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Image-Guided Radiation Therapy for Muscle-Invasive Carcinoma of the Urinary Bladder with Cone Beam CT Scan: Use of Individualized Internal Target Volumes for a Single Patient

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Key Words
Radiation therapy · Carcinoma of the urinary bladder · Urinary bladder volume · Individualized internal target volume

Abstract
Introduction: While planning radiation therapy (RT) for a carcinoma of the urinary bladder (CaUB), the intra-fractional variation of the urinary bladder (UB) volume due to filling-up needs to be accounted for. This internal target volume (ITV) is obtained by adding internal margins (IM) to the contoured bladder. This study was planned to propose a method of acquiring individualized ITVs for each patient and to verify their reproducibility.
Methods: One patient with CaUB underwent simulation with the proposed 'bladder protocol'. After immobilization, a planning CT scan on empty bladder was done. He was then given 300 ml of water to drink and the time (T) was noted. Planning CT scans were performed after 20 min (T+20), 30 min (T+30) and 40 min (T+40). The CT scan at T+20 was co-registered with the T+30 and T+40 scans. The bladder volumes at 20, 30 and 40 min were then contoured as CTV20, CTV30 and CTV40 to obtain an individualized ITV for our patient. For daily treatment, he was instructed to drink water as above, and the time was noted; treatment was started after 20 min. Daily pre- and post-treatment cone beam CT (CBCT)

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scans were done. The bladder visualized on the pre-treatment CBCT scan was compared with CTV20 and on the post-treatment CBCT scan with CTV30.
Results: In total, there were 65 CBCT scans (36 pre- and 29 post-treatment). Individualized ITVs were found to be reproducible in 93.85% of all instances and fell outside in 4 instances.
Conclusions: The proposed bladder protocol can yield a reproducible estimation of the ITV during treatment; this can obviate the need for taking standard IMs.

Introduction

Carcinoma of the urinary bladder (CaUB) is a relatively rare disease with annual incidence rate of 70,000 new cases in the United States [1]. Surgical management by radical cystectomy is considered the gold standard. Concurrent chemoirradiation has emerged as an equally effective option especially for early stages [2–8]. While planning radiation therapy for patients with CaUB, bladder filling during the treatment has to be accounted for. Therefore, a margin for internal movement of the urinary bladder (UB) has to be taken for calculating the internal target volumes (ITV) [9–13]. The proposed internal margins (IMs) for these movements range from 2 to 3 cm in various published reports [9–11, 14]. When these margins are applied to the contoured UB especially in the cranio-caudal direction, they can end up including a substantial amount of bowel within the target volumes [14, 15]. This increases the probability for small bowel toxicity. Therefore, it might be possible to limit the small bowel toxicity by an accurate prediction of the ITV. This study was planned to propose a method of acquiring individualized ITVs for each patient and to verify their reproducibility.

Methods

The selected patient was male with a biopsy-proven CaUB and was planned for upfront curative radiation therapy with concurrent chemotherapy. The patient had normal kidney function tests and was not suffering from lower urinary tract symptoms. Cystoscopy was suggestive of a disease in the trigone area, and a CT of the abdomen and pelvis did not reveal any lymphadenopathy. Informed consent was obtained from the patient after explaining the planned procedure. The patient's actual treatment planning was done with a standard margin of 2.5 cm, and only cone beam CT (CBCT)-based observations were used for this study. Ethical Committee clearance was therefore not required for this study. Radiation therapy was done on a Varian Trilogy linear accelerator (Varian Medical Systems, Inc., Palo Alto, Calif., USA).

CT Simulation

We instructed the patient to report for CT simulation after about 2 h of fasting, so that adequate dehydration could be achieved. Immobilization was done with a thermoplastic cast over the abdomen and pelvis clamped over an all-in-one board (THE AIO SOLUTION®, Orfit Industries) as per departmental protocol. After preparing the cast, the 'bladder protocol' for bladder volume predictability was followed. The patient was requested to empty his bladder. Upon return, the patient was given 300 ml of water to drink, and the time (T) was noted when he had finished. A contrast CT scan was performed exactly 20 min after that timepoint (T+20). The next scan was taken after 30 min (T+30) followed by another one after 40 min (T+40); both these scans were non-contrast scans.

Contouring

All scans done at T+20, T+30 and T+40 were co-registered on the Eclipse treatment planning system (Varian Medical Systems, Inc.). The T+20 scan was chosen for contouring the target volumes of the bladder and pelvic lymph nodes. The bladder was contoured as CTV20. The co-registered images

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of the scans taken at T+30 and T+40 were blended with the scan taken at T+20. These images were used to contour the bladder volumes at T+30 and T+40 as CTV30 and CTV40 (fig. 1). CTV30 and CTV40 were the predicted volumes of the bladder at 30 and 40 min, respectively, after the consumption of 300 ml of water (T).

Treatment Planning

The contoured volume of CTV40 was fused with the contoured CT volume for the lymph nodes and used for planning. According to ICRU 62, a margin for set-up error (SM) was added over CTV40 to create a planning target volume. This final volume was used for planning the IMRT, for phase I 45 Gy in 25 fractions would be delivered. Boost (phase II) was planned based on CTV20 to a dose of 19.8 Gy in 11 fractions after adding a SM. The SM was taken as 0.8 cm at all instances. Other organs at risk – bowel, rectum and femoral heads – were also contoured.

Treatment Delivery

Radiation therapy was delivered to the patient in accordance with the above-mentioned bladder protocol every day. After requesting the patient to empty the bladder, 300 ml of water was offered, and the time was noted when he had finished (T). The patient was taken for positioning and set-up after exactly 15 min, so that the beam could be switched on by 20 min after water intake (T+20). This gap of 5 min was allowed for positioning, set-up and CBCT scanning. Apart from time T, the time at which the beam was switched on and the time at which each daily fraction was completed were duly recorded. Similarly during phase II (boost), since planning was done on CTV20, the patient was taken in at 5 min after T, and treatment was started by 10 min after water intake (T).

Imaging during Treatment

The patient underwent CBCT scans before and after each treatment session.

Offline Review

The observations for this report were obtained according to Offline Review® (Eclipse treatment planning system; Varian Medical Systems, Inc.). All imaging sessions were reviewed offline to check whether the predicted bladder volumes contoured after simulation (CTV20, CTV30, etc.) were reproducible during actual treatment. As per the bladder protocol that was followed, the treatment was started by 20 min after time T. The average duration of each fraction in phase I was roughly 7 min. Therefore, during offline review, it was noted whether or not the bladder volumes were within CTV20 in the pre-treatment CBCT scan and within CTV30 in the post-treatment CBCT scan during phase I. The duration of treatment in phase II was about 4 1/2 min. Therefore, during offline review, it was checked whether the volumes fell within CTV20 in the post-treatment CBCT scans. If the volume was observed to be outside, then the maximum dimension of difference was recorded in millimeters.

Results

The total number of analyzable CBCT scans was 65, out of which 36 were pre-treatment scans and the remaining 29 were post-treatment scans (table 1). Of the 29 post-treatment scans, 19 were done during phase I and 10 during phase II (table 1). The volumes fell within the predicted volumes in 93.85% of all instances. The target was outside the predicted bladder volume in 4 instances: 2 in the pre-treatment CBCT scans and 2 in the post-treatment CBCT scans in phase I. Out of these 4 instances, at 1 instance it was outside of both the pre- and the post-treatment scans. For the remaining 2 instances, the bladder volume was within the predicted contours in at least 1 scan (either the pre- or the post-treatment CBCT scan). For each of these 4 instances, excessively loaded bowel was the reason of mismatch (fig. 2). The maximum dimension of mismatch in the pre-treatment CBCT scan with reference to CTV20 was 40 mm, and in the post-treatment CBCT scan with reference to CTV30 it was 17 mm. There were no mismatches during phase II.

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Discussion

The aim of this study was to test a methodology proposed to procure individualized ITVs for UB and to examine their reproducibility in daily practice. These individualized ITVs can help in decreasing the IMs taken during planning and can decrease the bowel dose. A possible drawback of the proposed methodology could be the fact that the movements of the bladder may not be reproducible over the course of a planned treatment. Our study was designed to address this concern by incorporating both pre-treatment and post-treatment CBCT scans at every fraction. Our results showed that in this patient the bladder volume was predictable in 93.85% of all instances. This figure is very encouraging because the reason for the mismatch in all instances was rectal fullness due to fecal matter, for which the patient was prescribed laxatives. He was instructed to use laxatives every day irrespective of constipation. We also changed the time for radiation therapy to the same time when simulation was done. After this there were no instances of mismatch seen. We also instructed the patient to not eat or drink anything for 2 h before treatment every day to maintain a similar level of hydration as on the simulation day.

There was a total of 4 instances of CBCT mismatch, twice in the pre- and twice in the post-treatment CBCT scan. In only one instance was there a mismatch in both the pre- and the post-treatment scans. It is worth noting that this patient was actually planned with a larger margin, as detailed before, to account for such instances. The reported mismatches of this study are the ones with respect to the expected volumes of CTV20 and CTV30, as detailed before. The maximum dimension of the reported mismatch was 4 cm. It is recommended in the published literature [9–11, 13] that a standard margin of 3 cm be applied to bladder volumes while undertaking 3D planning. It has also been discussed that such margins can lead to irradiation of normal bowel to a large extent [14, 15]. The bowel volume that would have been a part of CTV if the recommended margin of 3 cm had been taken was calculated and was found to be 204.28 ml as compared with the volume of 30.36 ml when CTV30 was considered. Therefore, the bowel volume within the ITV was substantially smaller when individualized ITVs were used. Since this can definitely have a considerable effect on bowel toxicity, we feel that this method of obtaining individualized ITVs using our proposed bladder protocol may be clinically useful. Indeed, our patient who received a total dose of 64.8 Gy in 36 fractions with concurrent gemcitabine injections to a weekly dose of 100 mg/m^2 tolerated the treatment very well with only RTOG grade II toxicity at discharge. He did not need any admission.

Our patient had polycystic kidney disease with borderline high values on kidney function tests; therefore, a cisplatin injection was not used as concurrent chemotherapy, and gemcitabine injections were used instead. The bladder volume might have been unpredictable if a cisplatin injection had been used, due to associated use of diuretics and hydration.

The reported findings are constrained by the fact that they were obtained from only 1 patient. However, the process we followed was very strict and merits discussion so that future studies may be performed. Since the study has been done on only 1 patient, we would like to analyze the results of our bladder protocol in a few more of our patients before we apply it to clinical use.

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Conclusion

We conclude that the proposed bladder protocol and the process of imaging for planning can yield reproducible IMs to bladder volumes which can be significantly lower than standard margins. This method can obviate the need for applying the same standard margins for all such patients. Since the ITV obtained with the bladder protocol was lower than the ITV obtained with the standard margin, this practice can reduce the bowel doses.

Table 1. Summary of the analyzable CBCT scans

Pre-treatment CBCT at T+20	
Total number of scans obtained	36
Number of times the volumes fell outside of CTV20	2 (5.55%)
Maximum value by which the contour was outside, mm	40
Post-treatment CBCT during phase I	
Number of scans done	19
Number of times the volumes fell outside of CTV30	2 (1.05%)
Maximum value by which the contour was outside, mm	17
Post-treatment CBCT during phase II (boost)	
Number of scans done	10
Number of times the volumes fell outside of CTV20	0
Maximum value by which the contour was outside, mm	0

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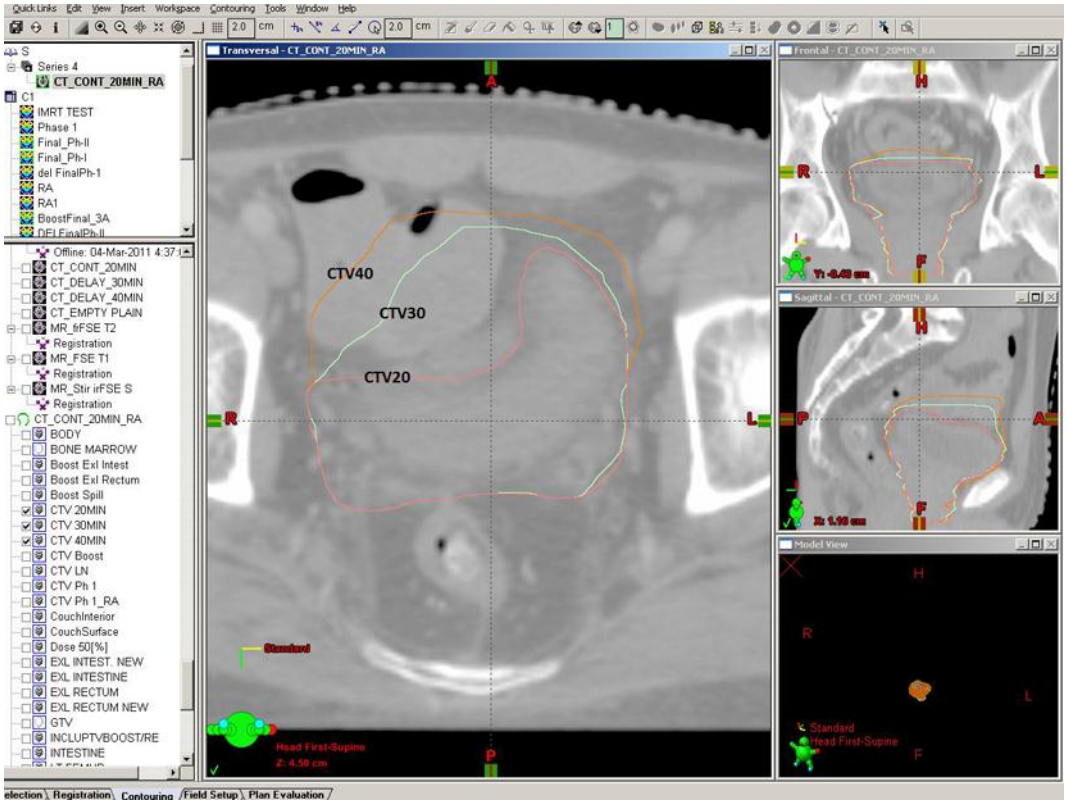

Fig. 1. A screenshot showing CTV20, CTV30 and CTV40 contoured after blending with CT scans obtained as per the bladder protocol.

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Fig. 2. A screen shot showing the mismatch between the bladder volume and CTV20 on a pre-treatment CBCT scan. Note the loaded rectum (arrowhead). Also note the CTV40 (arrow) which was the volume over which actual treatment was prescribed for the patient.

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