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Tafaul-Al-Ahsa Cancer Foundation Wins EXCELLENCE AWARD for Cancer Awareness Initiatives at Gulf Cancer Awareness Week 2024





The Gulf Oncology Society meeting resulted in fruitful outcomes, with young doctors showing keen enthusiasm for assuming leadership roles and implementing impactful initiatives.

The Official Journal of the Gulf Federation For Cancer Control

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Case Report

Managing Inconsistent Bladder Volumes in the Prostate Cancer Patient Using Daily Online Adaptive RT: A Case Report

Venkada Manickam Gurusamy, Yoganathan Sullimullur Arunachalam, Mohamed Riyaz Poolakundan, Sarah Fiona Mc Cabe, Rabih Wafiq Hammoud, Noora Al–Hammadi

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Abstract

Purpose: We report the use of online adaptive radiotherapy (OART) aiming to improve dosimetric parameters in the prostate cancer patient who had lower urinary tract symptoms that caused him not to adhere to the standard bladder filling protocol.

Methods and materials: The reference treatment plan for adaptive radiotherapy plan was generated for the pelvis and the solitary bony lesion using the Ethos treatment planning system. For each treatment session, high–quality iterative reconstructed cone beam CT (CBCT) images were acquired, and the system automatically generated an optimal adaptive plan after verification of contours. Image–guided RT (IGRT) plans were also created using the reference plan recalculated on the CBCT scan and were compared with adaptive plans.

Results: The reference bladder volume in the planning CT scan was 173 cc, and the mean bladder volume difference over the course was 25.4% ± 16.6%. The ART offered superior target coverage for PTV 70 Gy over online IGRT (V95: 90.5 ± 3.2 % Vs 97.3 ± 0.4%; p=0.000) and the bladder was also better spared from the high dose (V65 Gy: 17.9 ± 9.1% vs 14.8 ± 3.6%; p=0.03). However, the mean rectum V65 doses were very similar in both plans.

Conclusion: Managing the inconsistent bladder volume was feasible in the prostate cancer patient using the CBCT–guided OART and our analysis confirmed that adaptive plans offered better target coverage while sparing the bladder from high radiation doses in comparison to online IGRT plans.

Key Words: radiotherapy, CBCT, online adaptive radiotherapy, image–guided RT.

Introduction

Maintaining a consistent bladder volume is critically important for accurate radiotherapy (RT) treatment delivery in prostate cancer patients, and some studies have shown that bladder volume variation influences the daily position of the prostate [1,2]. A prospective randomized study was designed to provide evidence–based bladder–filling instructions to achieve a consistent bladder volume throughout RT treatment. Drinking 540 ml of water before radiotherapy was associated with reproducible bladder volumes and there was no deterioration in quality of life or increase in toxicities [3]. Most institutional protocols require patients to empty their bladder and drink about 500 mL of water and wait 30–40 minutes prior to RT treatment sessions.

However, some prostate cancer patients present with lower urinary tract symptoms and a significant proportion of patients experience acute radiation–induced symptoms of higher frequency, urgency, hematuria, incontinence, urinary obstruction, and noninfective cystitis, especially in the last few weeks of treatment [4,5]. These patients frequently struggle to follow the standard bladder–filling protocol, which results in a significant anatomical variation from the radiotherapy planning computed tomography (CT) scan.

Recently, online adaptive radiotherapy (OART) has been introduced, focusing on re–optimizing the treatment plan for every fraction based on patient's anatomy while

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he is on the treatment couch. We employed this advanced radiotherapy technique aiming to improve the dosimetric parameters in the patient who had lower urinary tract symptoms that caused him not to adhere to the standard bladder protocol. This case study was reviewed and approved by the institutional Medical Research Center.

Case presentation

The 77–year–old patient presented with high PSA levels and urgent and frequent urination. Biopsy confirmed prostatic acinar adenocarcinoma and the Gleason score was 4+4=8. Gallium–68 prostate–specific membrane antigen positron emission tomography (PSMA PET) CT whole body showed intense bilateral PSMA uptakes in the prostate gland with a separate focus in the left posterior peripheral zone, and an intense bony uptake in the cortical zone of the left ischial tuberosity.

MRI showed enlarged prostate with 80 ml in volume with intravesicular protrusion of the reteroourethral lobe and multiple suspicious lesions in the peripheral and transition zones. Based on the decision of the multidisciplinary team meeting, he was started on hormonal therapy. Radiotherapy was planned to the pelvis and the bony lesion.

Radiotherapy planning

Due to the patient's clinical symptoms, a strict bladder–filling protocol was not followed. The patient was instructed to take water as comfortably as before treatment. The patient was immobilized and underwent radiotherapy planning CT with a 3–mm slice thickness.

The prostate, seminal vesicles, the clinical target volume (CTV) and organs at risk (OARs) including the rectum, bladder and the bowel were contoured manually according to standard international and department guidelines in the Eclipse treatment planning system (Varian Medical System, Palo Alto, USA) [6]. Being rigidly registered to the planning CT scan, the MRI scan was used as a guide to aid in contouring the CTV 70 Gy, including the prostate and seminal vesicles. CTV 50.4 Gy included the elective lymph nodes in the pelvis, and the metastatic bone lesion was included in CTV 64.4 Gy. All these contours were transferred to Ethos Treatment Management for initial plan generation. In the Ethos system, planning target volume (PTV) 70 Gy was derived automatically with a 7 mm margin around the CTV 70 Gy except for 5mm in the posterior direction. PTV 64.4 Gy and PTV 50.4 Gy were also derived using a 5mm uniform margin. A single–phase treatment plan was generated to deliver 70/64.4/50.4 Gy in 28 fractions to the respective PTVs.

The clinical goals were included for each contour as per international guidelines for treatment plan optimization [6,7]. The optimal clinical goals finalized as the clinical intent were used for the reference plan generation during the initial planning phase as well as adaptive sessions. The dose calculation was performed using the Acuros XB algorithm and a twelve–field intensity modulated radiotherapy (IMRT) plan was selected as the reference plan for treatment.

Adaptive Treatment delivery

For each session, high–quality iterative reconstructed cone beam CT (CBCT) images were acquired after patient setup. The Ethos system automatically contoured structures (the bladder, rectum, bowel, prostate and seminal vesicles) on CBCT images using an artificial intelligence (AI) model. These structures are called influencers as they can alter the shape of CTVs while propagating them from planning CT to CBCT of the day. The auto–segmented contours were edited manually if needed. After the influencer contouring, the system transferred CTV 64.4 Gy and CTV 50.4 Gy onto the CBCT from the planning CT using structure guided deformation. The CTV 70 Gy included the prostate and seminal vesicles. While reviewing the accuracy of target propagation, the CTVs were manually edited if needed. Then, the system created all three PTVs automatically using the auto–PTV derivation. Once the PTVs were approved, the system automatically generated a new optimized adaptive treatment plan with beam geometry like the one in the initial treatment plan i.e. 12 field. In addition to the adaptive plan, the system also created a scheduled plan which is the reference or initial treatment plan re–calculated on the CBCT. The doses in the scheduled plan can be considered similar that in routine daily online image–guided RT (IGRT). Both plans were evaluated, and the better one was selected for treatment. An independent dose check of the adaptive plan was performed using Mobius3D. The Mobius3D calculated dose distribution (using collapsed cone algorithm) was compared against the Ethos calculated using 3D gamma evaluation (3% global /3mm, 10% tolerance), and we observed greater than 95% pixels passed the gamma criteria for all fractions. After the adaptive plan was approved by a Radiation Oncologist and a Physicist, it was sent to the Ethos treatment delivery system. The second CBCT was acquired before beaming on to check the anatomy of the patient had not changed and translational couch shifts were applied if needed.

All the planned treatment fractions were delivered, and the radiotherapy was tolerated well without any interruptions. The review of the dosimetric data was

done for target volumes and OARs. Statistical analyses between ART and online IGRT were performed using the Student's t–test (two–tailed, heteroscedastic). The difference was considered significant if the p–value was < 0.05. Daily variation in bladder volumes are shown in Fig 1 and the mean bladder volume difference ± standard deviation (SD) was 25.4% ± 16.6%. The comparison of dose volume parameters for online IGRT and adaptive radiotherapy is depicted in Table 1. The dose distribution of daily IGRT and adaptive radiotherapy for a fraction are shown in Fig 2 and 3.

Discussion

The Ethos system (Varian Medical Systems, Palo Alto, CA) is an AI–driven novel solution which can deliver CBCT–based daily OART [8]. It is possible to correct inter–fractional anatomical variation during radiotherapy with this system, which will probably improve the therapeutic ratio, especially in pelvic malignancies.

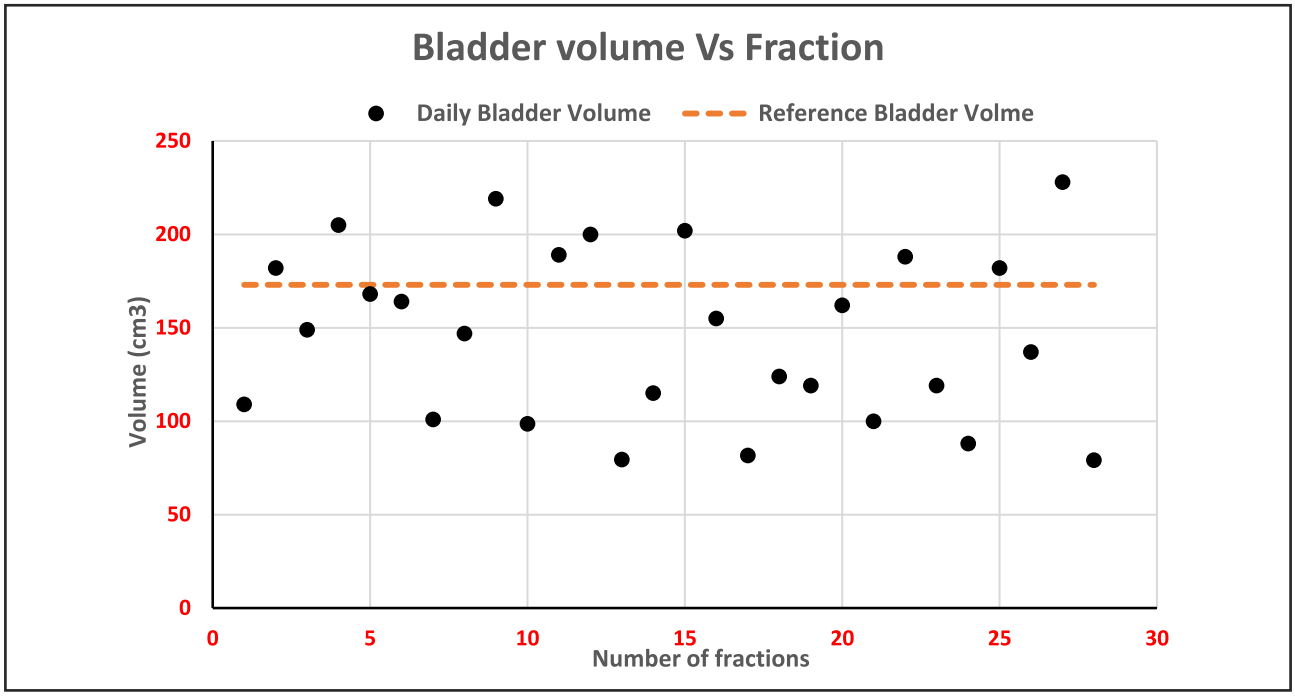


Figure 1. The bladder volume variation during treatment sessions. Reference bladder volume – the volume in the planning CT scan (173cc).

Targets/OARs	Volumes	Online IGRT Mean ± SD%	Adaptive RT Mean ± SD%	P–value
PTV 70 Gy	V95%	90.5 ± 3.2	97.3 ± 0.4	0.000
PTV 64.4 Gy	V95%	92.5 ± 8.0	98.6 ± 6.7	0.00002
PTV 50.4 Gy	V95%	98 ± 0.7	96.0 ± 7.3	0.19
Rectum	V65	4.6 ± 3.7	3.8 ± 0.8	0.32
	V55	9.8 ± 4.9	9.0 ± 1.5	0.43
	V45	17.5 ± 6.3	16.2 ± 2.6	0.33
Bladder	V65	17.9 ± 9.1	14.8 ± 3.6	0.03
	V45	54.3 ± 13.1	47.2 ± 8.3	0.0002
Bowel loops	D2 cc	189.6 ± 5.4 cGy	190.5 ± 6.6 cGy	0.50

Table 1. Comparison of dose volume histogram parameters

Abbreviations: OARs – organs at risk; IGRT – image guided radiotherapy; RT – radiotherapy; SD – standard deviation; PTV – planning target volume; V95% – the volume receiving at least 95% of prescribed dose; V65 – the volume receiving ≥65 Gy; V55 – the volume receiving ≥ 55 Gy; V45 – the volume receiving ≥ 45 Gy. D2 cc – the minimum dose received by the hottest 2 cc.

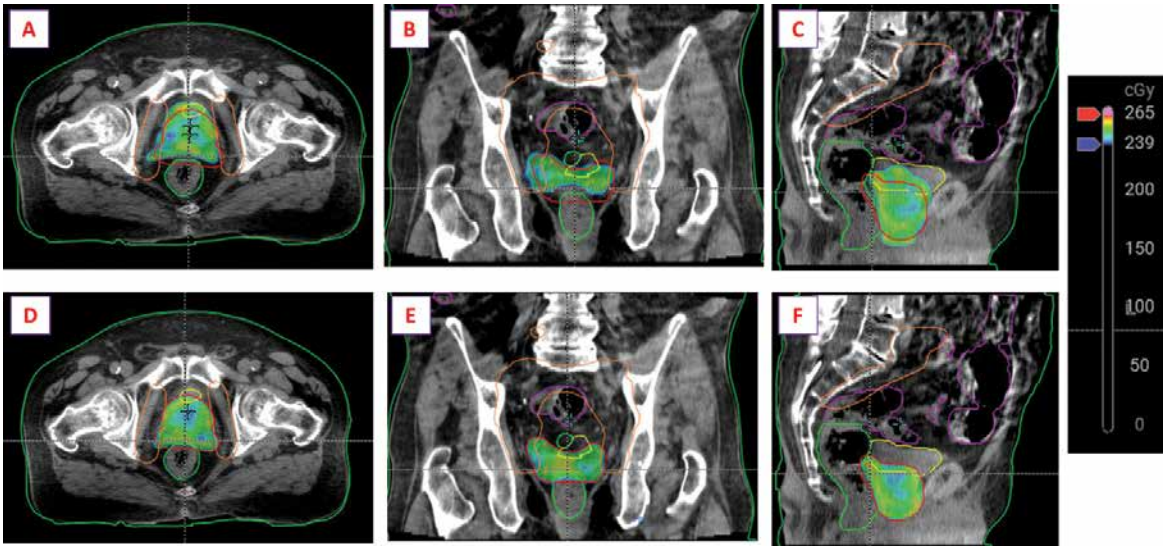


Figure 2. A–C: IGRT plan dose distribution on the cone beam CT taken during a treatment session. D–F: adaptive plan dose distribution. The panes on the left are the axial cross–section while the right panes are the sagittal cross–section and the middle are the coronal cross–section. Red – the planning target volume 70 Gy; Green – the rectum; Yellow – the bladder; **Magenta – bowel loops.**

In this report, the application of online adaptive RT to the prostate patient who was not able to hold urine during radiotherapy was demonstrated. OART was utilized in our patient based on the hypothesis that it could potentially reduce the doses of OARs. Despite huge inter fraction variation in bladder volumes and in prostate anatomy, significant improvement in PTV 70/64.4 Gy coverage and a decrease in bladder doses were achieved with adaptive planning. However, the mean rectum V65 doses were very similar in both plans. The auto derivation of the PTV by the system was very useful during adaptive sessions as only CTVs needed to be edited.

Similarly, the clinical use and potential benefits of adaptive radiotherapy have recently been demonstrated. Specifically, eleven prostate cancer patients were treated with CBCT–guided OART in a study using a fractionation scheme of 20 × 3 Gy. The mean V95% of PTV60 Gy ± SD was 86.7 ± 6.2% for the scheduled plans and 99.4 ± 0.5% for the adapted plans. Mean decrease of V60Gy of bladder and rectum ± SD was 3.9 ± 1.8% (range: 0.6–9.5%) for the adapted plan compared to the scheduled plan [9]. Moreover, sixteen patients with muscle–invasive bladder cancer received two or more (median = 23) fractions as OART, and the remaining fractions as non–ART in a study. The median (interquartile range) volume reduction in the PTV volume was 33.9% (24.2–45.0%), comparing OART and non–ART plans [10]. Results of selected studies that utilized adaptive radiotherapy in prostate cancer patients are summarized in Table 2.

Study	Patients	Adaptive sessions	Outcomes
Byrne et al. [11]	N=18	N=182	Adaptive plan was preferred in 95% of fractions Adaptive plan met more goals than scheduled plan in 78% of fractions Significant improvements in dosimetric parameters
Zoho et al. [12]	N=6	–	Confidence in the current OART workflow increased
Moazzezi et al. [13]	N=25	N=250	Minor auto–segmentation edits required in 96% of fractions Adaptive radiotherapy improved CTV coverage by 2.9% Bladder and rectum V90% decreased by 13.1% and 6.5%, respectively
Morgan et al. [14]	N=20	N=248	Online adaptive radiotherapy decreased PTV margins and improved rectal dosimetry With a symmetrical expansion of 3 mm from CTV achieved excellent target coverage

Table 2. A summary of selected studies that included adaptive radiotherapy in the treatment of prostate cancer patients.

Abbreviations: OART – online adaptive radiotherapy; CTV – clinical target volume; PTV – planning target volume; V90% – the volume receiving at least 90% of prescribed dose.

CBCT scans were used in our patient for daily online adaptation and planning. However, inferior image quality in comparison to the planning CT scan and artifacts might have resulted in some inaccuracies in the delineation of the prostate, and the bladder. In addition, the proper assessment of late toxicity needs more long–term follow–up. However, to best of our knowledge, it is the first report of using OART for the prostate cancer patient who was not able to follow the bladder protocol, and of achieving optimal dose volume constraints for radiotherapy.

In conclusion, managing the inconsistent bladder volume was feasible in the prostate cancer patient using the CBCT–guided OART and our analysis confirmed that adaptive plans offered better target coverage while sparing the bladder from high radiation doses in comparison to online IGRT plans. However, further prospective randomized studies with a large sample size are needed to further analyze and quantify the clinical benefit of this novel method in the future.

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Conflict of Interest:

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical information

Medical Research Center in Hamad Medical corporation, Qatar granted ethical approval and permission for this case report be published. We confirm that all steps of scientific research were performed by relevant guidelines and regulations. Informed consent for the study participation was not deemed necessary because of the retrospective nature of this study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Abbreviations

OART – online adaptive radiotherapy

CBCT – cone beam CT

RT – radiotherapy

CT – computed tomography

IGRT – image–guided RT

PSMA PET – prostate– specific membrane antigen positron emission tomography

CTV – clinical target volume

OAR – organs at risk

CTV – clinical target volume

Gy – Gray

IMRT – intensity modulated radiotherapy

SD – standard deviation

AI – artificial intelligence

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