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# The Impact of Residual Geometric Inaccuracies on Normal Organ Doses in Image Guided-Radiation Therapy of Prostate Cancer Using On-Board Kilovoltage Cone-Beam Computed Tomography

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ARTICLEINFO	ABSTRACT				
<i>Article type:</i> Original Article	<b>Introduction</b> : The aim of this retrospective study was to evaluate the variations in delivered dose to the bladder, rectum, and femoral heads of prostate cancer patients during a course of treatment by image-guided rediction therem: (CDT)				
<i>Article history:</i> Received: Oct 05, 2016 Accepted: Mar 28, 2017	<i>Materials and Methods:</i> Overall, 15 patients with prostate cancer were selected and. Each week, for each patient five consecutive cone beam computed tomography (CBCT) images were taken after bony anatomy alignment by using two orthogonal radiographic images, as well as CBCT images. Dose				
Keywords: Image Guided Radiation- Therapy Cone Beam Computed- Tomography Prostate Cancer Volumetric Modulated Arc- Therapy	distributions and dose volume histograms (DVH) for all the original and CBCT plans were obtained. Maximum, as well as mean doses and volumes of the bladder, rectum, and both femoral heads were recorded for each CBCT plan and compared with the original CT plan. For all the studied body parts, the differences in DVH between CBCT plans and original CT plan were calculated and compared. <i>Results:</i> Considering all the 75 CBCT images for the 15 patients, average of changes in mean doses and volumes were 17.8%, 41.8%, 7.1%, and 36.8% for the bladder and rectum, respectively. There was a significant (P<0.05) negative correlation between mean bladder dose and volume, while a weak and positive correlation was found between mean dose and volume of rectum in our patients. <i>Conclusion:</i> Our results showed that changes in volumes of the bladder and rectum alter their received inter-factional mean doses. Further attention to the volume variations of the bladder and rectum during a radiotherany course is recommended for more accurate IGRT treatment.				

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## Introduction

Anatomical changes in treatment area occur frequently during the course of cancer radiotherapy, which results in dose differences between planned and delivered doses to the tumor and critical organs. Additionally, the extent of anatomical changes is dependent on the site of treatment and it can be observed as positional and volumetric changes or organ deformation. [1]

In intensity-modulated radiation therapy (IMRT) of prostate cancer, two organs at risk (OAR) of bladder and rectum play critical roles in delivered dose to tumor volume. Thus, image-guided radiotherapy (IGRT) has been an increasingly adopted technique to reduce inter-fractional setup errors during treatment. [2-10] Pre-treatment kilovoltage cone beam computed tomography (kV-CBCT) images are taken daily or weekly to correct the possible setup variations and monitor organs' volumetric changes in the treatment area.

In busy centers, two diagonal radiographs are the main tools for setup corrections in most cases, and kV-CBCT is taken weekly for further correction. Besides, superimposition of original plan on weekly kV-CBCT images can be employed to evaluate the actual dose distribution in each treatment, and its application improves geometric and dosimetric accuracy of treatment. In other words, on-board CBCT images can be used for dose reconstruction in combination with the fluence maps from treatment plan. The accuracy of using a kV-CBCT for dose calculation has been studied for different cases. For prostate cancer, with negligible motion artifact, CBCT can be employed directly for dose calculation. [11] Additionally, studies on IGRT of prostate cancer reported significant differences between volume and dose of the bladder and rectum in original plans and registered CBCT plans. [6, 8, 12]

Several studies reported that the dosimetric analysis on CBCT images provides a helpful tool for clinicians to monitor treatment progress and to evaluate the actual delivered dose to target volumes. [6,

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10, 13, 14] In a study on IMRT of prostate cancer, a large discrepancy was found between the original treatment plan and the CBCT-based calculation. The results confirmed the importance of inter-fractional bladder and rectum movements. They also emphasized on the need for adaptive therapy to compensate for the anatomical changes in the future prostate treatments. [11]

According to the above-mentioned studies, it is evident that the existence of two inflatable and relatively moveable organs, the bladder and rectum, not only changes the location of prostate, but also alters their received dose during a treatment course. Therefore, their daily monitoring could improve the quality of treatment in IGRT of prostate cancer in terms of normal tissue complication probability (NTCP) and tumor control probability (TCP). To address this issue in our radiation therapy center, we used Varian TrueBeam for volumetric-modulated arc therapy (VMAT) of prostate cancer and weekly applied onboard KV-CBCT for all the patients. The aim of the current study was to investigate the extent of residual dosimetric errors in delivered dose to the bladder, rectum, and femoral heads due to volume changes of the bladder and rectum during a treatment course for the studied patients.

### Materials and Methods

This retrospective study was performed on prostate cancer patients treated with IGRT modality. Overall, 15 patients, 10 radical and 5 post-op, were randomly selected from among prostate cancer patients. Five CBCT images per patient and 75 CBCT images were evaluated. High-risk prostate cancer patients were treated with 56 Gy to pelvic CTV, 66 Gy to seminal vesicles, and 78 Gy to prostate in 37 fractions. Post-ops were treated with 68 Gy in 34 fractions and some were treated with 70 Gy in 35 fractions., OARs, including the bladder, rectum, and femoral heads, were delineated for each patient on five weekly CBCT datasets. Weekly target localization was performed using bone matching based on both orthogonal radiographs and kV-CBCT images. The treatment and CBCT imaging were performed using a Varian linac, TrueBeam system and its on-board CBCT system (Varian Medical Systems, Palo Alto, USA).

In clinical routine, prostate patients were treated in supine position and they were orally given 500 ml water 1 h before treatment to fill the bladder. To evaluate residual setup errors, volume changes, and their effect on whole treatment, five CBCT images were taken during the course of treatment. CBCT images were selected from Aria 11 system, and offline review segment and couch corrections were considered for each CBCT dataset. In Eclipse (version 11) treatment planning system (TPS), rectum wall, bladder, and femoral heads were contoured by one dosimetrist to avoid inter-observer variation for each CBCT image. Afterwards, original treatment plans were inserted to isocenter of each CBCT, and then couch corrections were applied to shift the treatment isocenter to obtain real treatment position. The dose calculations were performed by using Acuros XB algorithm. The dose calculations were carried out on CBCT provided plans and results were recorded and compared with original treatment plan. The comparisons between CBCT and original plans were performed based on dose-volume histogram results. Organ volumes, as well as maximum and mean doses for the rectum, bladder, and femoral heads were compared between CBCT and original plans.

To obtain more accurate results on CBCT-based dose distributions, CBCT and original CT simulator Hounsfield unit (HU) were verfied. According to the study of Hatton et al., [15] HU-mass density curves are measured with CIRS model 062M phantom (CIRS Tissue Simulation Technology Norfolk, VA, USA), which was made from tissue-equivalent epoxy resin materials. This phantom was originally designed for fan-beam CT imaging. To adapt it to CBCT imaging, tissue equivalent materials with a thickness of 5 cm were joined on both sides of the phantom. Then, the measured HU values for each given mass density were installed to TPS for Acuros XB dose calculation. The CBCT HU quality assurance tests were conducted with Catphan® 600 phantom. The comparison between CT simulator and CBCT provided HU for our CIRS phantom, which was consistent in ±2%.

To evaluate the correlation between the bladder and rectum mean doses and volumes, Pearson correlation coefficient was calculated using SPSS, version 19.

#### Results

In Table 1, the overall average doses for the rectum, bladder, and femoral heads are tabulated. Minus sign indicates decrease in both volume and dose and vice versa. Standard deviations show large organ volume fluctuations between fractions, but dose fluctuations did not follow volume changes in all the cases. The average volume and dose variations for each patient were calculated from absolute differences between the original CT and CBCT plans to avoid misinterpretation due to positive/negative dose and volume changes. Considering all the 75 CBCT images for the 15 patients, average dose and volume changes were 17.8%, 41.8%, 7.1%, and 36.8% for the bladder and rectum, respectively.

In Figure 1, the variation in mean and maximum doses and volumes of the bladder are illustrated for 12 patients. It is worth mentioning that 15 patients were investigated in the current study, but because of the limitation in inserting all the data in one figure, only 12 of them were presented in Figure 1. However, whole data for the 15 patients are summarized in Table 1.



**Figure 1.** Illustration of difference between original plan and CBCT replanning for five weeks during whole treatment course for bladder maximum dose, mean dose and bladder volume for prostate cancer patients treated volumetric arc radiation therapy of Varian True beam linac.

Table 1. The average and standard deviation of differences between original plan and weekly CBCT plans were calculated for every patient in our study. The data have been tabulated for mean doses of bladder, rectum and femoral heads as well as bladder and rectum volume.

	Bladder Mean	Bladder	Rectum mean	Rectum	Right Femoral	Left Femoral
	dose diff(%)	Volume diff	dose diff(%)	volume diff(%)	head mean	head mean dose
		(%)			dose diff(%)	diff(%)
Patient 1	-1.5±16.9	12.4±62.8	2.9±6.3	19.1±27.4	6.1±1.5	5.1±0.9
Patient 2	14.7±4.8	-68.7±15.3	5.6±4.1	9.1±34.3	-0.6±1.1	-1.9±1.2
Patient 3	3.7±5.7	-3.8±33.6	6.7±8.0	115.0±62.0	0.7±1.3	1.1±0.5
Patient 4	-11.1±5.1	51.2±56.7	8.9±10.3	4.4±8.7	28.0±6.0	26.3±1.9
Patient 5	23.6±19.8	-44.9±28.7	15.5±7.1	23.2±26.4	-0.7±1.4	0.5±1.3
Patient 6	10.8±7.2	-42.7±29.0	-2.6±2.9	100.8±42.3	-0.4±2.3	-1.6±0.6
Patient 7	-1.8±11.7	16.9±46.7	7.2±5.5	21.3±14.3	2.8±2.8	2.3±2.6
Patient 8	78.9±28.1	-50.5±18.0	-0.9±4.0	26.7±46.7	1.5±1.2	0.5±0.8
Patient 9	15.1±5.3	-68.3±13.6	13.0±4.3	6.2±7.5	-1.3±2.0	-0.19±1.6
Patient 10	4.3±11.9	-7.9±14.8	2.0±4.4	18.4±9.6	0.0±0.9	0.5±0.6
Patient 11	36.7±5.7	-72.9±7.1	-4.1±3.6	0.9±20.7	-0.3±12.0	-0.3±16.2
Patient 12	-31.2±19.5	93.9±73.8	13.0±19.6	31.5±26.3	1.6±1.8	1.5±1.2
Patient 13	24.7±2.0	-31.2±34.4	10.7±2.1	-16.4±17.8	32.4±3.3	35.1±5.1
Patient 14	-5.9±14.7	42.1±48.1	8.9±3.9	145.6±159.4	6.0±3.8	8.2±4.1
Patient 15	3.0±4.7	19.7±26.1	4.7±5.2	-12.9±16.7	2.0±0.94	35.7±3.0

It is observed that for most of the cases there is an inverse relationship between bladder mean dose and volume. In other words, for most cases, mean bladder dose increases significantly with reduction in its volume in each treatment session. However, the variation in bladder maximum dose with bladder volume was about 5% for all the cases. It might be due to the fact that when the bladder is filled more than that was in CT simulation, a smaller fraction of bladder volume remains in the vicinity of planning target volume and a greater volume of bladder is located far from the isocenter and receives lower doses than planned, consequently, the mean bladder dose is decreased.

In Figure 2, the results for variations in rectum dose and volume are shown for 12 patients. It is

noted that with increasing rectum volume, rectum dose increases, which is in contrast to the bladder. On the other hand, this direct relationship was not observed for all the cases and there are cases with inverse relationship between rectum mean dose and volume.

In Figure 3, dosimetric differences between planned and delivered doses for femoral heads are presented for 12 patients. Compared to the bladder and rectum, there were small mean dose changes of 5.6% and 8.1% for the right and left femoral heads, respectively, averaged for 15 patients. The volume changes in the femoral heads are attributed to small variations in contouring of femoral heads in original and CBCT plans.





Rectum maximum dose Rectum mean dose Rectum Volume

Figure 2. Illustration of difference between original plan and CBCT replanning for five weeks during whole treatment course for rectum maximum dose, mean dose and rectum volume for prostate cancer patients treated volumetric arc radiation therapy of Varian True beam linac.







Femur mean dose-R Femur mean dose-L

**Figure 3.** Illustration of difference between original plan and CBCT replanning for five weeks during whole treatment course for right and left femoral head maximum dose, mean dose for prostate cancer patients treated volumetric arc radiation therapy of Varian True beam linac.



**Figure 4.** The blended image composed of contoured CT and CBCT of second week for patient #8 and its related DVH for comparison. The bold yellow line representing the bladder contour for original plan and the dimmed yellow line is for CBCT of the same patient taken in second week. (a) The axial view. (b) The coronal view. (c) The mid-sagittal view. (d) DVHs of bladder obtained from original and CBCT





**Figure 5.** The blended image composed of contoured CT and CBCT of third week for patient #12 and its related DVH for comparison. The blue line representing the bladder contour for original plan and the dimmed purple line is for CBCT of the same patient taken in third week. (a) The axial view. (b) The coronal view. (c) The mid-sagittal view. (d) DVHs rectum obtained from original and CBCT

For better illustration of the volume changes in both bladder and rectum and their effect on received doses, figures 4 and 5 are provided. In Figure 4, bladder volume in CT and CBCT was depicted in two different views for the patient No. 8 and CBCT No. 3.

In addition, a DVH comparison of CT and CBCT plans is presented. In Figure 5, comparison of CT and CBCT (No. 3) planned rectum doses are seen for patient No. 12. Both patients had the maximum variation in bladder and rectum volume among the studied patients.

In Figure 6, the scatter plot of volume and mean dose changes for both bladder and rectum are depicted. As can be noted, there is a negative correlation between bladder volume and mean dose with a correlation coefficient of -0.65 (P<0.05). However, this correlation for the rectum was weak, that is, a non-significant positive correlation of 0.164 was found.



Bladder volume change (%)



Rectum volume change (%)

**Figure 6.** The scatter plot and regression line for mean dose changes in terms of volume changes for bladder (A) and rectum (B).

### Discussion

The purpose of the current study was to estimate the variations in received dose by the bladder, rectum, and femoral heads from IGRT treatments using weekly kV-CBCT image sets of Varian TrueBeam linac. There were large rectum and bladder volumetric changes for most of the patients with some exceptions (figures 1 and 2). Our results showed that reduced bladder volume increases mean bladder dose and vice versa. It can be explained that when volume decrease occurs in the bladder, whole volume of the bladder becomes closer to the planning target volume (PTV) and the distal segment of the bladder receives higher doses. Conversely, with greater volume of the bladder, the distal part of the bladder is located more distant from PTV, and the mean dose of the bladder decreases accordingly.

Our findings were consistent with the study of Huang et al. [6], whose results showed 18% and 44% changes in the bladder dose and volume. respectively. The inverse relationship between bladder volume and mean dose and their significant correlation was noted in the study of Hüttenrauch et al. [16] However, the relationship between bladder dose and mean dose was also influenced by treatment protocol and patient-specific criteria. For instance, when the patients #8, 9, and 11 were compared, there were significant differences between them. Patient No. 9 had the highest bladder volume reduction, whereas the increase of bladder mean dose was the lowest compared to patients 8 and 11. Patient 8 showed the slightest volume reduction, where bladder mean dose showed a considerable increase. This relationship might arise from the fact that patient No.8 was a high-risk radical prostate patient and treatment scheme included pelvic lymph nodes. Thus, a higher volume had to be irradiated around the prostate region. Furthermore, patient 9 had a post-op treatment with 68 Gy, while No. 11 was a low-risk radical prostate patient treated with 78 Gy, and pelvic lymph nodes were excluded. This indicates the reasons behind the observed fluctuations in the relationship between bladder volume and mean dose observed in our studied cases. However, several published studies remark that lower bladder volume results in higher dose, and irradiated volume affects mean dose of the bladder proportionally. [17, 18]

In most of the cases, mean dose increases with distension of the rectum, which can be explained by the fact that when rectum volume changes, it affects prostate position in anterior-posterior direction and rectum pushes prostate away from dose region, where rectum mean dose increases. Using bony structures for treatment alignment, rectum-prostate position cannot be evaluated; accordingly, rectum distension might push prostate anteriorly and a larger part of the rectum enters the high-dose region near the beam isocenter, which consequently raises the rectum mean dose. However, some patients show significant rectum volume changes, where variation in maximum and mean rectum doses were negligible (e.g., patients 3, 6, and 8).

It should be kept in mind that our study relied on pre-treatment CBCT images. In this regard, Reggiori et al. showed that treatment time is a big concern for intra-fraction dose uncertainties due to rectumprostate movements. [14] Nevertheless, compared to the other modalities used for IMRT, our employed technology of VMAT was fast enough to minimize this effect. It should be noted that we used CBCT images with lower quality than the images used for original treatment plans. Therefore, small differences in contouring between CBCT images and original plan could be a source of uncertainty in the current study.

The results for the femoral heads were different from both bladder and rectum cases, as the dosimetric difference between planned and delivered doses was minimum (less than 5% for most of the cases). This was expected as the femoral heads on both CT and CBCT images were superimposed for isocenter matching and patient setup before treatment. The observed small differences can be originated from lower quality of CBCT images and differences in femoral head contouring between original CT and CBCT images. However, in one of the cases, a difference of up to 35.7% was recorded, which was attributed to the difference between matching method used for this patient, where bony structure matching was affected by bladder contour matching (Figure 3). The largest variation in bladder mean dose was seen for patient No. 8. In this case, for the second CBCT, a reduction of about 60% in bladder volume resulted in 100% increase in mean dose (Figure 4).

Our results indicated residual geometric inaccuracies in IGRT based on orthogonal

radiographs and CBCT images in our department. This residual geometric misalignment caused dosimetric differences in planned and delivered doses to normal body parts such as the bladder and rectum. Our retrospective verification of CBCT images showed that the volume of the bladder was not constant for all the verified treatment sessions, and variation in bladder volume caused mean dose variations in CBCT plans. It means that the oral administration of water in our department did not guarantee the required bladder volume for all the treatments. Moreover, the matching method between planned geometry and CBCT images before treatment can be an influencing parameter in accuracy of IGRT. In this regard, Hirashima et al. evaluated the impact of prostate matching method in daily pretreatment CBCT on dose distribution in radiation therapy for prostate cancer. Compared to bony structure matching method, they showed that prostate matching provides more improvement in treatment due to better CTV dose coverage and lowering rectal and bladder received doses. [4] In our study, we used bony marks matching for two orthogonal kVp radiographs in correcting the position of patient before treatment and in taking weekly CBCT images. Besides, the extent of treatment volume could be another parameter for rectum dose. As Hille et al. remarked, higher toxicity can be observed in the rectum if seminal vesicles are included in treatment volume. [18] In our study, this effect can be observed between patients 9 and 10. Patient10 had three times more rectum volume increase compared to patient 9; however, rectum mean dose change was 13%, whereas mean dose variation of 2% was seen for patient 10. The reason might be that pelvic lymph nodes were included in the treatment of patient 9, while patient 10 was treated only for prostate region excluding seminal vesicles and pelvic lymph nodes.

## Conclusion

In this study, we emphasized the importance of residual geometric misalignment in pretreatment setup and analyzed its dosimetric consequences in a small group of VMAT-treated prostate cancer patients. Our results showed that changes in bladder and rectum volume alter their received interfractional mean doses. Insufficient filling of the bladder was the main reason of increase in bladder mean dose, and this effect was increased with administered dose to PTV, as well as extension of treatment volume. Our results showed that bladder volume change causes a pronounced effect on its mean dose. However, for the rectum, the mean dose variation with volume was smaller and in some cases negligible. It was shown that bone-matching technique for patient setup using CBCT image was susceptible to considerable geometric inaccuracies and attention to the volume and position of the bladder and rectum is required for more accurate IGRT treatment.

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