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A prospective observational study to analyse the influence of bladder and rectal volume changes on prostate radiotherapy using IMRT

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ABSTRACT

Aim: To analyse the interfractional bladder and rectal volume changes and the influence on prostate position.
Background: Interfractional displacement of prostate due to variation in bladder and rectal volume is usual. It is only rational to study the bladder and rectal volume changes and their effects on prostate position during intensity modulated radiotherapy of prostate cancer.
Materials and Methods: A prospective study was conducted on twenty patients with localized prostate cancer during the first phase of radiotherapy, where 50 gray in 25 fractions was delivered by the IMRT technique with daily cone beam computed tomography Bladder and rectum volumes were delineated on CBCT images and their volumes were noted. Prostate position was noted on each set of CBCT images with respect to specific reference points defined on the ileum and coccyx, and daily prostate displacement was noted.
Results: Mean setup errors in vertical, longitudinal and lateral directions were noted as 1.49, 0.498 and 0.17 cm, respectively. Mean change in bladder and rectal volumes in daily CBCT images with respect to that on the first day CT images was noted as 101.94 and 10.22, respectively. Mean lateral and vertical displacement in prostate position was noted as 0.53 and 0.49 cm respectively. No considerable changes in dosimetric parameters were observed because of bladder and rectal volume changes.
Conclusions: Daily CBCT should be done for accurate treatment delivery by the IMRT technique for prostate radiotherapy as prostate shifts physiologically with changes in rectal and bladder volumes.

1. Introduction

Prostate cancer is the fifth most common malignancy worldwide and it commonly affects older male patients belonging to the 6th and 7th decade of life.[1] The main modalities of treatment of prostate cancer include Surgery, Radiotherapy, chemotherapy and hormonal therapy either used individually or in combination depending upon the stage of the disease. For localized prostate cancer either surgery alone or Radiotherapy in the form of external beam radiotherapy or brachytherapy form the mainstay of the treatment.[2]

Several phase III trials have shown the benefit in terms of biochemical control rates by escalating the dose of radiotherapy up to 78–80 gray (Gy) from the conventional doses of 70 Gy. However, with conventional techniques, like three dimensional conformal radiotherapy (3DCRT), achieving this escalated dose becomes difficult because of increased rectal toxicity rates.[3–5] With evaluation of modern radiotherapy techniques, like intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT) etc. along with daily image guidance techniques like on board imaging techniques has allowed to deliver precise tumoricidal doses confined to target volumes with sharp dose gradient resulting in minimal doses to surrounding normal organs.

In the modern radiotherapy techniques, such as IMRT and VMAT, which deliver conformal dose, the main challenge is posed by the interfraction motion of the organs as there is a sharp dose gradient; therefore, any sort of motion may result from under dosing of the target region and increased doses to surrounding organs.[6] During prostate radiotherapy the problem of interfraction movement of the prostate becomes more important because of physiological change in the position of the prostate in relation to the change in bladder and rectal volumes and this may impact the treatment outcomes of the patients.

The current study has been conducted to analyse the bladder and rectal volume changes during the course of radiotherapy and its

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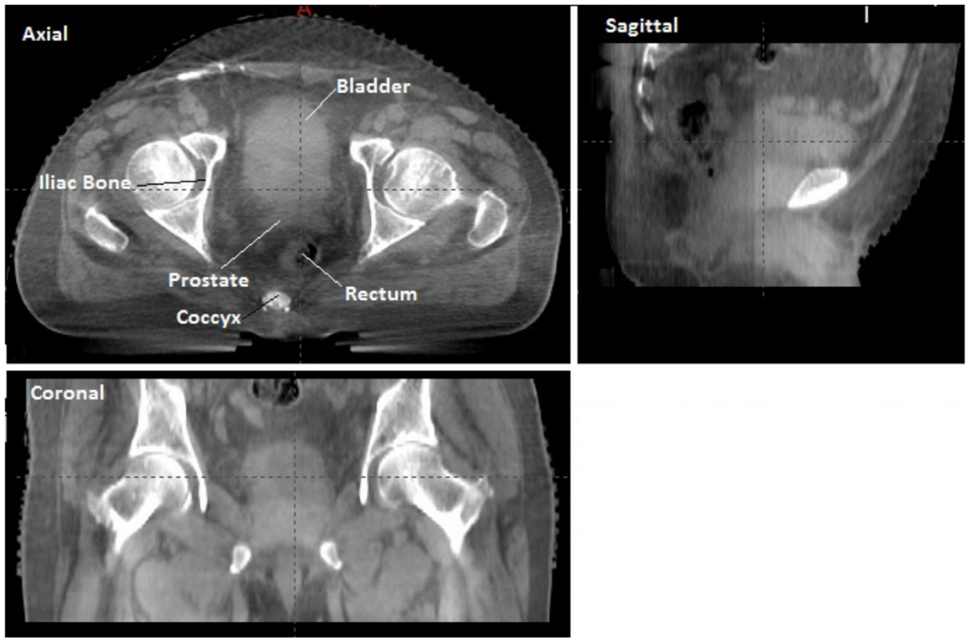

Fig. 1. Axial, coronal and sagittal view of cone beam computed tommography (CBCT) images of one of the prostate cancer patient.

effect on the prostate position by doing daily cone beam computed tomography (CBCT).

2. Materials and methods

In the present observational prospective study twenty patients with histologically proven early prostate cancer belonging to T1 & T2, N0, M0 categories and gleasons grade I between the age of 40–80 years with KPS ≥ 70% were taken. An Informed consent was taken from all of the patients who participated in this study. All the patients were planned and treated with intensity modulated radiotherapy (IMRT) with daily CBCT, to the dose of 78 Gy in 35 fractions (#) delivered to the planning target volume (PTV) in three phases with reduction of the target volume in all the subsequent phases. The present study was carried out during the first phase of the study only where patients were planned and treated for 50 Gy/25# delivered @2Gy /# with 5#/week.

Patients were simulated utilizing computed tomography (CT) machine Siemens SOMATOM Definition AS scanner (Siemens Medical Systems, Germany) with adequate immobilization devices, i.e. base plate and thermoplastic sheet. The contrast enhanced CT images with 3 mm slice thickness were obtained and transferred to the treatment planning system (TPS) Eclipse vs. 8.9 (Varian Medical Systems, Palo Alto, CA) for planning purposes. All the patients were asked to drink 200 ml water or as per individual patient's capacity 20 min before CT simulation.

The target volumes and organs at risk (OAR) were delineated as per the ICRU 83 Guidelines.[7] PTV was delineated by adding a 0.5 cm margin to the clinical target volume (CTV) as per the institutional protocol. Then IMRT plan for each patient was created by using 9 beams each of 6 megavoltage (MV) photon energy and Anisotropic Analytic Algorithm (AAA) was used for dose calculation. After approval of final treatment plan, patients were treated by dual energy linear accelerator (LA) Clinac DMX (Varian Medical Systems, Palo Alto, CA) having 6 and 15 MV photon energies with Millennium 80 multileaf collimators (MLC) system with each MLC thickness projected at the isocentre of 0.5 cm. On Board Imaging (OBI) system (Varian Medical Systems, Palo Alto, CA) having 125-kVp x-ray tube isocentrically mounted to the gantry of LA was utilized to take the kilo voltage (kV)-CBCT images.

Every patient was asked to drink the same amount of water which they did before CT simulation. After 20 min, the patient was set up on the LA couch using the immobilization devices and the Light Amplification by Stimulated Emission of Radiation (LASER) (LAP GmbH Laser Applications, Luneburg, Germany) installed in the LA room. Before delivery of each fraction, patient positional verification was done by CBCT. For the patient position verification, CBCT was performed by using OBI system with full Bowtie filter and keeping the vertical distance of the imager at 50 cm. The gantry was rotated from 179° to 180° i.e. 360° to obtain the CBCT images of the site. The patient setup was evaluated using Varian Portal Vision 7.5 (the anatomy matching software) by superimposing the CBCT images and the planning CT images. Prostate to prostate was matched following the standard procedure.[8] Setup errors were noted and applied to couch and then the plan was delivered to treat the patient.

These CBCT images were then transferred and opened on the Eclipse TPS. The bladder and rectum were contoured on the CBCT images. The volume of the bladder and rectum in each set of CBCT images for every patient was measured by using the tool available in the Eclipse TPS. Fig 1 shows the axial, coronal and sagittal view of CBCT images of one of the prostate cancer patient.

A point was specified for each patient on the edge of the iliac bone and another point on the upper edge of the coccyx on the first day of treatment. Both points varied from individual to individual but remained the same for a patient for all the 25 CBCT imaging sets. The lateral position of the prostate with respect to this specific defined position on the edge of the iliac bone and the vertical position of the prostate with respect to the specific point on the upper edge of the coccyx in the CBCT images and on the first day of planning CT images were measured for each patient. Using the obtained data, lateral and vertical displacement in the prostate position with respect to the defined points on the bones was calculated. The longitudinal displacement was not measured as the clear reference to measure the distance in longitudinal direction was not possible in most of the cases.

To measure the effect of bladder and rectum volume changes on the dosimetric parameters, the Re-CT was done for six suitable

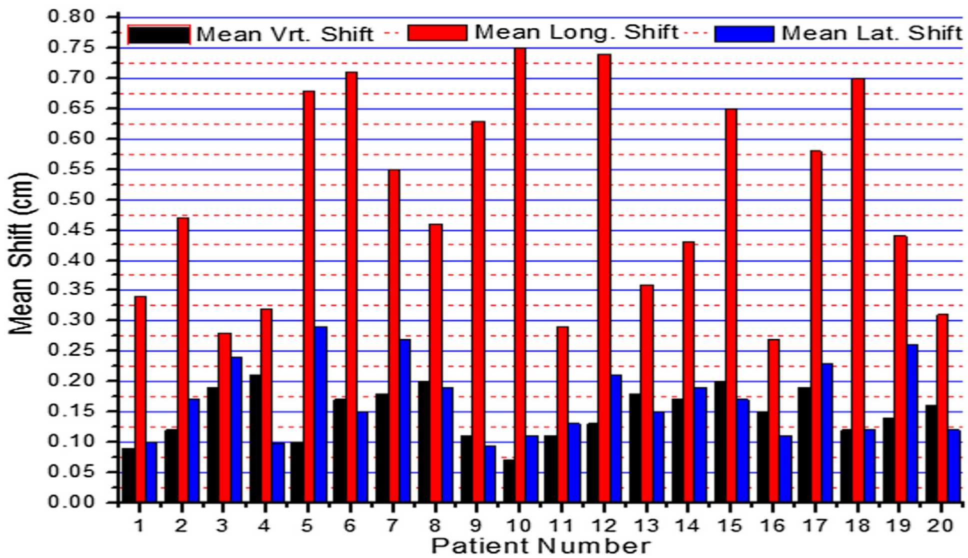

Fig. 2. The mean vertical, longitudinal and lateral shifts of 25 CBCT imaging sessions for each of 20 patients of prostate cancer.

patients whose bladder and rectum volume was observed to be highly variable in the CBCT images. Target volumes and normal organs covering the similar volumes as on the first day of planning CT images were delineated. The hybrid plan was created for each of these six patients, in which the actual plan done on day one of planning CT images was imported on the Re-CT images and isocentre was placed at the same anatomical place as that on day one of planning CT images. Dose was recalculated and monitoring units remained the same for all fields as in the actual plan. PTV coverage and the doses to the bladder and rectum were noted and analysed.

3. Results

Of the total of 500 CBCT imaging sessions for 20 patients, in 25 imaging sessions for each patient the mean vertical, longitudinal and lateral setup error was found to be 1.49 (SD: 0.041), 0.498 (SD: 0.171) and 0.17 (SD: 0.062) cm, respectively. Fig. 2 presents the mean setup errors of each patient in the vertical, longitudinal and lateral directions. The calculated mean isodisplacement vector (IDV) for all the twenty patients was calculated as 0.559 (SD: 0.169) cm. Fig. 3 shows the mean IDV of 25 CBCT imaging sessions for each of the 20 patients.

The mean volume of the bladder and rectum measured from the 25 set of CBCT images of each of the 20 patients was found to be 424.38 (SD: 122.28) and 50.86 (SD: 9.34), respectively. The mean change in the bladder and rectum volume in the CBCT images with respect to that on the first day of planning CT images was found to be 101.94 (SD: 64.29) and 10.22 (SD: 10.87), respectively. Detailed data of mean bladder and rectum volumes and the change in volume with respect to that in the first day CT images for all the 20 patients are given in Table 1.

The day to day mean lateral and vertical displacement in the prostate position with respect to its position on the first day of planning CT images (based on distances from the defined points on the edge of the iliac and the coccyx bone) was found to be 0.53 (SD: 0.26) and 0.49 (SD: 0.25) cm, respectively. Fig. 4 shows the mean lateral and vertical prostate displacement with respect to the bony landmarks (iliac and coccyx bones).

The doses to the bladder, rectum and PTV coverage in the actual plan done on the first day of planning CT images and in the hybrid plan done on re-CT images are given in Table 2. Fig. 5 is dose distribution on CT image of actual plan and of the hybrid plan, this image was taken as a good example to represent the impact of the rectum filled with air bubbles on the prostate position and target and bladder shift in dose distribution area.

4. Discussion

For the treatment of localized prostate cancer, commonly IMRT with daily imaging is used to provide highly conformal and adequate doses to the PTV and minimal doses to the surrounding tissue, thus increasing the therapeutic ratio. Different radiotherapy centers have different protocols on imaging, some do weekly CBCT and daily orthogonal portal imaging (OPI) while others do daily CBCT.[9] Studies shows that in the sites where target position may vary with respect to the bones, daily CBCT should be done before delivering every fraction.[6]

The patient setup errors reported in the current study as shown in Fig. 2 and the calculated IDV as shown in Fig. 3 are in agreement with the results published in the studies.[6,10,11] The setup error is a combined effect of errors in setup using the available immobilization devices and the prostate movement with respect to the pelvic bones. Since thermoplastic sheet molded for individual patient has the impressions of the pelvic site shape (pelvic bones, umbilicus, etc.), patients are immobilized in the same position every day during treatment with the help of the molded thermoplastic sheet references, however, the position of the prostate may vary inside the body physiologically which can be visualized by CBCT only. Thus, CBCT helps not only in accurate localization of prostate but also to nullify any setup errors if present.

Consideration and analysis of the additional imaging doses by CBCT is important. Moon et al.[12] presented in their study that imaging dose by single CBCT is 13.0 (±0.5) miligray (mGy) to the bladder, 12.5 (±0.5) mGy to the rectum, 11.5 (±0.4) mGy to the gonads, 1.04 (±0.06) to the stomach and an effective dose of 4.0 (±0.29) mGy is delivered. If the above doses are calculated for 38 fractions (full course of treatment) then they are approx. 49.4, 47.5, 43.7, 0.395 cGy to the bladder, rectum, gonads and stomach, respectively, and the effective dose is 15.2 cGy. These full doses are negligible as compared to the doses to these organs by treatment plan. So, imaging doses by CBCT are not the matter of concern when big advantage of accurate target positioning and proper dose delivery in the planned volume is achieved by the CBCT technique.

The change in volume of the bladder and rectum during the course of radiotherapy as noted in Table 1 and indicates that even after following the bladder full protocol, the volume of the bladder

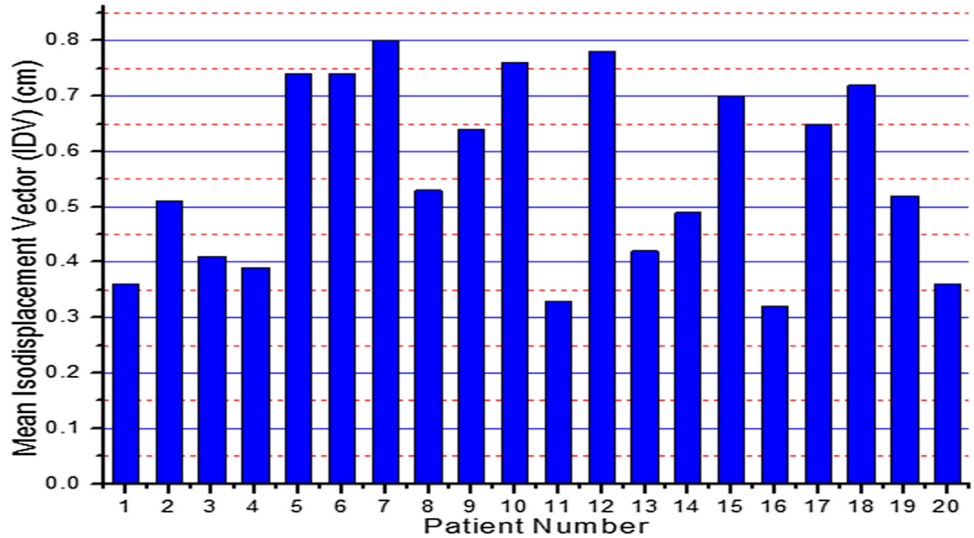

Fig. 3. The mean isodisplacement vector (IDV) of 25 CBCT imaging sessions for each of 20 patients of prostate cancer.

Table 1
Volume of bladder and rectum, and the difference from the volume of day one.

Patient No.	Mean volume measured from CBCT images of 25 imaging sessions (cc)		Mean change in volume from the volume measured from first day planning CT images (±cc)	
	Bladder	Rectum	Bladder	Rectum
1	292.82	38.44	66.4	9.43
2	195.93	52.14	51.4	14.96
3	209.51	52.21	71.63	6.84
4	463.39	46.96	97.97	6.18
5	487.82	47.79	220.53	7.95
6	304.72	57.15	80.33	5.45
7	488.64	42.61	71.76	5.61
8	550.5	46.13	73.33	4.4
9	527.13	41.57	53.87	3.24
10	356.8	62.76	96.84	31.23
11	460.77	45.03	35.08	5.45
12	506.38	43.5	108.99	2.53
13	301.24	76.28	113.75	8.17
14	529.93	57.15	211.64	39.64
15	653.69	50.98	32.96	2.3
16	536.84	44.79	64.34	4.99
17	311.43	62.32	81.53	6.27
18	421.42	59.31	214.23	3.76
19	432.79	49.13	233.79	32.16
20	455.91	40.91	58.39	3.89
Mean	**424.383**	**50.858**	**101.938**	**10.2225**
SD	**122.2822**	**9.335144**	**64.28583**	**10.86879**

CBCT: cone beam computed tomography; CT: computed tomography, cc: cubic centimeter; SD: standard deviation.

is varying. Although no control on the rectum volume, a large volume change in the rectum is caused by air bubbles which can be managed to a certain limit. In the cases of prostate cancer, the bladder volume change is more significant as compared to that of the rectum, air bubbles are only the major reason for significant variation in the rectum volume.[13] In some of the cases, the change noted in the bladder volume is very high as compared to the rest of routine and usual cases, it is because some patients failed to follow the full bladder protocol due to difficulty in voiding or other medical reasons, while other patients become very nervous and drink more water. Chen et al. have also presented the same kind of reasons.[13] In all these cases, it is obvious to have a big change in the bladder volume.

The change in the bladder volume directly influences the prostate position, increased volume of the bladder pushes the prostate and cause it be displaced either in the lateral or posterior direction.[14,15] Similarly increased rectum volume will push up the prostate in the anterior direction and will also push up the bladder.[16] From the Fig. 5 it can be clearly seen that the position of the prostate with respect to the reference point on the iliac bone and the coccyx is varying significantly. High dose gradient is planned in IMRT and in such cases if prostate displacement with the values as shown in Fig. 4 takes place then, definitely, it will directly impact the delivery of planned dose on the defined target volume and, eventually, the target coverage and doses to the bladder and rectum will differ from the planned ones.

The change in dosimetric parameters, as shown in Table 2, because of the change in volumes of the bladder and rectum are not significant. Although the number of patients included in the study to evaluate dosimetric changes is too small and a large number of cases is required to conclude whether the change in dosimetric parameters is statistically significant or not; however, based on the results shown in Table 2 it can be assumed that no big differences observed in the dosimetric parameter, except in one case where the

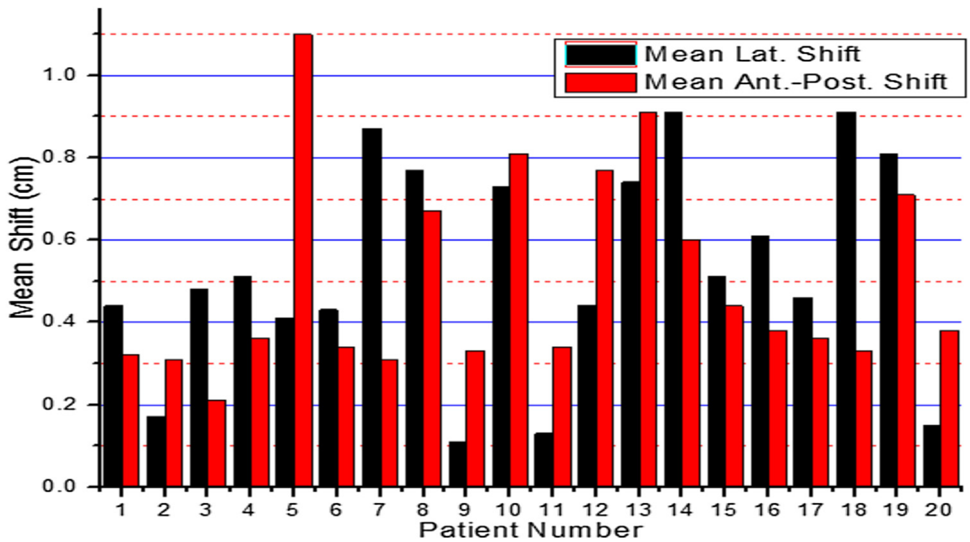

Fig. 4. Day to day displacement of prostate in lateral and vertical directions with respect to the bony landmarks (iliac and coccyx bones).

Table 2
Impact of bladder and rectum volume changes on the dosimetric parameters.

Patient No.		Bladder			Rectum			PTV Coverage $V_{95\%}$ (%)		
		Actual Plan	Hybrid Plan	Difference	Actual Plan	Hybrid Plan	Difference	Actual Plan	Hybrid Plan	Difference
1	Volume	151.2	196.6	45.40	81.1	78.80	−2.30	100.67	99.12	−1.55
	Dmean	26.96	21.83	−5.12	24.80	13.03	−11.78			
	D1/3	38.45	33.60	−4.85	38.25	13.60	−24.65			
	D2/3	33.00	2.40	−27.60	16.20	4.07	−12.13			
2	Volume	277.60	248.90	−28.7	96.10	41.70	−54.40	100.73	100.67	−0.06
	Dmean	36.08	37.11	1.04	32.05	28.38	−3.67			
	D1/3	41.45	42.60	1.15	37.20	31.70	−5.50			
	D2/3	30.30	30.95	0.65	26.55	21.30	−5.25			
3	Volume	128.80	142.3	13.5	46.2	57.90	11.70	101.66	103.65	1.99
	Dmean	35.64	37.73	2.10	33.50	34.24	0.74			
	D1/3	44.75	48.15	3.40	40.95	43.75	2.80			
	D2/3	27.35	30.00	2.65	27.05	26.55	−0.50			
4	Volume	636.30	543.50	−92.80	48.10	54.70	6.60	100.85	92.2	−8.65
	Dmean	30.67	31.27	0.60	31.08	35.64	4.56			
	D1/3	36.05	36.70	0.65	38.20	44.45	6.25			
	D2/3	25.55	26.60	1.05	26.20	31.40	5.20			
5	Volume	460.40	316.20	−144.20	70.5	37.2	−33.30	100.63	100.24	−0.39
	Dmean	32.90	31.70	−1.19	30.17	33.96	3.80			
	D1/3	37.15	35.40	−1.75	33.95	40.60	6.65			
	D2/3	26.60	25.55	−1.05	23.95	26.10	2.15			
6	Volume	360.23	311.19	−49.04	85.46	59.12	−26.34	101.19	102.89	1.70
	Dmean	29.85	30.92	1.07	27.94	26.15	−1.79			
	D1/3	38.13	39.09	0.96	40.15	37.10	−3.05			
	D2/3	25.74	26.81	1.07	25.87	22.45	−3.42			

Dmean: mean dose; D1/3: dose to one third volume; D2/3: dose to two third volume; V95%: volume receiving 95% of prescribed dose.

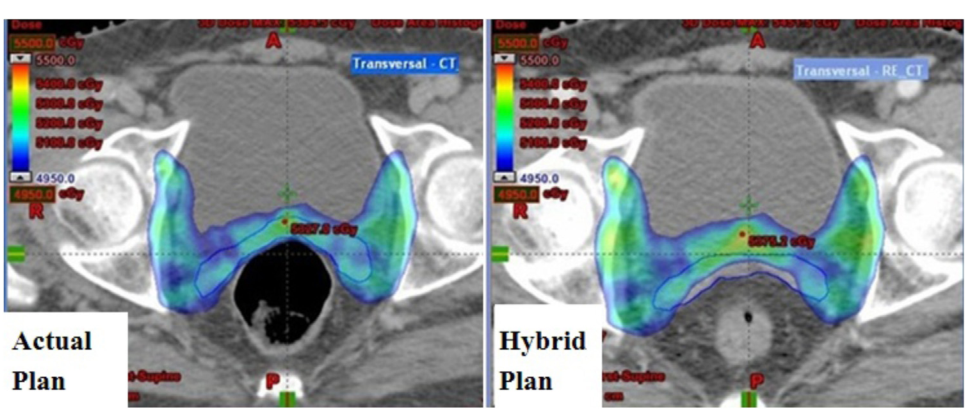

Fig. 5. Dose distribution on one of the CT image of actual plan done on first day planning CT images having rectum filled with gas, and of the hybrid plan on re-CT images without significant gas in the rectum.

main reason for the large difference is well noted as a large rectal distension in the first day of planning CT images.

The full bladder protocol should be followed to maintain the bladder volume but Hynds et al.[17] reported in their study that bladder filling protocol does not provide consistent and reproducible bladder volumes for radiotherapy, similar observations were made in the current study where those patients who strictly followed the full bladder protocol were also reported to show daily variation in bladder volume. However it was small. It means that the full bladder protocol helps in preventing the large change in volume. Since no significant variation was observed in dosimetric parameters because of bladder and rectum volume changes, based on all the observation of the study, it can be stated that an accurate radiotherapy of prostate cancer can be done by IMRT technique if setup verification is done by CBCT before delivering each fraction.

5. Conclusion

Change in the bladder and rectum were noted in daily CBCT causing prostate displacement with respect to the bony landmarks. Negligible difference was observed in dosimetric parameters because of the bladder and rectum volume changes. So, it can be concluded that daily CBCT should be done for setup verification in the cases of prostate cancer even when following the full bladder protocol. If daily CBCT is done, then accurately planned dose can be delivered to accurately planned volumes irrespective of volume changes in the bladder and rectum.

Conflict of interest

None declared.

Financial disclosure

None declared.

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