monaco planning system (version: 5.11.02, Elekta-CMS Software, MO, USA,) with the CTV (encompassing the whole bladder), PTV and organs at risk – rectum, small bowel, sigmoid and femoral heads – contoured on the planning CT. Isotropic expansions of 0.5, 1.0 and 1.5 cm and an anisotropic expansion of 1.5 cm superiorly and 1.0cm inferiorly, anteriorly and posteriorly were generated from the CTV and applied to the reference planning CT (Fig. 1). All structures delineated on the reference scan were exported to our X-ray volumetric imaging (XVI) stations, Elekta 5.0.4, for daily image verification. Daily verification was performed to ensure the bladder was covered by the original planning PTV. Prior to implementation of our VMAT program for curative bladder cases, we conducted a small in-house study which showed that VMAT was delivered faster than IMRT for

comparable plans. For curative bladder cases, we opted for the efficiency of VMAT over IMRT to reduce the risk of potential underdosing of the target from bladder filling. The maximum timeline from CT to treatment was three weeks.

Concurrent chemotherapy, with the minimum required hydration, was delivered one day per week. Radiotherapy was delivered shortly after completion of the infusion, typically within an hour.

Prior to the patient's daily radiation treatment, each patient received a CBCT and image matched per departmental protocol. With XVI software (version: 5.0, ELEKTA), the bony anatomy adjacent to the target was initially auto-registered with the planning CT scan information. A second automatic match of the soft tissue target (PTV + 1 cm) was then applied. The PTV + 1 cm was the primary structure for the soft tissue registration match. The CBCT was best matched to the soft tissue anatomy with CTV to the whole bladder while ensuring the whole bladder was encompassed within the planned PTV. The match was finally assessed and approved by two radiation therapists for treatment validation.

The evaluation study margins were analysed offline posttreatment either on our XVI unit or after the images were exported to our electronic medical record system (MOSAIQ, version: 2.64, Elekta), following the completion of the patient's treatment course, to determine the smallest suitable margin which encapsulated the bladder. The smallest suitable margin was chosen by a visual assessment comparing the evaluation margins on the reference image with the bladder on the acquired image overlaid. This analysis was performed by visual inspection to replicate on-set image matching. The smallest suitable margin was recorded in Excel 2010 and was cross-checked by another radiation therapist to minimise observer bias. If delineation

between the bladder wall superiorly and small bowel inferiorly could not be discerned without doubt over which margin was appropriate, a cautious approach was employed with the larger margin chosen. In total, 382 CBCTs from twelve patients were assessed for acceptable margins which encompassed the bladder.

In order to quantify a possible benefit of reduced margins for doses to OAR, specifically the small bowel, rectum and sigmoid colon, we compared the plans of 1.0-cm IM and ANIM vis-a-vis with a plan with margins as recommended by EviQ. For the plan with the recommended margins, we employed the smallest margins recommended by EviQ, that is, 2.0 cm superiorly; 1.5 cm anteriorly, posteriorly, and laterally; and 1.0 cm inferiorly. The plans with the recommended margins were calculated first with the target volumes to ideally achieve 100% of the prescribed dose (64 Gy) to 99% of the CTV and 95% of the PTV to receive 95% of the prescribed dose. The minor violations for the CTV and PTV were 95% of CTV to receive 100% of the prescribed dose and between 95% of the PTV to receive 90–95% of the prescribed dose. The dose constraints for the OARs (small bowel, rectum and sigmoid) are shown in Table 1. Where possible, we aimed to reduce the OAR doses to either ideal or minor per our organisational protocol while maintaining our target volumes doses, but if this was not achievable, as low as reasonably achievable (ALARA). Once the plans were optimised for the margins recommended, this plan was applied to the 1.0 IM and the ANIM plans with change to neither the IMRT prescription nor parameters within the optimiser of our planning system to assess the difference of the margin reduction alone. The evaluation criteria for all plans remained the same. The average treatment times, from CBCT correction to end of treatment, were derived from MOSAIQ.
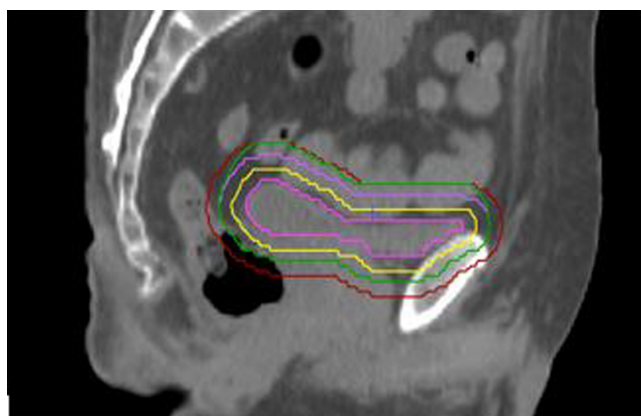
Statistical methods

Generalised estimating equations were used to estimate the proportion of scans that encompassed the bladder by the smallest acceptable margin and to account for the correlation in the data. This method – which includes 95% confidence intervals (CI) – accounts for the correlation among repeat images for each patient and reduces the effective sample size to closer to the number of patients studied, rather than the number of fractions assessed. Doses to OARs were summarised using nonparametric statistics; plans were compared with EviQ guidelines using the Wilcoxon test (paired samples). $P < 0.05$ was considered statistically significant. Representative box and whisker plots derived from the actual data were prepared for V45 small bowel, V40 rectum and V40 sigmoid,

Figure 1. Sagittal slice showing expansions applied to the CTV – CTV (pink), 0.5 IM (yellow), 1.0 IM (purple), 1.5 IM (red) and ANIM (green).

respectively. In these representative graphs, the box shows the median and interquartile range, whereas the whiskers show the lowest and highest values.

Results

In total, 382 CBCTs were assessed for the suitable margin/s which encompassed the bladder. In brief, the 1.5IM and ANIM covered all the CBCTs examined; the 1.0IM covered most of CBCTs and 0.5IM less than half of the CBCTs studied. As summarised in Table 2, the 0.5IM covered the CTV in 46.1% of scans (95% CI: 30.1, 62.7), the 1.0IM covered the CTV in 96.8% (93.7, 98.4) of scans and the 1.5IM and ANIM covered the CTV in 100% of scans. Considered another way, the 0.5IM was the *smallest* acceptable margin in 45.9% of the CBCTs (95% CI: 30.1, 62.7), the 1.0IM the smallest margin in 50.9% of the CBCTs (34.6, 67.0) and the ANIM the smallest margin in 3.2% of the CBCTs (1.6, 6.3; Table 3). None of the CBCTs required an isotropic expansion of 1.5IM.

There was no correlation between the need for larger margins and the coincidence of same-day chemotherapy and radiation treatments. On average, the duration of our patients' VMAT treatment was 3 min and 20 s (range: 2 min 55 s to 3 min 32 s).

Doses to OAR for the plans with the 1.0IM and ANIM were compared with a plan with the recommended guidelines as per EviQ (Table 4). Doses to the sigmoid were significantly lower for the 1.0IM and ANIM plans, compared with the recommended margins plan, for all the dose levels examined (Table 4). The maximum dose for the 1.0IM (median = 62.7) and ANIM (median = 64.1) was significantly lower than that of the maximum dose for the recommended margins plan (median = 65.2; $P < 0.02$ and $P < 0.03$ respectively). The differences between the reduced margin plans and the recommended margin plans were particularly significant for V40 Gy and V60 Gy ($P < 0.002$ for the 1.0-cm IM and $P < 0.003$ for ANIM plans respectively): V60 Gy (%) medians were 18.3 for EviQ, 2.5 for 1.0IM and 5.2 for ANIM. The comparisons for 40 Gy (%) showed a similar trend and are illustrated in the box plot shown in Fig. 2A. This representative plot of the raw

Table 1. OAR dose constraints for small bowel, rectum and sigmoid bowel.

Organs at risk	Ideal	Minor violation
Small bowel (EviQ, Banerjee et al, RTOG 0822)[7,23,24]	No hot spots within the small bowel Maximum dose < 67 Gy 15 Gy<230cc (RTOG 0822) 35 Gy<180cc (RTOG 0822) 40 Gy<100cc (RTOG 0822) 45 Gy<90cc	Maximum dose < 68 Gy 15 Gy < 275cc (Banerjee et al) 35 Gy <230cc (RTOG 0822) 40 Gy<130cc (RTOG 0822) 45 Gy<120cc
Rectum (Foroudi et al, 2012, EviQ)[7,10]	V40<50% V50 Gy ≤ 40% V60<25%	V40 Gy ≤ 60% V50 Gy ≤ 50% V60 Gy ≤ 35%
Sigmoid (referenced from in-house prostate protocol)	V40 Gy = 35% V65 Gy < 17% Max Dose 5cc < 102.5%	V40 Gy = 35–60% V60 Gy = 25–40% Max dose 5.1–10cc < 102.5%
Femoral heads (Foroudi et al, 2012)[10]	V35 Gy<100% V45 Gy<60% V50 Gy<10%	Same as ideal

Table 2. Number (percent) of CBCTs with acceptable margins which encompassed the bladder – assessed from each patient's daily CBCT.

Patient No.	Number of fractions	Acceptable margins which encompassed the bladder: Number of scans (%)			
		0.5IM	1.0IM	1.5IM	ANIM
1	32	32 (100)	32 (100)	32 (100)	32 (100)
2	32	16 (53.3)	30 (93.8)	32 (100)	32 (100)
3	30	6 (20.0)	27 (90.0)	30 (100)	30 (100)
4	32	3 (9.4)	32 (100)	32 (100)	32 (100)
5	32	7 (21.9)	30 (93.8)	32 (100)	32 (100)
6	32	22 (68.8)	32 (100)	32 (100)	32 (100)
7	32	7 (21.9)	32 (100)	32 (100)	32 (100)
8	32	13 (40.6)	32 (100)	32 (100)	32 (100)
9	32	20 (62.5)	29 (90.6)	32 (100)	32 (100)
10	32	19 (59.4)	30 ((93.8)	32 (100)	32 (100)
11	32	29 (90.6)	32 (100)	32 (100)	32 (100)
12	32	2 (6.3)	32 (100)	32 (100)	32 (100)
Total	382	176 (46.1% [30.1, 62.7])*	370 (96.8% [93.7, 98.4])*	382 (100%)	382 (100)

*Percentages and confidence intervals estimated using generalised estimating equations [95% confidence interval].

Table 3. Number (percent) of CBCTs with the *smallest* acceptable margin which encompassed the bladder – assessed from each patient's daily CBCT.

Patient No.	Number of fractions	Smallest acceptable margin required to encompass the bladder: Number of scans (%)*			
		0.5IM	1.0IM	1.5IM	ANIM
1	32	32 (100)	0 (0)	0 (0)	0 (0)
2	32	16 (53.3)	14 (43.8)	0 (0)	2 (6.3)
3	30	6 (20.0)	21 (70.0)	0 (0)	3 (9.4)
4	32	3 (9.4)	29 (90.6)	0 (0)	0 (0)
5	32	7 (21.9)	23 (71.9)	0 (0)	2 (6.3)
6	32	22 (68.8)	10 (31.3)	0 (0)	0 (0)
7	32	7 (21.9)	25 (78.1)	0 (0)	0 (0)
8	32	13 (40.6)	19 (59.4)	0 (0)	0 (0)
9	32	20 (62.5)	9 (28.1)	0 (0)	3 (9.4)
10	32	19 (59.4)	11 (34.4)	0 (0)	2 (6.3)
11	32	29 (90.6)	3 (9.4)	0 (0)	0 (0)
12	32	2 (6.3)	30 (93.8)	0 (0)	0 (0)
Total	382	176 (45.9% [30.1-62.7])[†]	194 (50.9% [34.6-67.0])[†]	0	12 (3.2% [1.6-6.3])[#]

*For Patient 2, for example, bladder volumes were encompassed by an isotropic margin of 0.5 cm on 16 occasions; an isotropic margin of 1.0 cm was required on 14 occasions.
[†]Percentages and confidence intervals estimated using generalised estimating equations [95% confidence interval].

Table 4. Doses to organs at risk, comparing EviQ guidelines with 10-mm (1.0IM) and anisotropic margins (ANIM).

Parameter	EviQ guidelines Median (range)	1.0IM Median (range)	P*	ANIM Median (range)	P*
Small bowel, *n* = 12					
Max Gy	66.4 (19.3–67.9)	66.1 (5.8–68.0)	0.08 (ns)	66.3 (8.0–68.7)	0.2
15 Gy (cc)	137.8 (0.5–266.0)	87.6 (0.0–163.2)	0.002	89.8 (0.0–136.5)	0.002
35 Gy (cc)	84.70 (0.0–133.8)	50.1 (0.0–100.0)	0.003	57.7 (0.0–114.2)	0.003
40 Gy (cc)	74.3 (0.0–131.0)	43.1 (0.0–92.8)	0.003	52.7 (0.0–105.9)	0.003
45 Gy (cc)	65.8 (0.0–128.0)	34.0 (0.0–84.3)	0.003	42.45 (0.0–98.5)	0.003
Rectum, n = 12					
V40 Gy (%)	19.6 (1.9–47.2)	12.6 (0.8–31.3)	0.002	10.3 (0.6–31.5)	0.002
V50 Gy (%)	10.7 (0.0–26.7)	3.5 (0.0–17.7)	0.003	2.3.0 (1.1–14.7)	0.003
V60 Gy (%)	3.1 (0.0–16.6)	0.5 (0.0–8.7)	0.005	0.4 (0.0–6.8)	0.005
Max dose (Gy)	64.6 (19.4–67.8)	62.5 (17.2–66.9)	0.002	62.4 (18.8–66.2)	0.002
Sigmoid colon, *n* = 12					
Max dose (Gy)	65.2 (53.3–68.2)	62.7 (5.8–67.8)	0.02	64.1 (9.4–69.9)	0.03
V40 Gy (%)	39.5 (3.9–83.6)	12.2 (0.0–64.6)	0.002	23.12 (0.0–74.7)	0.002
V60 Gy (%)	18.3 (0.0–66.7)	2.5 (0.0–39.1)	0.003	5.2 (0.0–53.2)	0.003

*Compared with EviQ guidelines.

data compares the estimated dose levels with the EviQ recommended margin plan and illustrates the dose variability within the patient cohort.

Similarly, doses to the rectum were significantly lower for V40 Gy (%), V50 Gy (%), V60 Gy (%) and maximum dose in the 1.0-cm IM and ANIM plans than the recommended margins plan (Table 4). To illustrate this, V50 Gy (%) medians were 10.7 for EviQ, 3.5 for 1.0IM ($P < 0.003$) and 3.0% for ANIM ($P < 0.003$). The comparisons for V40 Gy (%) are illustrated in the box plot shown in Fig. 2B.

For the small bowel, the differences between the reduced margin plans and the recommended margin plans for the dose levels of 15 Gy (cc), 35 Gy (cc), 40 Gy (cc) and 45 Gy (cc) were all highly significant. For example, 35 Gy (cc) medians were 84.7 for EviQ, 50.1 for
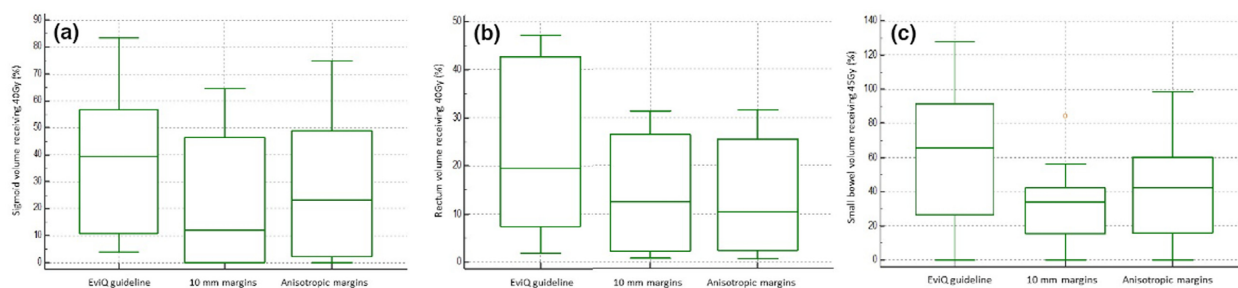
Figure 2. Comparison of the EviQ guidelines, 1.0IM and ANIM. Box and whisker plots illustrating the volumes of (A) sigmoid receiving 40 Gy (%) (B) rectum receiving 40 Gy (%) (C) small bowel receiving 45 Gy (cc).

1.0IM ($P < 0.003$) and 57.7 for ANIM ($P < 0.003$). The comparisons for 45 Gy (cc) are illustrated in the box plot shown in Fig. 2C.

Discussion

The present study suggests that a reduction in PTV margins is feasible for radical bladder cancer radiotherapy treatments using a rigid bladder protocol, daily CBCT and VMAT. In our study, a 1.0-cm isotropic margin would have been suitable to cover the bladder in 96.8%, with a 95% CI of 93.7–98.4%, of the CBCTs acquired and an anisotropic margin of 1.0cm in all dimensions, except for 1.5 cm superiorly would have encapsulated the bladder in the remaining 3.2%. Thus, our anisotropic margins would have covered the CTV in 100% of the CBCTs.

The benefits of adopting smaller margins may include a reduction in integral dose to normal tissue,[13] a decrease in dose to surrounding critical organs, as given in this study and, subsequent to this, a possible reduction in treatment-related toxicities.[11,12] Although neither integral doses nor treatment related toxicities were verified in this study, there is scope to assess these aspects in future evaluations. In this study, we showed that the doses to the small bowel, rectum and sigmoid bowel were lower in the reduced margin plans than the recommended margins and were statistically significant. This finding was across all the dose levels specified within our organisational protocol for each organ at risk, except for the maximum dose of the small bowel. Further decreases of doses to the OAR may have been possible with further optimisation of the reduced margins plans. However, to determine the effect of reducing the margins alone on the OAR, we chose the same dosimetric parameters, physical constraints, IMRT constraints and calculation and sequencing parameters as used for the recommended margins plan.

Although these are welcome benefits for the patient, caution should be exercised so that underdosing of the bladder does not become an unintentional consequence of reducing margins without a stringent bladder preparation protocol to reduce the risk of bladder filling. Henry et al[16] noted that bladder filling occurs predominantly in the cranial aspect of the bladder; hence, underdosing could have a negligible clinical outcome as tumours in the dome of the bladder are less common. In effect, for bladder cancers where the tumour is not in the dome, if the superior aspect of the CTV is *not* within the PTV due to bladder filling, this would constitute a partial bladder treatment where clinical outcomes are comparable with whole bladder treatments.[1] In our study, the fact that lack of coverage, based on a 1.0IM, was only seen at the dome, one could make an argument that most patients (i.e. patients without superior/dome involvement) could be treated with 1.0-cm expansion margins. If only 3.2% of CBCTs are not covered by the 1.0-cm IM, the dose the dome receives the remaining 96.8% of the time will be well above a 50 Gy equivalent used in a two-phase treatment approach.[7] Thus, there may be scope for considering 1.0-cm margins for MIBC patients without superior/dome involvement.

Control of fluid intake was an important consideration in the present study as variable bladder filling rates could impact the consistency of the PTV. One study involving 150 patients found that the natural bladder filling rate was approximately 1.4 mL/min.[17] In a study which investigated volume changes with cine MRI in both diseased and nondiseased bladders, filling in diseased bladders averaged 2.0 mL/min.[18] We requested the patients in our study to double void their bladder prior to their CT and treatment appointments. This action resulted in a near, if not completely, empty bladder, unless the patient had residual volume within their bladder. Validation of the bladder preparation protocol was supported when, on at least two occasions, patients declined to void immediately prior to their treatment appointment with the resultant CBCT showing the bladder volume beyond the PTV margins. Following a subsequent void and rescan, the bladder volume was within the PTV.

One finding of interest from this study was that every patient in the study had at least two CBCTs which showed the 0.5-cm isotropic margin was suitable for bladder coverage. There may be reasons why a 0.5-cm margin was appropriate in some instances: for example, patient compliance with our bladder protocol, a treatment CBCT comparable with the planning scan, or the observer's ability to discern the bladder dome from the bowel abutting the organ superiorly. An extension in time from one hour to longer for our request of nil fluid by mouth prior to the treatment appointment may give promising results, but this may have a negative effect on some patients. All patients in this study were elderly, which are a group vulnerable to the effects of dehydration, especially those consuming numerous medications and during warm weather.[19,20] Another observation was that concurrent chemotherapy appointments did not result in the need for larger margins, which supported our requirement for patients to double void prior to their treatment.

Although one can conclude that our data support plan-of-the-day radiation therapy for radical bladder cases, this technique can be a resource burden on the department with an increased risk of choosing the incorrect plan for daily treatment. In light of this, our organisation opted for one PTV margin only for our radical bladder cases with emphasis placed on a rigid bladder protocol to assist with the maintenance of a consistent bladder volume.

There are a number of limitations to this study. Firstly, we did not acquire post-CBCTs following daily treatment. As discussed, we aimed to limit the bladder inflow rate and bladder residual volume and avoided additional patient irradiation. Foroudi et al[21] argued that care should be taken when reducing margins based on pretreatment CBCTs due to intrafraction changes. In their study, the treatment time was approximately 13 mins. A recent study of PTV margins by Adil et al[22] found minimal differences between the bladder volumes pre- and post-CBCTs. They suggested that the median time of approximately seven minutes between the scans was insufficient for intrafraction changes to occur. In our study, the duration of the VMAT treatment delivery (from CBCT correction to treatment completion) was even shorter, with an average of 3 min 20 s.

Secondly, posttreatment bladder ultrasound scans were not performed as we were reliant on patient compliance and visualisation of the bladder on the patient's daily CBCT. Although the bladder scanner is a useful tool in prostate RT,[15] CBCT gives superior representative volumetric data compared with the bladder scanner.

Thirdly, the present study was retrospective in nature, with no intervention given to patients if their bladder volume was encompassed within their original planning PTV. Intervention was only applied twice to patients whose bladder volume expanded beyond their planning PTV. As the 1-cm isotropic margin was sufficient for 96.8% of CBCTs studied, therein lies the possibility that a 1-cm margin may have been appropriate for all patients as the other 3.2% of CBCTs could have had an intervention if studied prospectively. Thus, a 1-cm isotropic margin may have been achieved for 100% of cases with active intervention.

A further limitation to the present study is the relatively small patient sample size. The sample size was determined by the low number of patients with bladder cancer who present to our cancer centres for curative radiation therapy treatment. However, with 382 CBCTs acquired, the study provided sufficient information to support a change in our organisational protocol.

Conclusion

From this study, we consider it appropriate to reduce our margins for curative bladder cancer treatments with VMAT and soft tissue matching to 1.0–1.5 cm superiorly and 1.0cm in all other dimensions. The margin size reduction is feasible with 100% of CBCTs covered by the proposed anisotropic margin. The decrease in margins gives statistically significant lower doses to OAR, compared with the recommended guidelines, and could result in further reduction in side effects from treatment.

Conflicts of interest

There are no conflicts of interest.

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