

Volume and dosimetric analysis of rectum and bladder for prostate carcinoma patients by using kilo voltage cone beam computed tomography (CBCT)

K. Venkatesan^{1,3}, C.J. Raphael¹, K.M. Varghese¹, P. Gopu¹,
S. Sivakumar¹, M. Boban¹, N.A.N. Raj², K. Senthilnathan³,
P. Ramesh Babu^{3*}

¹Department of Radiation Oncology, Amala Institute of Medical Sciences, Thrissur-680555, Kerala, India.

²Centre for Biomaterials, Cellular and Molecular Theranostics (CBCMT) VIT University, Vellore-632014, India

³Department of Physics, School of Advanced Sciences VIT University, Vellore 632 014, Tamil Nadu, India

ABSTRACT

Background: To study and analyze the variations in delivered doses to rectum and bladder of carcinoma prostate patients by using kilo Voltage (kV) 'Cone Beam Computed Tomography' (CBCT) images. **Materials and Methods:** 2-Dimensional kilo Voltage (2D kV) Imaging and CBCT were done for seven prostate cancer patients. The deviations among their shifts were correlated and the volumetric changes of the rectum and bladder were analyzed. Rectum and bladder contours were redrawn on every boost fractions and dose calculation were performed on CBCT images to study the effect on dose volume histograms. **Results:** A correlation coefficient for set-up variations was within 0.78 for all directions between CBCT soft tissue matching and kV bone match. The mean deviation of bladder and rectum volume over the boost fractions was -12% to +9% (SD 31cc to 70cc) and -10.2% to +12% (SD 3.1cc to 14.9cc), respectively. Bladder mean dose variation was <1.5Gy for all three positions whereas it was <3.65Gy for rectum. D1% dose deviation from reference plan for bladder was 1.1Gy (CBCT matched position), 1.4Gy (kV matched position), and 1.7Gy (no correction), and for rectum, the deviations were 1.2Gy, 2.2Gy, 3.6Gy, respectively. No significant deviation was found statistically significant at the low dose region. **Conclusion:** It is possible to achieve good dose delivery and conformity in target (prostate) with CBCT image guidance rather than kV bone match, but dose contribution to the rectum is dependent on the patient's anatomy, bladder filling, and rectum filling, pertaining to the day of examination.

Keywords: Image-guided radiotherapy, prostate, bladder, rectum.

► Original article

*Corresponding authors:

P. Ramesh Babu, Ph.D.,

E-mail:

prameshbabu@vit.ac.in

Revised: July 2019

Accepted: August 2019

Int. J. Radiat. Res., July 2020;
18(3): 557-569

DOI: 10.18869/acadpub.ijrr.18.3.557

INTRODUCTION

In prostate cancer, conventional radiotherapy (RT) at conventional low doses has not been very satisfactory when comparing clinical outcomes, but it has a lower risk of biochemical failure if high-dose is received rather than conventional-dose and conformal radiation⁽¹⁻³⁾. Highly conformal radiation therapy for the treatment of prostate cancer has been shown to reduce the risk of rectal toxicity compared with

conventional radiation therapy⁽⁴⁻⁶⁾. Intensity modulated radiotherapy (IMRT) has been shown to be superior to three-dimensional conformal radiotherapy (3D-CRT) in terms of both comprehensive nodal coverage and decreased dose to the surrounding normal tissue^(7,8). Rapid development in image-guided radiation therapy (IGRT) has provided powerful tools for improving the accuracy of patient positioning and target localization⁽⁹⁻¹¹⁾. Many studies have been devoted to the understanding of set-up

uncertainties for target localization. During the course of radiotherapy, the inter-fractional movement of prostate position has to be verified by using CBCT or 2D planar imaging (with the help of implanted fiducial marker) ⁽¹²⁻¹⁴⁾. Adaptive IGRT reduces the risk of geometric miss and results in excellent bio-chemical control that is independent of rectal volume/distension, while maintaining very low rates of chronic gastrointestinal toxicity ^(15,16).

Maud et al. ⁽¹⁷⁾ showed that margin reduction is possible when using daily CBCT for prostate to prostate matching during IGRT and it could be more useful than 2D planar imaging (without fiducials). Yoo et al. ⁽¹⁸⁾ and Kaliyaperumal et al. ⁽¹⁹⁾ showed that the dose calculation on CBCT is comparable with fan beam planning CT and dose difference is minimal. Adamczyk et al. ⁽²⁰⁾ studied about combining the bony anatomy and soft tissue positioning can improve the precision and effectiveness of the dose delivery to the target. They stated that CBCT could be used for minimization of the setup error further, but imaging time is the limiting factor. Yartsev et al. ⁽¹²⁾ studied the target margins in prostate cancer and found that online adaptation should improve the radiation delivery. Maggio et al. ⁽²¹⁾ studied the impact of the rectal and bladder filling with the patient's treatment outcome and concluded that bladder and rectal preparation significantly decreases the biochemical and clinical failures. Zhichen et al. ⁽²²⁾ evaluated the variation of bladder and rectal filling with dose delivery and found that bladder volume is significant to the dose changes to the prostate. Gill et al. ⁽²³⁾ studied about the margins required for accurate dose delivery without increasing the rectal dose. They stated that 3mm margin could be adequate for target without increasing the rectum dose when soft tissue match was performed.

In our study, the volumetric changes of the rectum and bladder have been analyzed during the radiotherapy treatment of Carcinoma Prostate. Our aim in this work was whether the volumetric imaging with soft tissue matching can reduce the dose to normal structures (rectum and bladder), and whether dose

delivery accuracy can be improved if adaptive radiotherapy was performed using CBCT. We have analyzed and compared three possible scenarios of daily treatment with and without image guidance, so that we can quantify the impact of different imaging methods. The deviation between 2D kV and CBCT match has been correlated. The dose calculation has been performed on CBCT with modified rectum and bladder contours on every fraction of boost phase with three methods of matching, i.e., CBCT matched prostate position, bony match with 2D kV imaging, and no match applied (for studying the variation without any imaging).

MATERIALS AND METHODS

Patient selection and simulation

Totally, seven patients were taken in this study (table 1). The patients were simulated with thermoplastic cast and other immobilization devices. Before simulation, the patients were advised to empty their bladder and drink two glass of water (500 ml). After 30 minutes, patient CT scan was performed with the slice thickness of 3mm in GE dual scan CT scanner. The volume of bladder and rectum were observed in CT images, and if the bladder was not sufficiently filled or the rectum was filled with gas, the patient was re-simulated with prior preparations to achieve optimal bladder and rectum filling. The images were exported to Eclipse treatment planning system (TPS) version 11.0 (Varian medical systems Palo Alto). The prostate, seminal vesicles, and other normal structures were drawn in CT images with standard guidelines. The prostate was taken as gross tumor volume (GTV). GTV and microscopic spread (including seminal vesicles) were taken as clinical target volume (CTV_t). For the first phase, the margin taken from CTV_t to planning target volume (PTV) was 0.9cm for superior-inferior, 1.5cm for anterior, 0.5cm for posterior, and 0.9cm for lateral (left to right) directions, and it was defined as PTV_t. The lymph nodes were drawn and 0.7cm margin was given uniformly and it was termed as PTV nodal (PTV_n). For the second phase, a margin of 1.0cm

for anterior, 0.4cm for posterior, 0.9cm for superior-inferior, and 0.5cm for lateral

directions (left to right) wastaken from CTV_t and it was termed as PTV_{boost}.

Figure 1. Modified Ondo Google Satellite Map Showing Zones of Sample Collection. Map data ©2017 Google (14)

	Age	Stage	Dose Prescription		Cumulative BED*(Gy)	Cumulative EQD2* (Gy)
			Initial Phase	Boost Phase		
Case1	69	T3N0M0	54Gy/30f	19.8Gy/9fr	177.44	71.8
Case2	66	T3N1M0	50Gy/25fr	24Gy/10f	179.07	76.7
Case3	62	T2N0M0	50Gy/25fr	28Gy/14fr	182.00	78.0
Case4	68	T3N0M0	45Gy/25fr	30Gy/12fr	179.00	76.7
Case5	60	T3N0M0	46Gy/23fr	32Gy/14fr	188.10	80.7
Case6	65	T3N1M0	45Gy/25fr	30Gy/13fr	175.17	77.1
Case7	60	T3N0M0	50Gy/25fr	28Gy/14f	184.87	78.0

Dose prescription and treatment delivery

The radiation treatment plan was divided into two phases. In the first phase, 46-50Gy was delivered in 23 to 25 fractions (2Gy per fraction) for PTV primary and PTV nodal. In the second phase, the treatment plan was generated 24Gy to 30Gy in 10 to 12 fractions (2.4Gy to 2.5Gy per fraction) to PTV primary. In some patients, the 8Gy in four fractions was planned after 46Gy to PTV primary. For the second phase, the re-simulation of CT was taken with the same procedure as mentioned in the first phase. IMRT or volumetric modulated arc therapy (VMAT) dose plan was generated with 6MV in Trilogy linear accelerator (Varian medical system Palo Alto). Quality assurance of the treatment plan was performed with electronic portal imaging device with portal dose image prediction.

During the first phase, the patients were advised to follow the rectum and bladder protocol before each treatment (same as the simulation procedure). After patient setup, 2D kV image was taken to verify the bone match and patient rotation. If the patient's translation error was less than 3mm in all directions and rotational error was less than 0.7 degree, then the CBCT was taken for the verification of PTV prostate, rectum, and bladder. The bladder and rectum volumes were compared to the volumes in planning CT and if the variations were less, then the treatment was continued. Otherwise, the patient was released and advised to come again after bladder and rectum preparation. For the first three fractions, the same procedure explained above was repeated to verify the

reproducibility of rectal and bladder volumes, followed by the changing of the imaging protocol (daily-kV and weekly twice-CBCT). In the second phase, before the treatment, 2D kV image was taken for the verification of bone match and if minimum translational and rotational error was found, then CBCT was taken. In CBCT, the rectum and bladder were observed and soft tissue match (prostate to prostate) was performed. Finally, the CBCT matched shifts were applied and the treatment was performed.

Dose calculation on modified bladder and rectum volume in CBCT

The CBCT images were analyzed for boost phase and the rectum and bladder were re-drawn on CBCT for every fraction. Figure 1 shows the overlying of different rectum and bladder contours redrawn in different fractions. All the beam parameters of reference plan with planning CT were assigned to the CBCT and dose calculation was performed with the same monitor units and fluence in eclipse TPS by using anisotropic analytical algorithm. According to International Commission on Radiation Units and Measurements (ICRU) Report No. 42, CBCT has to be calibrated for Hounsfield Units (HU) versus relative electron density for dose calculation²⁵. For this, Catpha phantom 504 was used, which has different inserts with HUs ranging from -1000 to 990. This HU-electron density curve for CBCT pelvis mode was assigned in TPS (table 2 and figure 2). Dose calculation was performed on CBCT with the three types of match, namely, CBCT soft

tissue match, 2D kV Bone match, and No Match, applied. The dose volume histograms (DVH) of bladder and rectum were analyzed over the fractions (figure 3a and 3b). The averaged DVH values were compared with the planned DVH. The first phase and second phase DVHs were summed up in a single DVH and it was compared with the planned DVH for the above three perspectives (figure 4a and 4b). The correlation of shifts between 2D kV match and CBCT match

was compared. The frequency distributions of superior-inferior (SI), anterior-posterior (AP), and left-right (LR) lateral directions were analyzed. The Pearson spearman correlation was used for comparison of shifts obtained from 2D kV and CBCT match. Normal distribution was used for frequency distribution. Statistical package for social sciences (SPSS version 24) was used for statistical analysis.

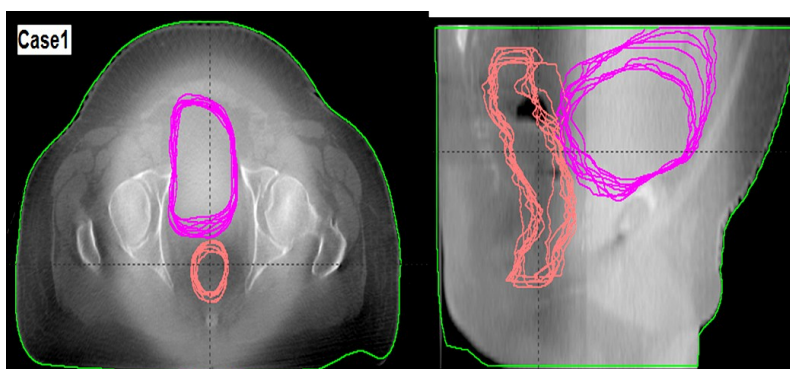


Figure 1. Contours of bladder and rectum drawn in daily cbct images overlaid in single axial and sagittal slice.

Table 2. Electron density of different inserts in Catphan phantom and Relative electron density versus Hounsfield unit calibration for cone beam computed tomography (pelvis mode) in treatment planning beam configuration.

Material	Electron Density $\times 10^{23}$ e/gram	Relative Electron Density	Hounsfield Units (reference)	Hounsfield Units (actual)	Relative Electron Density (actual)
Air	3.007	0.899491475	-1000	-1000	0
PMP	3.435	1.027520191	-200	-231	0.769
LDPE	3.429	1.025725396	-100	-121	0.879
Polystyrene	3.238	0.968591086	-35	-82	0.918
Water	3.343	1	0	-5	0.995
Acrylic	3.248	0.971582411	120	115	1.1072
Delrin	3.209	0.959916243	340	308	1.19984
Teflon	2.889	0.864193838	990	956	1.51088

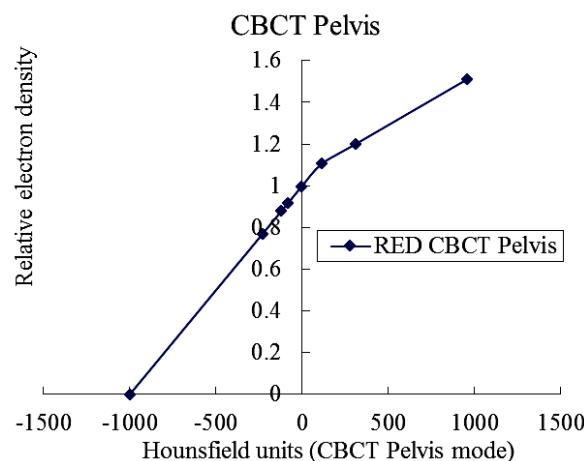


Figure 2. Relative electron density versus Hounsfield unit calibration curve for cone beam computed tomography (pelvis mode).

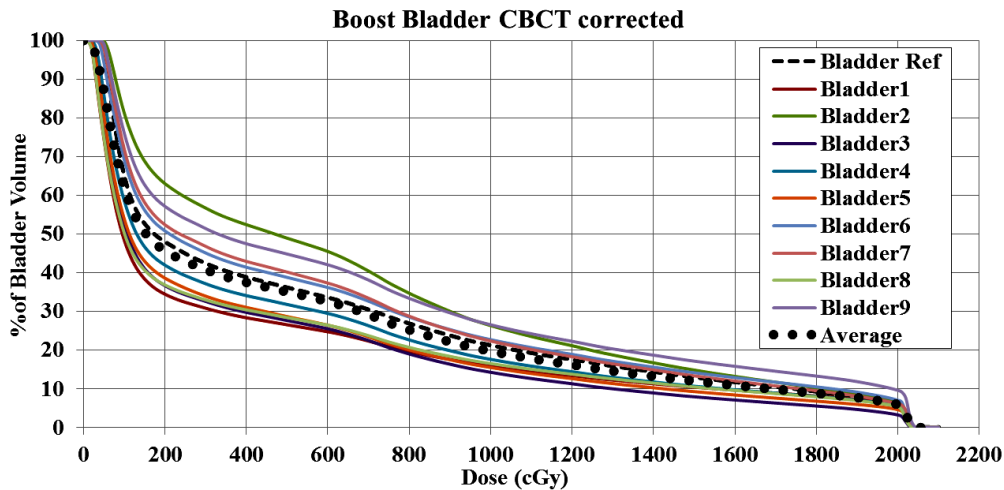


Figure 3a. Daily CBCT image was matched (soft tissue) with planning CT. Bladder was re-drawn on each CBCT and dose calculation was done. DVHs shows the daily bladder dose variation for boost phase (for one patient).

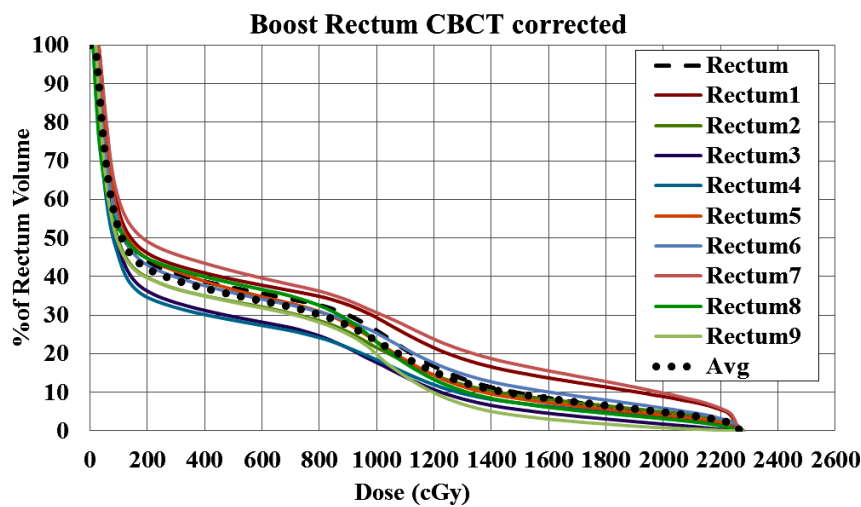


Figure 3b. DVH of rectum volumes drawn and calculated on daily cbct after soft tissue matching with planning CT for boost phase treatment. Rectum dose deviation shown in daily DVH with planned DVH-Boost Phase(for one patient).

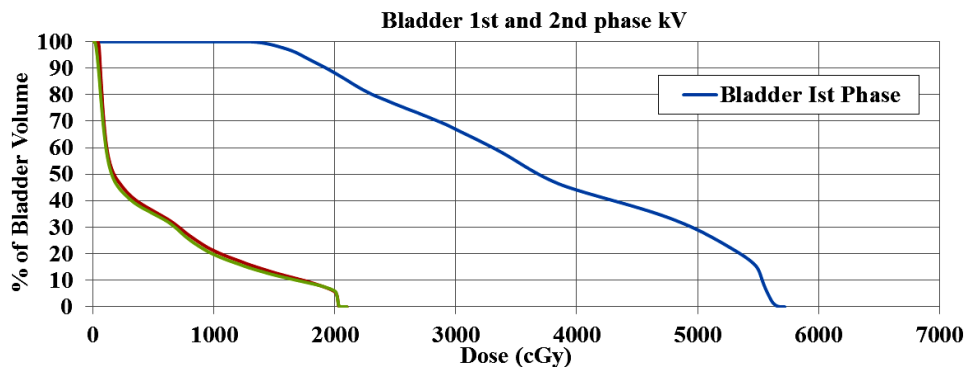


Figure 4a. Daily 2D kV bone match was performed. Based on the translational shift, the co-ordinates were given in CBCT and dose calculation was performed with modified Bladder volume. DVH shows dose deviation- 1st(planned) and 2nd phase (planned and kV match calculated) for one patient.

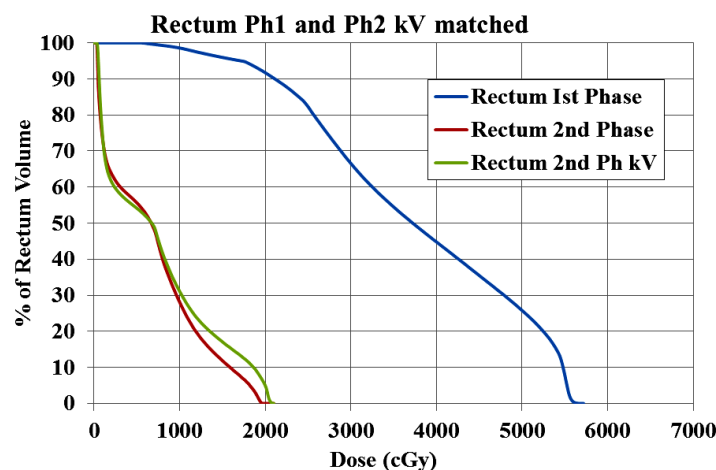


Figure 4b. Daily 2D kV bone match was performed. Based on the translational shift, the co-ordinates were given in CBCT and dose calculation was performed with modified rectum volume. DVH shows dose deviation- 1st (planned) and 2nd phase (planned and kV match calculated) for one patient.

RESULTS

Comparison of shifts between 2D kV and CBCT match

The correlation co-efficient between 2D kV and CBCT match was 0.4517 for AP, 0.6456 for SI, and 0.7793 for LR directions. The mean value of shifts was 0.2mm (SD=2.292mm) for AP

direction in CBCT match and 0.17mm (0.87mm) in 2D kV match. Mean value of shifts was -1.13mm (SD=1.988) for SI directions in CBCT and -0.52mm (1.795mm) in 2D kV match. In LR directions, the mean shift was -0.12mm (SD=1.629mm) for CBCT match and -0.22mm (SD=1.419mm) for 2D kV match (figure 5).

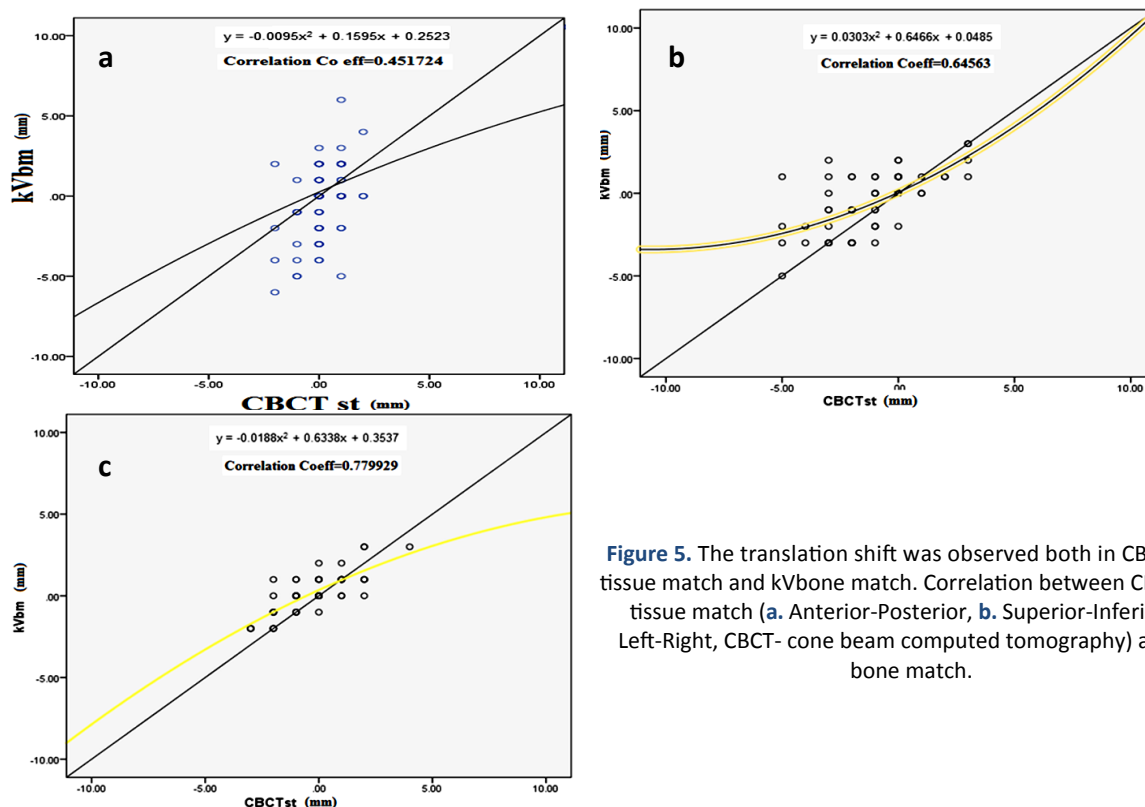


Figure 5. The translation shift was observed both in CBCT soft tissue match and kVbone match. Correlation between CBCT soft tissue match (a. Anterior-Posterior, b. Superior-Inferior, c. Left-Right, CBCT- cone beam computed tomography) and kV bone match.

Bladder and rectum volume changes during the course of radiotherapy

Several authors have reported bladder and rectum volume changes during the course of radiotherapy (26-28). The mean value of bladder volume was ranging from 85cc to 406.7cc over seven patients (figure 6a). The standard deviation for the bladder volume was ranging from 29.28cc to 109.72cc, which shows that volume of bladder differs according to the patient's retention ability. The mean deviation of bladder volume was ranging from 59.2cc to 115.42cc with the standard deviation of 22.84cc

to 78.01cc. In one patient, the reference bladder volume was 126cc and the average volume of bladder volume was 85.54cc, because of the patient's inability to control the bladder.

The mean value of the volume of rectum was ranging from 42.15cc to 68.29cc with the standard deviation ranging from 3.69cc to 11.85cc (figure 6b). The mean difference from reference value was 2.83cc to 11.03cc and the standard deviation was 2.27cc to 11.14cc from the reference volume. It shows that the variation in the volume of rectum was significantly less when compared to bladder.

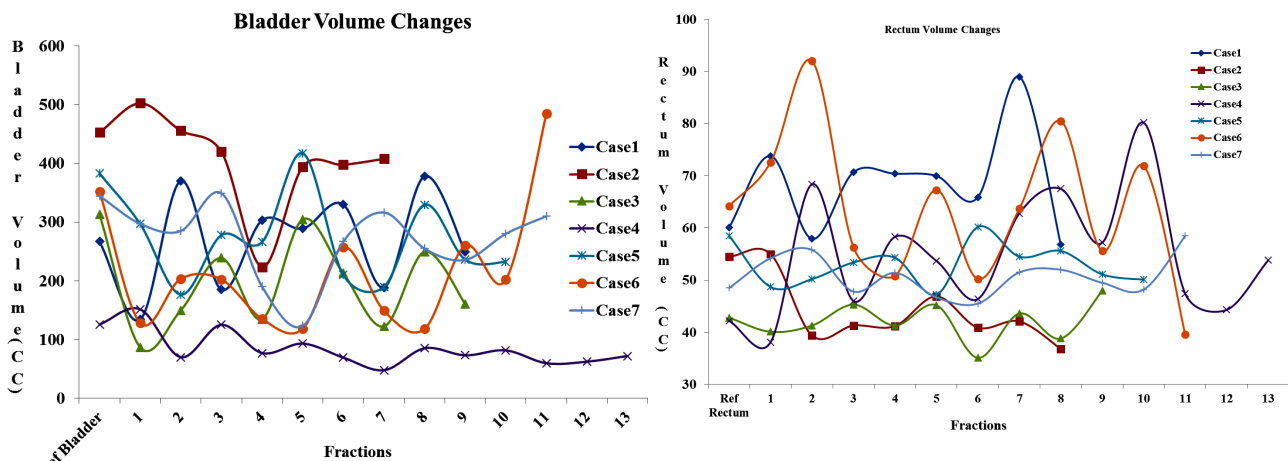


Figure 6. a) Bladder was contoured on daily CBCT and compared with reference planning CT bladder volume. b) Rectum was contoured on daily CBCT and compared with reference planning CT rectum volume.

Delivered doses to bladder and rectum

In the first patient, we observed 0.8Gy dose difference from planned rectum dose to CBCT matched rectum dose. 2.7Gy difference was found between planned and without imaging position. In the bladder, no significant deviation (<1Gy) was observed in high dose region as well as low dose region between reference and CBCT, and kV matched position; but, 1.5Gy to 3.5Gy dose deviation was found between planned and no imaging position (1% to 20% bladder volume). In the second patient, 2Gy to 4Gy dose difference was observed between these three positions with a reference-planned value in bladder at high and medium dose regions (50-65Gy). No significant variation was observed in the low dose region. In rectum, the dose difference was 5Gy-7Gy at high dose region

while comparing to planned, CBCT matched, and kV matched values. In the third patient, 1Gy to 2.5Gy difference was observed in high dose region for bladder between planned and CBCT matched or kV matched values. 0.4Gy (planned vs. CBCT matched value), 1.6Gy (planned vs. kV-matched value), and 3.6Gy (planned vs. no imaged position) for 75Gy-82Gy dose region were observed in rectum. 2.5Gy-3Gy dose difference was observed in medium dose region (50Gy-65Gy dose region) for bladder. In rectum, no significant dose difference was found in medium dose region. In the fourth patient, 1.5Gy to 2Gy dose difference was observed in bladder (at 70-80Gy dose region) between planned and CBCT matched, kV matched, and no imaging positions. In rectum, 1.5Gy-2.5Gy (65Gy-70Gy region) and 3-4Gy difference in medium dose

region (45Gy-55Gy) was observed. In the fifth patient, the dose difference between planned and delivered (CBCT matched, kV matched, or without imaging) 0.5Gy-2.5Gy (60Gy-80Gy region) for bladder and 0.8Gy-1.2Gy in rectum was observed (60Gy-79Gy region). In the sixth patient, 4Gy dose difference was found in

medium dose region for bladder and in rectum, no significant dose difference was found in medium dose region. In the seventh patient, 0.5Gy-7.3Gy dose difference was found in bladder and 2Gy-4.7Gy difference was observed in rectum between planned and delivered at high dose region (table 3, figure 7a and 7b).

Table 3. Dose calculation in CBCT was performed with three different corrections and compared to planned referencedose for Rectum and Bladder.

	Dose Received by Rectum (Gy)						Dose Received by Bladder (Gy)				
	Vol(%)	1(%)	5(%)	10(%)	20(%)	50(%)	1(%)	5(%)	10(%)	20(%)	50(%)
Case 1	Reference	77.8	74.0	69.3	63.5	37.5	76.6	75.5	72.0	63.5	38.5
	CBCT Corrected	78.6	74.5	69.5	64.3	39.0	77.0	76.0	71.9	64.0	39.0
	kV Corrected	80.0	75.0	73.3	66.0	43.5	77.5	76.1	72.9	66.0	40.0
	No Correction	80.5	75.0	74.0	65.5	44.0	78.0	77.0	73.0	67.0	39.0
Case 2	Reference	75.8	71.6	68.0	60.5	38.0	75.0	65.8	60.0	55.8	37.3
	CBCT Corrected	80.3	79.1	75.0	66.0	39.0	74.0	67.0	61.0	56.0	38.0
	kV Corrected	80.3	78.6	74.0	65.5	38.0	78.0	70.0	62.0	57.0	37.9
	No Correction	80.3	79.6	77.0	67.5	38.0	78.0	69.8	61.5	56.5	39.0
Case 3	Reference	81.9	79.0	78.1	72.5	49.5	82.0	81.8	79.0	78.0	53.0
	CBCT Corrected	82.3	80.5	78.7	75.0	51.5	83.0	82.0	80.5	79.5	56.0
	kV Corrected	83.5	81.5	79.0	74.5	51.5	83.5	82.8	82.1	80.5	56.0
	No Correction	85.5	83.0	79.8	74.5	51.0	84.5	83.5	83.0	82.5	57.0
Case 4	Reference	77.8	70.0	67.5	60.0	37.4	76.5	72.8	56.0	53.5	37.2
	CBCT Corrected	79.3	76.0	69.5	63.0	38.0	77.0	73.8	57.0	53.8	38.0
	kV Corrected	80.5	77.0	70.5	63.0	38.0	78.0	74.0	57.5	55.0	39.0
	No Correction	81.0	77.5	70.5	63.0	38.0	78.0	74.5	57.5	57.0	39.5
Case 5	Reference	78.5	71.0	64.3	56.2	37.0	80.5	76.0	68.8	60.5	37.0
	CBCT Corrected	78.0	72.0	65.8	57.0	37.0	81.5	76.5	69.0	60.5	39.0
	kV Corrected	79.0	74.0	68.0	58.0	38.0	82.0	77.0	70.0	62.0	40.0
	No Correction	79.5	75.0	69.3	58.2	37.0	81.8	78.0	70.3	63.0	41.0
Case 6	Reference	76.5	70.0	63.8	58.0	31.0	78.5	76.5	76.5	72.0	49.0
	CBCT Corrected	77.5	67.0	61.8	57.0	33.0	79.0	77.0	76.0	72.0	51.0
	kV Corrected	77.5	68.0	61.5	57.0	33.0	80.0	77.5	76.5	72.5	51.5
	No Correction	77.5	69.0	61.8	57.0	33.0	81.0	76.5	75.5	73.0	52.0
Case 7	Reference	77.5	76.5	69.8	59.8	29.5	79.0	79.0	76.0	70.0	39.8
	CBCT Corrected	78.3	77.9	71.5	59.9	31.5	78.5	77.8	77.1	70.5	41.0
	kV Corrected	79.0	78.5	74.0	60.5	32.0	79.0	78.5	77.5	70.2	46.0
	No Correction	79.5	79.1	70.8	61.5	31.0	79.5	79.0	78.0	70.5	47.0

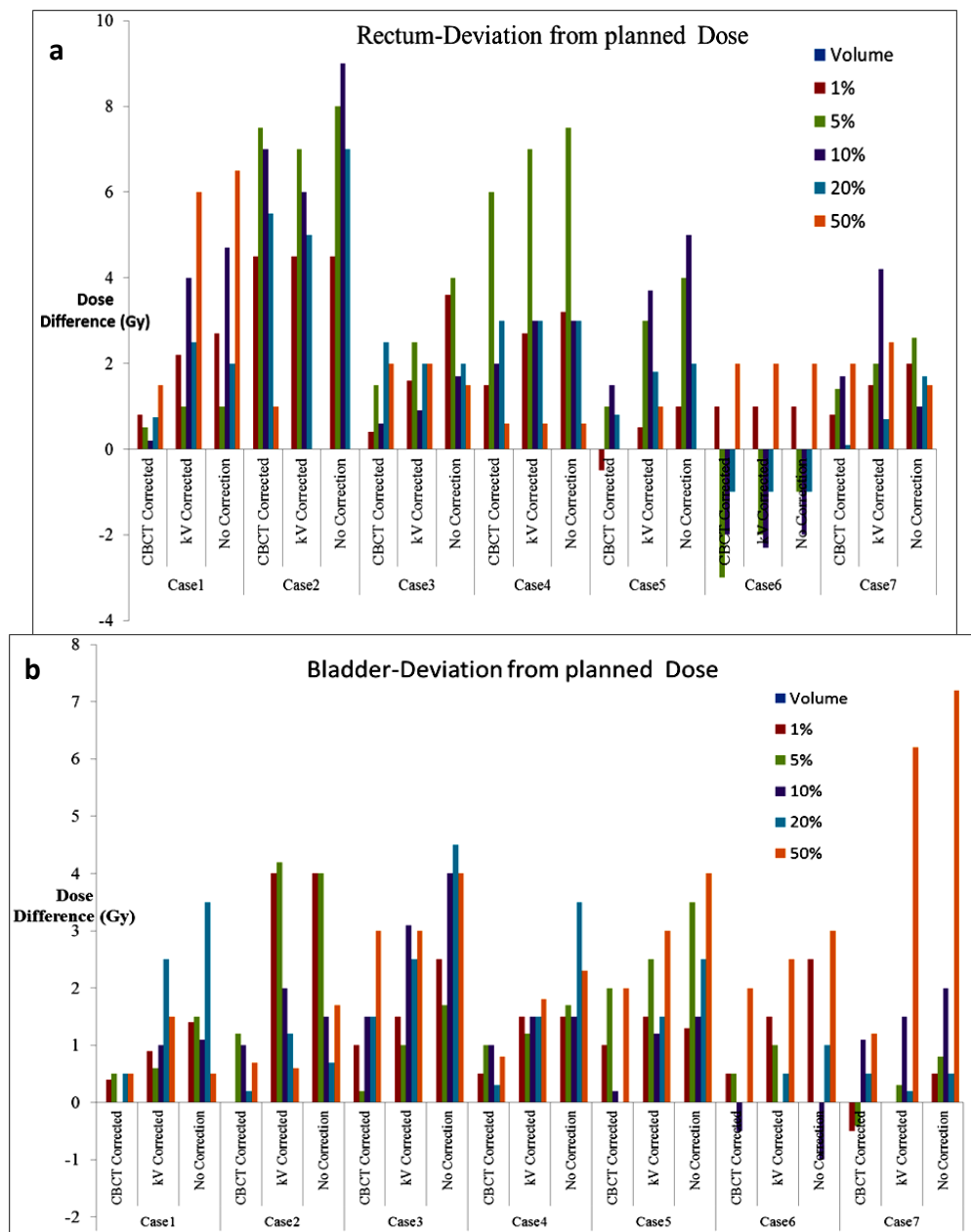


Figure 7. a) Dose deviation between three correction methods and its effect on 1% to 50% volume from planned dose –Rectum.
b) dose deviation between three correction methods and its effect on 1% to 50% volume from planned dose –Bladder.

DISCUSSION

Dose escalation in prostate cancer can increase the biochemical control and reduce toxicity if tighter margins are used for treatment delivery. Barney *et al.*⁽²⁹⁾ stated that implanted fiducial with 2D match is better than soft tissue matching in view of the prostate movement. However, they did not correlate the dose to

rectum and bladder due to the deviation of these two organs. Without fiducial marker in prostate, the matching with bony landmark was unable to provide the exact position of the prostate. In this study, we evaluated the importance of soft tissue prostate image guidance. The correlation coefficient of the AP shifts shows the minimum value. This is due to the increase in bladder filling compared to planning CT, which pushes

the prostate in posterior and inferior directions, and vice-versa. In rectum, the presence of gaseous and fecal matter pushes the prostate into an anterior direction. These changes will not be reflected in the 2D kV bone match, as these are soft tissues. In the AP direction, bony

match is not always similar to soft tissue match. As these changes affect the movement of prostate mostly in AP and SI direction, the correlation coefficient is near to 1 in LR direction, showing a minimum difference between 2D kV and CBCT match (figure 8).

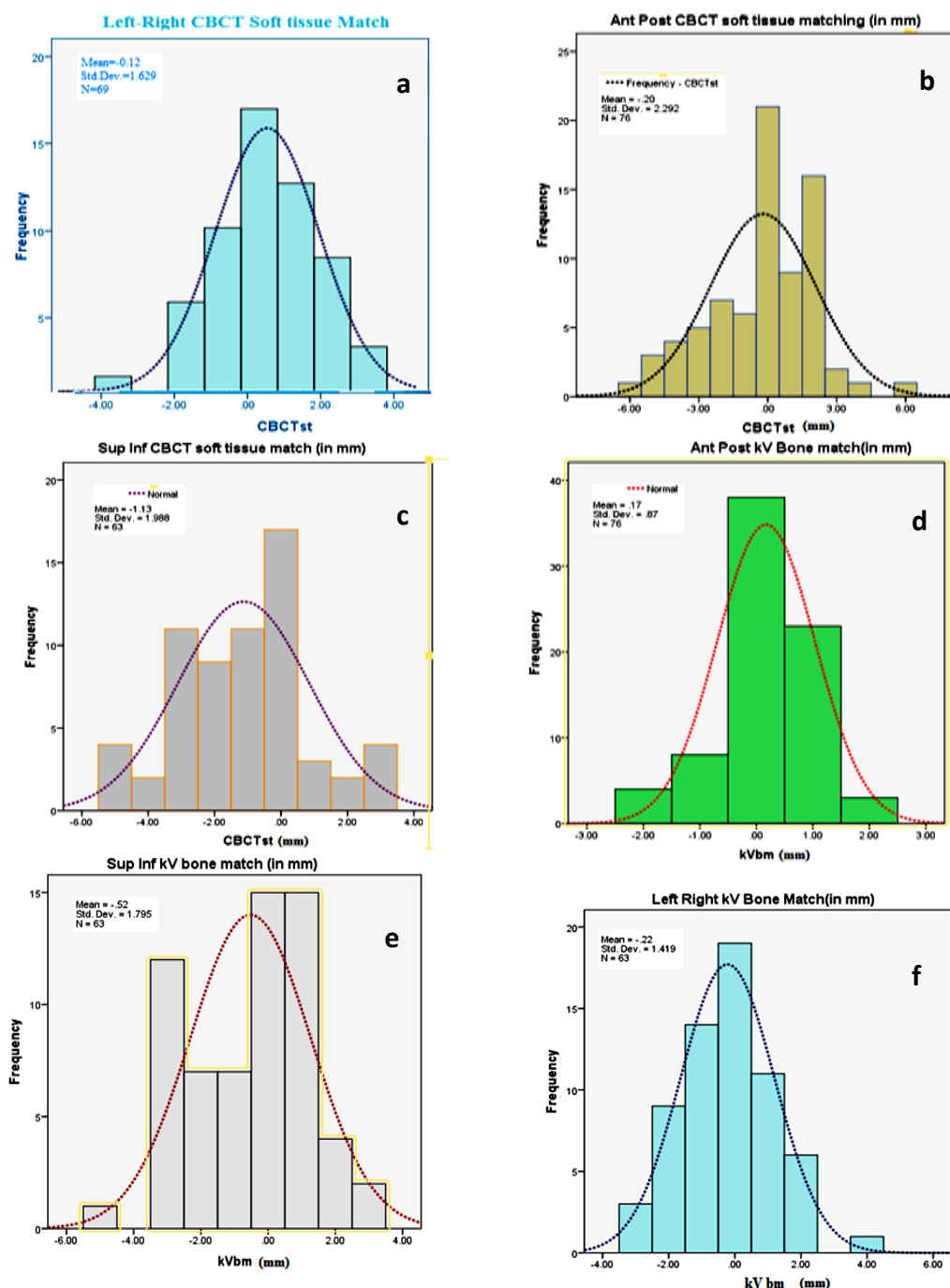


Figure 8. Frequency distribution of CBCT (a. left-right b. anterior-posterior c. superior-inferior) and 2D kV match (d. anterior-posterior e. superior-inferior f. left-right); BCT-cone beam computed tomography 2DkV- 2 dimensional kilo-voltage

The frequency distribution shows that the 2D kV bone match is sharp and shifts towards zero mm, showing that interfraction patient set-up was reproducible. However, at the same time, the frequency distribution for CBCT match in AP direction and the center is flattened, showing an increase in the prostate movement between fractions.

Chen *et al.*⁽²²⁾ studied the dosimetric impact of rectum and bladder volume and concluded that the bladder volume is a more significant factor in respect of the bladder dose. In our study, the soft tissue matching with image guidance could provide the value closer to the planning dose. The variations of bladder as well as rectum can change the delivered dose for both normal structure as well as prostate, with reduced margins.

Bell *et al.*⁽³⁰⁾ showed that the bladder and rectal size changes during the treatment could affect the prostate position. Thus, the dose coverage to upper prostate area will be shifted due to pressure from the rectal and bladder volumes. It can affect the delivered dose to prostate due to a lesser margin in higher doses. Therefore, the bladder and rectal volume has to be same throughout the simulation up to the end of the treatment (by reducing the margin) to achieve the full dose to prostate without increasing the doses to bladder and rectum. In our study, Figure 9a and 9b shows the cumulative dose volume histogram (DVH) of

planned and delivered dose for bladder and rectum for a patient. The DVH obtained from CBCT match shows the bladder and rectum received comparable (minor deviation) doses with our planned dose for four patients. For two patients, the delivered rectum dose was more due to the overlapping PTV margin in rectum. The DVH of CBCT with no match applied (hypothetical situation) shows the bladder and rectum receiving more doses when compared to planned value and these differences were higher than CBCT match and 2D kV match values. This overdosage was due to two factors, namely, bladder filling or rectum overlapping (which comes in the field) and movement of prostate. In case of 2D kV match, the patient set-up error is minimized by bony matching, but still soft tissue movements are not taken care of. This leads to more deviation of bladder and rectum doses when compared with CBCT match, but is lesser than no correction applied. Using CBCT match, we can assure 100% dose to prostate and at the same time, a reduced dose to bladder and rectum. Using the 2D kV bone match, we were unable to know how much dose was delivered to prostate. In case of no imaging done, there were two possibilities. The first possibility was either prostate would get full dose or partial dose. The second possibility was the rectum could receive more doses than the reference planned dose.

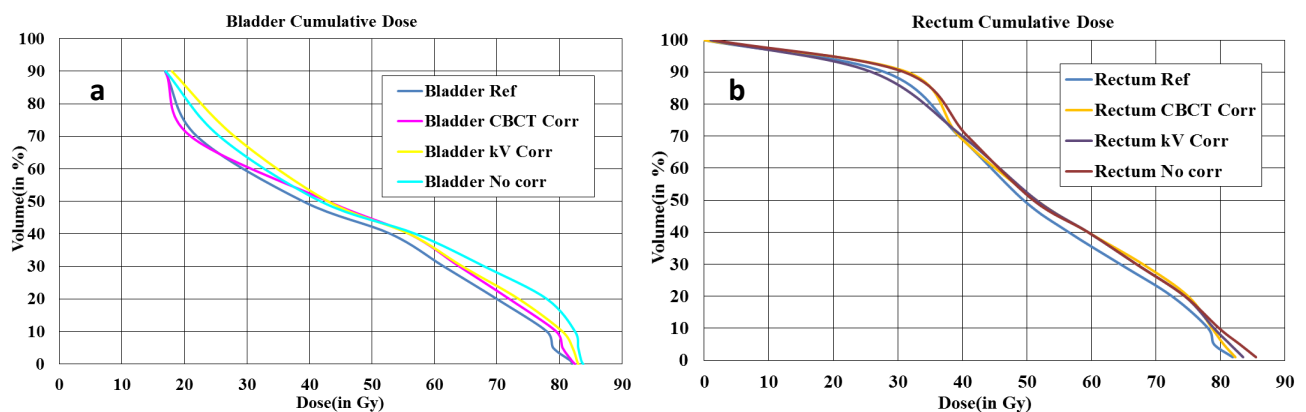


Figure 9. a) Cumulative dose volume histogram (DVH) of planned and delivered dose- Bladder. **b)** Cumulative dose volume histogram (DVH) of planned and delivered dose- Rectum.

Boersma *et al.* ⁽³¹⁾ quoted that dose escalation up to 78Gy using a conformal technique is feasible and rectal bleeding is increased above certain sharp dose volume thresholds. The dose escalation should be performed with caution, i.e., by reducing the margin at the intercept of the prostate and the rectum wall to 0 mm, above 75Gy. Therefore, above 75Gy, the delivered dose should be within prostate. If isodose curve shifted 1mm posteriorly, then the dose was delivered to rectum instead of prostate. In this situation, our study is in line with De Crevoisier *et al.* ⁽³²⁾, and shows that the daily image guidance can provide a comparatively better solution with planar imaging to verify the prostate position. Therefore, the dose escalation beyond certain doses is only possible with volumetric image guidance to avoid acute rectal complications.

CONCLUSION

In this study, we found that rectum in the high dose region is a significant factor for delivering 100% dose to target. With image guidance (CBCT), we can match the prostate position, but dose contribution to the rectum is dependent on the patient's anatomy. Bladder filling and rectum filling pertains to the day of treatment. It is possible to achieve good dose delivery and conformity in target (prostate) with CBCT image guidance, rather than 2D kV bone match.

Conflicts of interest: Declared none.

REFERENCES

1. Kuban DA, Tucker SL, Dong L, Starkschall G, Huang EH, Cheung MR, *et al.* (2008) Long-term results of the M. D. Anderson randomized dose-escalation trial for prostate cancer. *Int J Radiat Oncol Biol Phys*, **70**(1): 67-74.
2. Kalbasi A, Li J, Berman AT, Swisher-McClure S, Smaldone M, Uzzo RG *et al.* (2015) Dose-escalated irradiation and overall survival in men with non metastatic prostate cancer. *JAMA Oncol*, **1**(7): 897-906.
3. Zaorsky NG, Keith SW, Shaikh T, Nguyen PL, Horwitz EM, Dicker AP, *et al.* (2018) Impact of radiation therapy dose escalation on prostate cancer outcomes and toxicities. *American Journal of Clinical Oncology*, **41**(4): 409-415.
4. Wortel RC, Incrocci L, Pos FJ, Lebesque JV, Witte MG, van der Heide UA, *et al.* (2015) Acute toxicity after image-guided intensity modulated radiation therapy compared to 3D conformal radiation therapy in prostate cancer patients. *Int J Radiat Oncol Biol Phys*, **91**(4): 737-44.
5. Zelefsky MJ, Levin EJ, Hunt M, Yamada Y, Shippey AM, Jackson A, *et al.* (2008) Incidence of late rectal and urinary toxicities after three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys*, **70**(4): 1124-9.
6. Dearnaley DP, Jovic G, Syndikus I, *et al.* (2014) Escalated-dose versus control-dose conformal radiotherapy for prostate cancer: long-term results from the MRC RT01 randomised controlled trial. *Lancet Oncol*, **15**(4): 464-473.
7. Dolezel M, Odrázka K, Zouhar M, Vaculikova M, Sefrova J, Jansa J *et al.* (2015) Comparing morbidity and cancer control after 3D-conformal (70/74Gy) and intensity modulated radiotherapy (78/82Gy) for prostate cancer. *Strahlenther Onkol*, **191**(4): 338-46.
8. Bhardwaj AK, Kehwar TS, Chakravarti SK, Oinam AS, Sharma SC (2007) 3-Dimensional conformal radiotherapy versus intensity modulated radiotherapy for localized prostate cancer: Dosimetric and radiobiologic analysis. *Int J Radiat Res*, **5**(1): 1-8.
9. Mayyas E, Chetty IJ, Chetvertkov M, Wen N, Neicu T, Nurusev T, Ren L, *et al.* (2013) Evaluation of multiple image-based modalities for image-guided radiation therapy (IGRT) of prostate carcinoma: a prospective study. *Med Phys*, **40**(4): 041707(1-9).
10. Zelefsky MJ, Kollmeier M, Cox B, Fidaleo A, Sperling D, Pei X, *et al.* (2012) Improved clinical outcomes with high-dose image guided radiotherapy compared with non-IGRT for the treatment of clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys*, **84**(1): 125-9.
11. Dang A, Kupelian PA, Cao M, Agazaryan N, Kishan AU (2018) Image-guided radiotherapy for prostate cancer. *Transl Androl Urol*, **7**(3): 308-320.
12. Yartsev S and Bauman G (2016) Target margins in radiotherapy of prostate cancer. *Br J Radiol*, **89**(1067): 20160312.
13. Mahdavi SR, Jazayeri Gharehbagh E, Mofid B, Jafari AH, Nikoofar AR (2017) Accuracy of the dose delivery in prostate cancer patients using an electronic portal imaging device (EPID) *Int J Radiat Res*, **15**(1): 39-47.
14. Jason CY, Qureshi MM, Clancy P, Dise LN, Willins J, Hirsch AE (2015) Daily patient setup error in prostate image guided radiation therapy with fiducial-based kilovoltage onboard imaging and conebeam computed tomography. *Quant Imaging Med Surg*, **5**(5): 665-672.
15. Ghilezan M, Yan D, Martinez A (2010) Adaptive radiation therapy for prostate cancer. *Semin Radiat Oncol*, **20**: 130-137.
16. McVicar N, Popescu IA, Heath E (2016) Techniques for adaptive prostate radiotherapy. *Phys Med*, **32**(3): 492-8.

17. McPartlin AJ, Li XA, Kershaw LE, Heide U, Kerkmeijer L, Lawton C et al. (2016) MRI-guided prostate adaptive radiotherapy - A systematic review. *Radiother Oncol*, **119**(3): 371-80.
18. Maund IF, Benson RJ, Fairfoul J, Cook J, Huddart R, Poynter A (2014) Image-guided radiotherapy of the prostate using daily CBCT: the feasibility and likely benefit of implementing a margin reduction. *Br J Radiol*, **87**: 1044-51.
19. Yoo S and Yin FF (2006) Dosimetric feasibility of cone-beam CT-based treatment planning compared to CT-based treatment planning. *Int J Radiat Oncol Biol Phys*, **66**(5): 1553-61.
20. Kaliyaperumal V, Raphael CJ, Varghese KM, Gopu, Sivakumar S, Boban M et al. (2017) Study of variation in dose calculation accuracy between kV Cone-Beam computed tomography and kV fan-Beam computed tomography. *J Med Phys*, **42**(3): 171-180.
21. Adamczyk M, Piotrowski T, Adamiak E (2012) Evaluation of combining bony anatomy and soft tissue position correction strategies for IMRT prostate cancer patients. *Rep Pract Oncol Radiother*, **17**(2): 104-9.
22. Maggio A, Gabriele D, Garibaldi E, Bresciani S, Delmastro E, Di Dia A, Miranti A, et al. (2017) Impact of a rectal and bladder preparation protocol on prostate cancer outcome in patients treated with external beam radiotherapy. *Strahlenther Onkol*, **193**(9): 722-732.
23. Chen Z, Yang Z, Wang J, Hu W (2016) Dosimetric impact of different bladder and rectum filling during prostate cancer radiotherapy. *Radiat Oncol*, **11**: 103.
24. Gill SK, Reddy K, Campbell N, Chen C, Pearson D (2015) Determination of optimal PTV margin for patients receiving CBCT-guided prostate IMRT: comparative analysis based on CBCT dose calculation with four different margins. *J Appl Clin Med Phys*, **16**(6): 252-262.
25. Brenner DJ, Martinez AA, Edmundson GK, Mitchell C, Thames HD, Armour EP (2002) Direct evidence that prostate tumors show high sensitivity to fractionation (low alpha/beta ratio), similar to late-responding normal tissue. *Int J Radiat Oncol Biol Phys*, **52**: 6-13.
26. Use of Computers in External Beam Radiotherapy Procedures with High-Energy Photons and Electrons; International Commission of Radiation Units and Measurements (ICRU) Report 42; 1987.
27. Rijkhorst EJ, Lakeman A, Nijkamp J, Bois J de, Herk M van, Lebesque J V, et al. (2009) Strategies for online organ motion correction for intensity-modulated radiotherapy of prostate cancer: Prostate, rectum, and bladder dose effects. *Int J Radiat Oncol Biol Phys*, **75**: 1254-1260.
28. O'Doherty UM, McNair HA, Norman AR, Miles E, Hooper S, Davies M, et al. (2006) Variability of bladder filling in patients receiving radical radiotherapy to the prostate. *Radiother Oncol*, **79**: 335-40.
29. Tsai CL, Wu JK, Wang CW, Hsu FM, Lai MK, Cheng JC, et al. (2009) Using cone-beam computed tomography to evaluate the impact of bladder filling status on target position in prostate radiotherapy. *Strahlenther Onkol*, **185**: 588-95.
30. Barney BM, Lee RJ, Handrahan D, Welsh KT, Cook JT, Sause W (2011) Image-guided radiotherapy (IGRT) for prostate cancer comparing kV imaging of fiducial markers with cone beam computed tomography (CBCT). *Int J Radiat Oncol Biol Phys*, **80**(1): 301-5.
31. Bell LJ, Cox J, Eade T, Rinks M, Kneebone A (2014) The impact of rectal and bladder variability on target coverage during post-prostatectomy intensity modulated radiotherapy. *Radiother Oncol*, **110**: 245-50.
32. Boersma LJ, van den Brink M, Bruce AM, Shouman T, Gras L, Velde A, et al. (1998) Estimation of the incidence of late bladder and rectum complications after high-dose (70-78Gy) conformal radiotherapy for prostate cancer, using dose-volume histograms. *Int J Radiat Oncol Biol Phys*, **41**: 83-92.
33. De Crevoisier R, Bayar MA, Pommier P, Muracciole X, Pène F, Dudouet P (2018) Daily versus weekly prostate cancer image guided radiation therapy: Phase 3 multicenter randomized trial. *Int J Radiat Oncol Biol Phys*, **102**(5): 1420-1429.

