



Research Article

A study on prostate movement and dosimetric variation because of bladder and rectum volumes changes during the course of image-guided radiotherapy in prostate cancer

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ABSTRACT

Aim: To study the impact of bladder and rectum volume changes on prostate positioning and the dosimetric parameters.

Background: Prostate is a moving organ, and its position is also affected by bladder and rectum volumes. Image-guided radiotherapy (IGRT) is being practiced widely for the treatment of prostate carcinoma (Ca). So, it is important to accurately study the effect of bladder and rectum volume changes in treatment.

Materials and methods: Thirty patients with Ca prostate were included in this study, and all were treated with 50 Gray (Gy) in 25 fractions for the first phase of treatment. A total of 750 cone-beam computed tomography (CBCT) sessions were performed. Prostate position w.r.t. its day one position was noted, and the bladder and rectum volumes were compared with their volumes on day one. Also, repeat CT was done for five patients after 10 fractions. The initial plan was imported as it was on the repeat CT images, and a hybrid plan was prepared by putting the plan isocenter at the relative anatomical reference point in repeat CT images as it was in primary CT images. The multileaf collimators (MLC) fluence was put as it is, and the dose was calculated using the monitoring units (MU), which were in the initial plan. Doses to bladder, rectum, and the target were analyzed.

Results: The mean prostate motion in lateral and anterior-posterior direction was found to be 0.71 (± 0.69) centimeter cm) and 0.77 (± 0.57) cm, respectively. The mean change in bladder and rectum volumes as compared to that in day one CT images was found to be 110.51 (± 84.25) cubic centimeters (cc) and 10.89 (± 10.17) cc, respectively. No significant variation was observed in the doses to bladder, rectum, and the target volume in a hybrid plan, as compared to that in actual initial plan.

Conclusions: Bladder and rectum volume affects the position of prostate, rather the dosimetric parameters, and therefore, it can be concluded that daily CBCT should be done for accurate IGRT delivery to the prostate cancer.

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1. Introduction

Prostate cancer primarily occurs in old age, with more than three-quarters of the cases in men above the age of 65 years. Prostate cancer has become the major health issue globally in the last few decades. The worldwide prostate cancer burden is expected to grow to 1.7 million new cases and 4,99,000 new deaths by

2030, simply due to the growth and aging of the global population. It is the second most frequently diagnosed cancer in men worldwide and the fifth most common cancer overall.¹

According to population-based cancer registries (PBCRs) of India, prostate cancer is the second leading cancer among men in big Indian cities, e.g., Pune, Kolkata, Thiruvananthapuram, and Delhi, while it is third leading cancer in the cities like Mumbai and Bangalore. The prostate is among the top ten leading cancer sites in the rest of the register. The PBCRs recorded a significant increasing trend in incidence rates over time with an annual

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percentage increment of 0.9% in Mumbai, 3.3% in Delhi, 3.4% in Bangalore, Chennai in 4.2%, and 11.6% in Kamrup Urban District.²

For the treatment of prostate cancer, radiotherapy, and surgical resection along with neoadjuvant or concurrent chemotherapy are the mainstays of treatment. Most of the prostate cancer patients require radiotherapy during treatment, and radiotherapy provides an enhanced compatible functional outcome with better organ preservation.³

Radiotherapy has gained revolutionary progress from very low activity sources and ortho-voltage x-ray machines to the modern state-of-the-art technology medical linear accelerators having multiple megavoltage photon and electron energies. Conventional two-dimensional (2D) open field treatment planning technique has been replaced by three-dimensional (3D) target confined techniques, such as three-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), stereotactic radiotherapy (SRT), stereotactic radiosurgery (SRS), and volumetric-modulated arc therapy (VMAT). Because of the remarkable upgradation in radiotherapy treatment techniques, therapeutic ration has improved because of improved tumor coverage and decreased dose to the surrounding normal organs.⁴

Along with new radiotherapy techniques, the patient position verification technique has also been dramatically enhanced; currently, kilovoltage cone-beam computed tomography (kV-CBCT) facility is coming with all the linear accelerators, which gives 3D information of the patient in the treatment position, which is fused with planned CT images, and the accurate position of the patient can be made possible, which helps in improving the geometrical accuracy of target localization.^{5–7}

Position verification by CBCT in case of prostate cancer radiotherapy not only helps in accurate prostate (CBCT) to prostate (planning CT) matching,⁸ but also helps in finding out the daily variation in volume of bladder and rectum because of variable filling and the possible volume change of prostate during the course of radiotherapy, and based on which the dosimetric alteration can be guessed which may affect whole treatment.

The current study has been carried out to find out the volume changes in bladder, rectum, and prostate during the course of radiotherapy and their dosimetric implication.

2. Materials and Methods

A prospective observational study was carried out in which thirty patients diagnosed with localized prostate cancer were included and were treated with IGRT technique. As a standard procedure of the Department, all the patients were explained about benefits, possible radiation, acute and late toxicities, and the protocol to be followed during the course of radiotherapy. Informed consent form was taken from each patient as usually given by every patient who takes radiotherapy in the Department.

The patients involved in the study were of primary prostate cancer histologically proven and were aged between 40–80 years. The Karnofsky Performance Status (KPS) was $\geq 70\%$ and all the patients of early prostate cancer (T1 & T2) stage that is medically inoperable as a result of any associated comorbid conditions.

All the patients were taken to the mold room and were made to lie down in the supine position on the pelvic baseplate, both the arms were placed toward the head, alignment was set by using LASER, and then the thermoplastic sheet was molded to the pelvic region. Then the patients were taken to the computed tomography (CT) room, and after positioning the patients on the CT table top using baseplate and molded thermoplastic sheet, contrast-enhanced CT images of 3 mm slice thickness were taken using Siemens SOMATOM Definition AS scanner (Siemens Medical

Systems, Germany). The CT images were transferred to the treatment planning system (TPS) Eclipse version 8.9 (Varian Medical Systems, Palo Alto, CA).

Gross tumor volume (GTV), Clinical target volume (CTV), Planning target volume (PTV) and Organ at risk (OAR) were delineated on the CT images following the guidelines of the International Commission on Radiation Units and Measurements report No. 83 (ICRU 83).⁹ The PTV was marked as 0.5 cm margin around the CTV in all the cases. IMRT was created with 6-MV photon beams, and Varian leaf motion calculator version 8.9.08 was utilized to calculate the leaf motion for dynamic dose delivery. A dose-volume optimizer (DVO) was used for planning optimization. Anisotropic Analytic Algorithm (AAA) with grid size 0.25 cm was used for dose calculation. After evaluation of the target coverage, doses to OARs and analysis of DVH, plans were approved for delivering to the patients by high energy medical linear accelerator (LA) Clinac DMX (Varian Medical Systems, Palo Alto, CA) equipped with Millennium 80 MLC system and having photon energies of 6 and 15 MV and electron energies of 6, 9, 12, and 15 MeV.

Patients were scheduled for IGRT, 50 Gy in 25 fractions (#) at the rate of 2Gy/# in the first phase of treatment. This study was conducted during the first phase of treatment only, although a total dose of 78Gy/39# was planned and delivered in the first, second, and third phases of the treatment plan.

All the patients were positioned and immobilized on the couch of the LA by using the thermoplastic sheet molded for them. On-Board Imaging (OBI) system (Varian Medical Systems, Palo Alto, CA) consisting of a 125-kVp x-ray tube isocentrically mounted to the gantry of the LA was used for patient position verification. Since the prostate is a soft tissue organ whose position may vary w.r.t. the bones; therefore, to verify the prostate position with the planned position, cone-beam computed tomography (CBCT) was performed in each session before treatment delivery. The CBCT was performed at an imager vertical distance of 50 cm and by using a full-bowtie filter. CBCT was performed by rotating the gantry in the counter-clockwise direction from 179° to 180° (360° rotation).

Anatomy-matching software (Varian Portal Vision 7.5) was used to study patient setup deviations and to determine the spatial coordinates in the images. The CBCT images were fused with the reference CT images and prostate to prostate was matched, as shown in Fig. 1 with the help of transversal, frontal, and sagittal views by using the spyglass method, in which a movable inner window separated the reference image on the inside from the CBCT image on the outside. The encompass is appraised by examining the continuity of the bones across the edges of the inner window.⁸ The shifts along three translational directions, namely the lateral, longitudinal, and vertical directions were noted and applied to the LA couch, and then the plan was delivered. This imaging and plan delivery process was followed for each day during the course of radiotherapy.

A total of 750 imaging sessions were performed for 30 patients with 25 sessions for each patient. In each of the 750 sessions, shifts in all three translational directions were noted and analyzed. The isocentre shifts along all the three translational directions were combined in a 3-D isodisplacement vector (IDV), which is defined as $E = (\text{vert}^2 + \text{long}^2 + \text{lat}^2)^{1/2}$.⁸

2.1. Evaluation of change in volume of bladder and rectum

The bladder and rectum on the CBCT images were contoured on TPS, as shown in Fig. 2. The position of the prostate with respect to its position on day one was noted in the anterior-posterior and lateral directions; however, longitudinal position change was not noted, as in many of the CBCT images, a clear reference in the longitudinal direction was not possible. The bladder and rectum

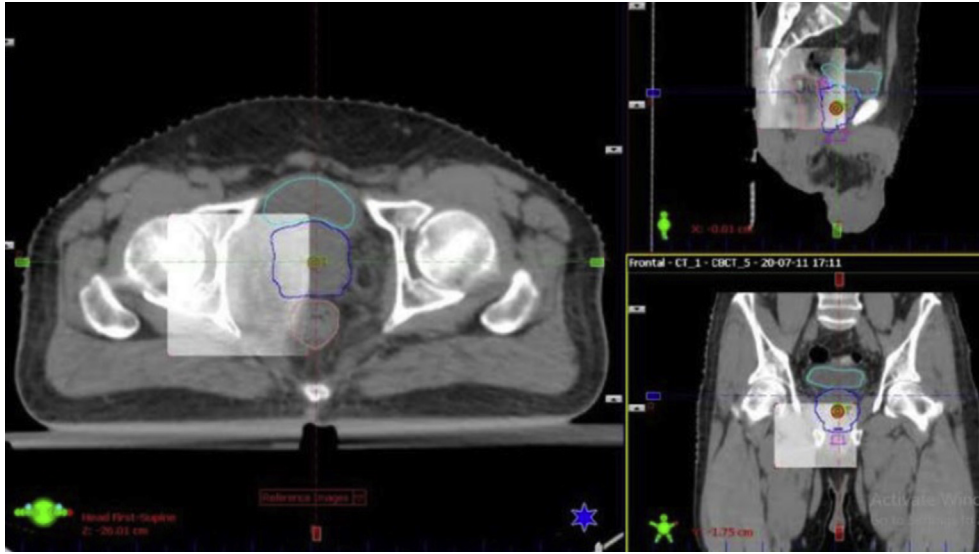


Fig. 1. Prostate to prostate matching by superimposing the cone-beam computed tomography (CBCT) and CT images by spyglass method.

were contoured on all the CBCT images, and their volumes were measured and compared with the volume of both the organs on day one.

2.2. Creation of hybrid plans for analyzing the impact of volume changes on dosimetric parameters

Since CBCT images are not the CT Hounsfield units calibrated, so accurate dose calculation is not possible on CBCT images if a plan is done on these images. Therefore, CT was repeated for five patients whose rectum/bladder volume seemed highly variable in the CBCT images. Bladder, rectum, and prostate were delineated on the repeat CT images. CTV and PTV were delineated, and the prostate was considered as GTV. The CT images of the plan done on the first day were imported on repeat CT images, and the isocenter of the plan was set at the identical position w.r.t. the pelvic bones, similar to the first day CT images taken for the first phase of treatment. The MU of all the fields were noted from the first plan and were entered into the hybrid plan for all the fields. The dose was calculated. Maximum dose (D_{max}) and doses to bladder and rectum were noted. Also, the volume of all these three structures was noted. Dose coverage of 95% ($V_{95\%}$) and 93% and ($V_{93\%}$) of the prescribed dose for PTV was noted. The difference between volume and doses of bladder and rectum was calculated, and the impact of volume change on doses was analyzed. Fig. 3 shows dose distribution on

plan done on day one CT images and the hybrid plan on repeat CT images.

3. Results

All the thirty patients were in the age of 50 to 80; however, the selection criterion was 40 to 80. The most number of cases were in the age group of 61 to 70. Most cases had adenocarcinoma, and the most common stage was T2N0M0, as shown in Table 1.

Position verification of all the thirty patients in 750 imaging sessions ($30 \text{ patient} \times 25 \text{ sessions}$) was done by CBCT, the mean shift in vertical, longitudinal, lateral directions, and mean isodisplacement vector (IDV) calculated have been described in Table 2.

The prostate position change w.r.t. the pelvic bones because of bladder and rectum filling and movement, was noted in each session for every patient. The mean lateral movement and the inferior-superior movement in prostate position w.r.t. its day one position was found to be 0.71 (SD: 69) and 0.77 (SD: 0.57), respectively. The detailed results have been given in Table 3.

The change in volume of bladder and rectum w.r.t. the volume on day one, was calculated by measuring the volume of these organs from CT images of day one and the daily CBCT images. The mean change in the volume of bladder and rectum was found to be 110.51 (SD: 84.25) and 10.89 (SD: 10.17), respectively, as shown in Table 4.

3.1. Impact of volume change of bladder and rectum on dosimetric parameters

The change in volume of bladder, rectum, and prostate and its impact on the dosimetric parameters are as shown in Table 5. The p -value by the student's unpaired t -test was calculated for comparing the doses in actual plans and hybrid plans. The calculated p -value for D_{mean} , $D_{1/3}$ and $D_{2/3}$ was 0.8801, 0.9305 and 0.3484 for bladder, while 0.7825, 0.6362 and 0.6930 for rectum. Also, the calculated p -value for the volume of bladder and rectum in both the plans was found to be 0.7371 and 0.2680, respectively, which is statistically not significant. The detailed results have been depicted in Table 5.

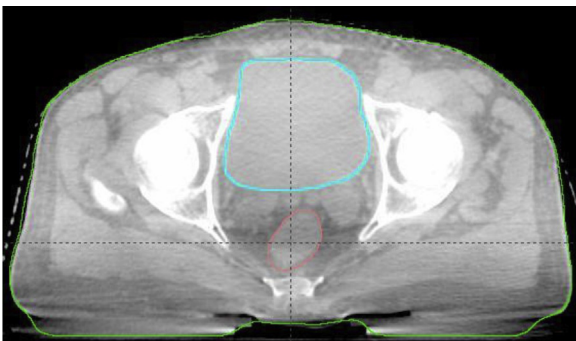


Fig. 2. CBCT image of one of the cases having delineated bladder and rectum.

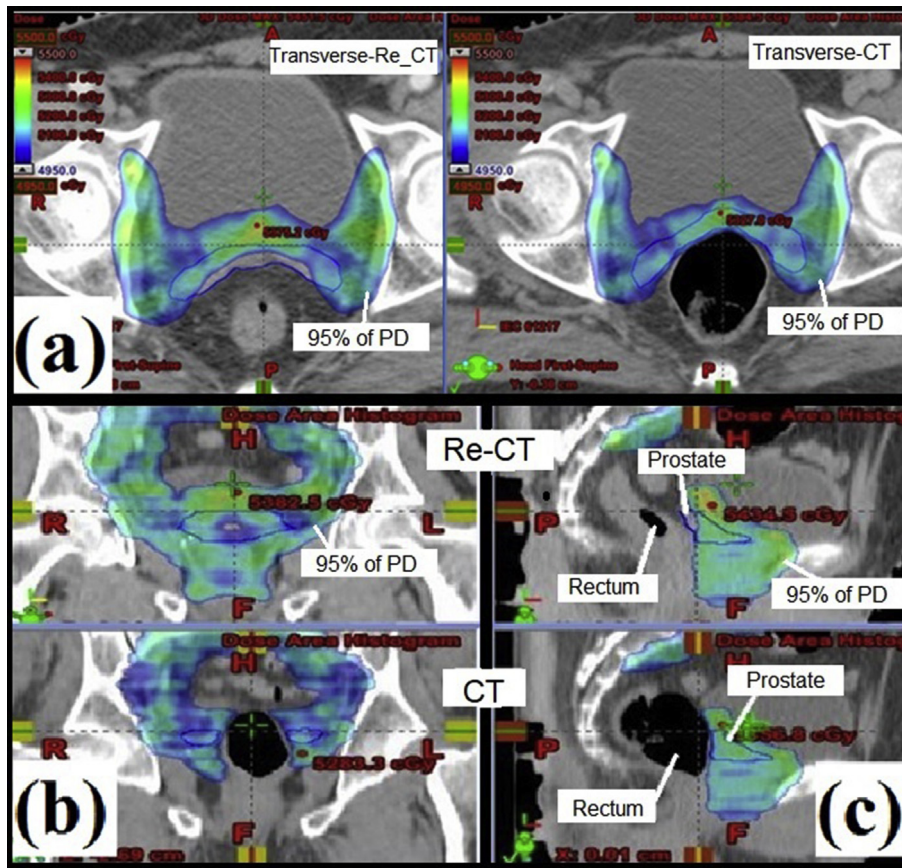


Fig. 3. Dose distribution on the hybrid plan on repeat CT images and plan done on day one CT images in (A) transversal, (B) coronal, and (C) sagittal view of repeat CT and CT images of one of the prostate cancer patient.

Table 1
Patients statistics of age group, histopathological diagnosis, and the stage of the cancer.

Clinical factors	Age Group			Histopathological Diagnosis	Stage of the Cancer			
	51–60	61–70	71–80		T1N0M0	T2N0M0		
Divisions of Clinical factors				Well differentiated adenocarcinoma	moderately differentiated adenocarcinoma	Poorly differentiated carcinoma		
No. of patients	10	13	7	16	7	7	12	18

The change in PTV coverage because of bladder and rectum volume changes has been given in Table 6. Since totally, there are total five patients only, and their data of difference in PTV coverage vary largely, the mean has not been calculated.

4. Discussion

This study was carried out to investigate the change in volume of bladder, rectum, and prostate during the course of radiotherapy and the impact of bladder and rectum volume variation on the position of prostate. The study also covered the dosimetric impact of volume changes, although this was done by repeat CT required only for five patients and other patients for whom repeat CT was

not required, were not prescribed repeat CT to avoid charges for additional CT simulation. The results of the study underline the multiple factors, which need to be considered in doing IMRT of the prostate carcinoma.

The setup errors noted by CBCT are in good agreement with the results published by other studies.^{8,10} Also, doing daily CBCT has advantages over negligible additional imaging doses. The main object of CBCT is better image guidance, which has high benefits. As per the published data by Walter *et al.*¹¹ onetime CBCT of the pelvic region delivers 17.2 mGy to the rectum, ≤ 28 mGy to the surface, and 10.2 mGy to the center of the body, and the peripheral computed tomography dose index (CTDI) is 23.6 mGy. So, if it is calculated for 38#, then the dose will remain at 65.36 cGy to the

Table 2
The mean measured vertical, longitudinal, lateral shifts, and the calculated isodisplacement vector (IDV) of 750 imaging sessions of 30 patients with prostate cancer.

Mean of 750 imaging sessions of 30 patients	Mean vrt. Shift (cm)	Mean long. Shift (cm)	Mean lat. Shift (cm)	Mean IDV (cm)
Mean	0.22	0.62	0.23	0.72
SD	0.1	0.18	0.04	0.16
Median	0.195	0.615	0.225	0.725

vrt.: Vertical; long.: Longitudinal; lat.: Lateral.

Table 3
Change in position of the prostate with respect to bony landmarks.

Patient no.	No. of CBCT sessions	Mean lateral shift from the position on day one (cm) (either side)	Mean anterior-posterior shift from the position on day one (cm) (either side)
1	25	0.44	0.32
2	25	0.34	1.23
3	25	0.17	0.31
4	25	0.48	0.21
5	25	2.96	0.17
6	25	0.51	0.36
7	25	0.97	1.37
8	25	0.20	1.88
9	25	0.64	1.97
10	25	0.41	1.10
11	25	0.43	0.34
12	25	0.87	0.31
13	25	0.77	0.67
14	25	0.11	0.33
15	25	0.73	0.81
16	25	0.13	0.34
17	25	0.44	0.77
18	25	0.74	0.91
19	25	0.91	0.60
20	25	0.51	0.44
21	25	3.16	0.19
22	25	0.61	0.38
23	25	0.97	1.37
24	25	0.30	1.76
25	25	0.69	1.89
26	25	0.43	1.21
27	25	0.46	0.36
28	25	0.91	0.33
29	25	0.81	0.71
30	25	0.15	0.38
Mean		0.71	0.77
SD		0.69	0.57

rectum, ≤ 106.4 cGy to the surface, and 38.76 cGy to the center, and the CTDI will be 89.68 cGy. These values are in 38# and hence are negligible if compared with the pelvic dose tolerance values for OAR.

The bladder, rectum, and prostate are the movable structures and are not fixed with any kind of bones. The normal position of the prostate may vary daily; however, the major variation in its position happens because of the filling of the bladder and rectum. The filled rectum pushes the prostate toward the patient's anterior, while the filled bladder pushes the prostate toward the posterior. Since the prostate is a structure between the bladder and rectum, the change in the volume of both these organs has a high impact on the position of the prostate. If the bladder is filled and is having a higher volume as compared to that on day one, then it will press the prostate toward the posterior direction, but the rectum in the posterior side will oppose it, and the prostate will have a shift to the lateral side. Although the standard protocol of an empty rectum and fixed bladder volume gives the limited solution to the above problem, still rectum volume management on a daily basis is a challenge; moreover, many of the prostate cancer patients are unable to follow the fixed bladder volume protocol. In the current study also all the patients were asked to follow the fixed bladder volume protocol in which the individual patient was asked to drink 200–300 ml of water daily (depending on individual's capacity) 20 minutes before being taken for radiotherapy. Since the prostate position is directly associated with the bladder and rectum volume, which affects their position, in most of the cases, patients who do not lose weight significantly and follow the rectum bladder volume protocol properly, the prostate shift will be less observed, and in such cases, the accuracy of treatment will be good.

The least mean change in volume of the bladder was 32.96 cc, while the highest change in volume was observed as 395.93 cc. The

least change in volume and nearly other results are because such patients strictly followed bladder protocol, while the highest change in volume and similar results were observed for those patients who were not comfortable in holding urine while some patients did not realized the importance of drinking water even after proper counseling to keep the bladder full, and so they did not always drink water in fixed quantity as suggested. Furthermore, some patients may be too nervous, and therefore, drink more water, making the bladder full.¹²

The least and highest change in volume of rectum was found because of large rectal distension, which may be related to chronic constipation and can result in bowel hypotonia; therefore, subsequently, impaired rectal movement and activities. Rectal peristalsis and passage of flatus also have a contribution to rectal filling and rectal changes. The rectum expands and presses up toward the prostate.¹³

Hybrid plans were created on repeat CT images of five suitable patients to know the impact of change in organ volumes on the dosimetric parameters. Since it was not possible to get the daily repeat CT images, repeat CT was only done once after ten fractions for only five suitable patients. From the Table 5, it is clear that on increasing the bladder volume, dose to it decreases and vice versa. In case of rectum, on increasing the volume its dose also increases and vice versa. However in one case, the dose to bladder increased on increasing volume, the CT images were analyzed and found that on increasing the volume of bladder, it did not expand in the anterior direction, rather it expanded in the lateral and posterior directions, which is the area of PTV, and it pushed the prostate in the posterior direction. These results concurred with the results published by Pearson *et al.*¹⁴

Similarly, in one case, the dose to rectum increased even after its volume reduction. On analyzing the CT images, it was found that

Table 4
Volume of bladder and rectum, and the difference from the volume of day one.

Patient No.	No. of Imaging Sessions	Mean Volume (cc)		Mean Change in volume from day one (\pm cc)	
		Bladder	Rectum	Bladder	Rectum
1	25	292.82	38.44	66.4	9.43
2	25	499.9	42.96	87.74	29.03
3	25	195.93	52.14	51.4	14.96
4	25	209.51	52.21	71.63	6.84
5	25	370.26	41.29	395.93	19.6
6	25	487.82	47.79	220.53	7.95
7	25	221.86	48.49	288.1	6.98
8	25	313.42	38.65	44.29	3.08
9	25	420.9	42.05	102.83	6.66
10	25	463.39	46.96	97.97	6.18
11	25	304.72	57.15	80.33	5.45
12	25	488.64	42.61	71.76	5.61
13	25	550.5	46.13	73.33	4.4
14	25	527.13	41.57	53.87	3.24
15	25	536.84	44.79	64.34	4.99
16	25	301.24	76.28	113.75	8.17
17	25	506.38	43.5	108.99	2.53
18	25	460.77	45.03	35.08	5.45
19	25	529.93	57.15	211.64	39.64
20	25	653.69	50.98	32.96	2.3
21	25	286.72	42.34	76.4	11.52
22	25	356.8	62.76	96.84	31.23
23	25	295.63	65.34	71.6	24.74
24	25	107.63	41.37	64.51	8.72
25	25	565.62	72.53	82.85	6.73
26	25	480.42	39.96	62.41	5.32
27	25	311.43	62.32	81.53	6.27
28	25	455.91	40.91	58.39	3.89
29	25	421.42	59.31	214.23	3.76
30	25	432.79	49.13	233.79	32.16
Mean		401.67	49.74	110.51	10.89
SD		129.93	10.11	84.25	10.17

the patient was overstretched at the time of taking repeat CT images, which resulted in lifting the body portion at the level of rectum, prostate, and bladder. Because of this lifting upward, rectum came in dose area. So, it can be suggested from this observation that during the setup of patient for daily treatment, it has to be made sure that the patient's back is in the flat position,

Table 5
Change in doses to bladder and rectum due to change in volume of bladder and rectum.

Patient No.	Actual plan				Hybrid plan				Actual plan – hybrid plan			
	Volume (cc)	D _{mean} (cGy)	D _{1/3} (% of PD)	D _{2/3} (% of PD)	Volume (cc)	D _{mean} (cGy)	D _{1/3} (% of PD)	D _{2/3} (% of PD)	Volume (cc)	D _{mean} (cGy)	D _{1/3} (% of PD)	D _{2/3} (% of PD)
1.												
Bladder	151.2	2695.6	76.9	66.0	196.6	2183.2	67.2	10.8	+45.4	-512.4	-9.7	-55.2
Rectum	81.1	2480.3	76.5	32.4	78.8	1302.5	27.2	8.14	-2.3	-1177.8	-49.3	-24.26
Prostate	56.8	5113.9			50.6	5119.5			-6.2	+5.6		
2.												
Bladder	277.6	3607.5	82.9	60.6	248.9	3711.2	85.2	61.9	-28.7	+103.7	+2.3	+1.3
Rectum	96.1	3205	74.4	53.1	41.7	2838.0	63.4	42.6	-54.4	-367	-11	-10.5
Prostate	20.5	5150.2			17.8	5039.0			-2.7	-111.2		
3.												
Bladder	128.8	3563.5	89.5	54.7	142.3	3773.4	96.3	60.0	+13.5	+209.9	+6.8	+5.3
Rectum	46.2	3349.8	81.9	54.1	57.9	3423.6	87.5	53.1	11.7	+73.8	+5.6	-1
Prostate	11.6	5144.9			14.2	5141.6			+2.6	-3.3		
4.												
Bladder	636.3	3067.3	72.1	51.1	543.5	3127.2	73.4	53.2	-92.8	+59.9	+1.3	+2.1
Rectum	48.1	3107.6	76.4	52.4	54.7	3563.9	88.9	62.8	+6.6	+456.3	+12.5	+10.4
Prostate	20.1	5001.3			13.2	5096.0			-6.9	+94.7		
5.												
Bladder	460.4	3289.7	74.3	53.2	316.2	3170.4	70.8	51.1	-144.2	-119.3	-3.5	-2.1
Rectum	70.5	3016.9	67.9	47.9	37.2	3396.4	81.2	52.2	-33.3	379.5	+13.3	+4.3
Prostate	11.2	5121.3			13.6	5104.0			+2.4	-17.3		

Table 6
Changes in doses to PTV due to volume changes of bladder and rectum.

Patient No.	PTV coverage				Difference in PTV coverage	
	CT		Repeat CT		V _{95%} (%)	V _{93%} (%)
	V _{95%} (%)	V _{93%} (%)	V _{95%} (%)	V _{93%} (%)		
1.	100.67	100.85	99.12	99.82	-1.55	-1.03
2.	100.73	100.94	100.67	100.87	-0.06	-0.07
3.	101.66	101.92	103.65	103.82	+1.99	+1.9
4.	100.85	101.1	92.2	95	-8.65	-6.1
5.	100.63	100.82	100.24	100.49	-0.39	-0.33

similar to when taking planning CT images; otherwise, even after bone to bone matching and even prostate to prostate matching, the rectum will remain in the dose area, and in this way, it will receive higher dose than the planned dose. On increasing the volume of rectum, it pushes the prostate in the anterior direction and in this way, the PTV around the prostate goes out of the dose area. Similarly, if the volume of rectum in planning CT images is higher and on any treatment day, it decreases, then the prostate placed above the rectum shifts toward the posterior direction and goes out of the dose area, as shown in Fig. 3(a) and (b).

Matching prostate to prostate by CBCT before treatment delivery will ensure the dose delivery in PTV volume, specially on the prostate volume, but the maximum dose (D_{max}) and the doses to bladder and rectum cannot be managed by CBCT imaging, although by this imaging, dose to the area of interest i.e. PTV can be delivered with some error in % of dose coverage, maximum and minimum doses in the PTV. Bladder and rectum filling is a major factor along with the other reasons for the shift in the prostate during the radiotherapy. Rectum volume maintaining on daily basis is not easy as is the bladder volume; however, the rectum should be free of air bubbles at the time of taking planning CT images as it is the major factor in high rectum volume, which may not be there on most of the other treatment days.

Moiseenko *et al.*¹⁵ concluded in their study that daily variation in bladder volume causes the undesirable dose delivery to it, as compared to bladder volume, which does not affect prostate shift and PTV underdosing/overdosing that significantly. Similarly, Chen *et al.*¹² also, in their study, analyzed the influence of volumetric

changes of bladder and rectum filling on the 3D dose distribution in prostate cancer radiotherapy. The maximum dose difference between the initial treatment plan and recalculated dose for the CBCT in the central area was not more than 3.50 Gy, about 5.1–4.2% of the prescription dose (64.8–79.2 Gy) to the PTV. They concluded that an increase of 10% of bladder volume will cause a 5.6% reduction of the mean dose. They demonstrated that the volume change of the bladder is more significant than changes in rectal volume for prostate cancer patients. The volume changes of the rectum are not significant except for the air bubbles in the rectum, but bladder volume variations will cause bladder dose changes proportionately. These published studies are in good agreement to findings of our study where we found that the dose to bladder and rectum and dose to 95% and 93% of target volume altered because of volume changes, as shown in Tables 5 and 6.

Although the dosimetric data in the current study are of a very limited number, it is not rational to make a clear statement, but still, it can be seen that the huge dosimetric difference is not there except one exceptional case of patient number 4 in Table 6. So, if the rectum remained empty and free of air at the time of planning CT and bladder full protocol is adopted, then reasonably accurate radiotherapy can be done by doing daily CBCT in which dosimetric data will not be affected too much because of routine minor changes in volumes of the organs. The empty rectum protocol gives good setup results as per already published studies.^{16,17} The daily CBCT is required; many of the centers follow weekly or biweekly CBCT, which actually increases the setup errors.¹⁸

5. Conclusions

The results of this study clearly highlight that the change in the volume of the bladder and rectum makes a significant prostate positional shift. Also, the volume changes vary largely among the patients. The dosimetric results of the hybrid plan represent the changes in doses to bladder and rectum, as well as the target coverage. So it can be concluded that a proper and strict protocol of empty rectum free of air bubbles and full bladder should be followed, and daily CBCT for positional verification prior to treatment delivery will be a good standard of practice for accurate radiotherapy delivery in the case of prostate cancer.

Ethics approval and consent to participate

N/A.

Consent for publication

N/A.

Availability of data and material

All the data are original, and no data available online.

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Authors' contributions

All authors have given consent for publication.

Conflicts of interest

N/A.

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References

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Canc* 2010;127:2893–917.
2. Jain S, Saxena S, Kumar A. Epidemiology of prostate cancer in India. *Meta Gene* 2014;2:596–605.
3. Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and radiation therapy: current advances and future directions. *Int J Med Sci* 2012;9:193–9.
4. Ashamalla H, Rafla S, Parikh K, Mokhtar B, Goswami G. The contribution of integrated PET/CT to the evolving definition of treatment volumes in radiation treatment planning in lung cancer. *Int J Radiat Oncol Biol Phys* 2005;63:1016–23.
5. Kim GY, Pawlicki T, Le QT, Luxton G. Linac-based on-board imaging feasibility and the dosimetric consequences of head roll in head-and-neck IMRT plans. *Med Dosim* 2008;33:93–9.
6. Oelfke U, Tücking T, Nill S, Seeber A, Hesse B, Huber P, et al. Linac-integrated kV-cone beam CT: technical features and first applications. *Med Dosim* 2006;31:62–70.
7. Morin O, Gillis A, Chen J, Aubin M, Bucci MK, Roach M, et al. Megavoltage cone-beam CT: system description and clinical applications. *Med Dosim* 2006;31:51–61.
8. Gurjar OP, Mishra SP, Bhandari V, Pathak P, Pant S, Patel P. A study on the necessity of kV-CBCT imaging compared to kV-Orthogonal portal imaging based on setup errors: Considering other socioeconomic factors. *J Canc Res Therapeut* 2014;10:583–6.
9. ICRU Report 83. *Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT)*. Bethesda: International Commission on Radiation Units and Measurements; 2010.
10. Dickie CI, Parent AL, Chung PW, Catton CN, Craig T, Griffin AM, et al. Measuring interfractional and intrafractional motion with cone beam computed tomography and an optical localization system for lower extremity soft tissue sarcoma patients treated with preoperative intensity-modulated radiation therapy. *Int J Radiat Oncol Biol Phys* 2010;78:1437–44.
11. Walter C, Boda-Heggemann J, Wertz H, Loeb I, Rahn A, Lohr F, et al. Phantom and in-vivo measurements of dose exposure by image-guided radiotherapy (IGRT): MV portal images vs. kV portal images vs. cone-beam CT. *Radiother Oncol* 2007;85:418–23.
12. Chen Z, Yang Z, Wang J, Hu W. Dosimetric impact of different bladder and rectum filling during prostate cancer radiotherapy. *Radiat Oncol* 2016;11:103.
13. Padhani AR, Khoo VS, Suckling J, Husband JE, Leach MO, Dearnaley DP. Evaluating the effect of rectal distension and rectal movement on prostate gland position using cine MRI. *Int J Radiat Oncol Biol Phys* 1999;44:523–33.
14. Pearson D, Gill SK, Campbell N, Reddy K. Dosimetric and volumetric changes in the rectum and bladder in patients receiving CBCT-guided prostate IMRT: analysis based on daily CBCT dose calculation. *J Appl Clin Med Phys* 2016;17:107–17.
15. Moiseenko V, Liu M, Kristensen S, Gelowitz G, Berthelet E. Effect of bladder filling on doses to prostate and organs at risk: a treatment planning study. *J Appl Clin Med Phys* 2006;8:55–68.
16. Poli APDF, Dias RS, Giordani AJ, Segreto HRC, Segreto RA. Strategies to evaluate the impact of rectal volume on prostate motion during three-dimensional conformal radiotherapy for prostate cancer. *Radiol Bras* 2016;49:17–20.
17. Redding DJ, Bragg CM. Assessment of the dosimetric consequences of prostate movement through rectal distension for patients receiving 3DCRT. *J Radiother Pract* 2011;10:147–58.
18. Kupelian PA, Lee C, Langen KM, Zeidan OA, Mañon RR, Willoughby TR. Evaluation of Image-Guidance Strategies in the Treatment of Localized Prostate Cancer. *Int J Radiat Oncol Biol Phys* 2008;70:1151–7.