Original Article

Assessment of Inter-fraction Target Motion using On-board Imaging System for Prostate Cancer

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Objective: To determine inter-fraction errors from setup and target motion of prostate cancer treated with intensity modulated radiation therapy [IMRT] by using on-board cone beam computed tomography [CBCT].

Materials and Methods: We analyzed retrospective data of on-board CBCT images of 14 prostate cancers over 395 sessions. We performed image matching of CBCT and planning CT, using two methods, prostate soft tissue matching to determine total error (tumor motion and setup error), and bone matching for setup error only. Target motion values were estimated by subtracting setup error from total error. Systematic error of target motion and setup error were calculated from individual mean values.

Results: Inter-fraction errors for target motion were 0.9±0.6 mm (0 to 8 mm), 0.7±0.5 mm (0 to 6 mm), and 0.5±0.3 mm (0 to 6 mm) for vertical [Vrt], longitudinal [Lng], and lateral [Lat] directions, respectively. Inter-fraction of setup errors were 2.7±1.2 mm (0 to 13 mm) for Vrt direction, 2.2±1.0 mm (0 to 8 mm) for Lng, and 2.8±1.6 mm (0 to 14 mm) for Lat.

Conclusion: With bone matching, planning target volume [PTV] margins should be at least 6 mm in all directions. Systematic setup errors are within 3 mm in all directions.

Keywords: Target motion, Setup error, Inter-fraction, Cone-beam CT, Prostate cancer

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Prostate radiation therapy requires a higher dose with narrow margins to spare the surrounding healthy tissue, such as bladder and rectum, with improved tumor control[1]. Intensity modulated radiation therapy [IMRT] and volumetric arc therapy [VMAT] can facilitate delivery of highly conformed dose[2]. Image-guided radiotherapy [IGRT] has been suggested to improve tumor control and is associated with lower late urinary and gastrointestinal toxicities for definitive radiotherapy[3,4].

IGRT for prostate cancer has been used as a standard verification for delivery of external beam radiation treatment due to a more accurate dose delivery to the patient. There are different strategies for IGRT verification used in prostate cancer[5]. One of them is cone beam computed tomography [CBCT] technology, which is a non-invasive verification delivery via on-board volumetric imaging by an on-board imager [OBI]. As a result, CBCT can report inter-fraction error that occurs from both setup error and internal organ motion. As IGRT leads to a more precise treatment, several studies related to IGRT verification in prostate cancer[6-8]. This study aimed to determine the inter-fraction error from setup error and target motion of prostate cancer treated with IMRT using on-board cone beam CT.

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Materials and Methods

Patient data

We analyzed retrospective data from 14 patients with prostate cancer who were treated with

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IMRT technique from November 2008 to May 2011. All patients were simulated and treated in supine position with a foot support device to facilitate setup reproducibility. The patients each ingested 2 glasses of water (500 ml) for full bladder, 30 to 45 minutes before undergoing CT scans and each daily treatment. Each patient's skin was marked to set the position. Planning CT images were taken at 3 mm slice thickness using a helical 16 slice Brilliance Big Bore CT scanner (Philips Medical Systems, Cleveland, OH, USA). Parameters for scanning were 120 kVp, 250 mAs, 512x512 matrix. Contour of the planning target volume [PTV] and organ at risk [OARs] were then delineated by radiation oncologist with Eclipse version 10.0.42 (Varian Medical System) based on the institutional protocol. For each patient, the PTV margin was expanded by adding 8 mm in superior, inferior and lateral directions, and 5 mm in the posterior direction from the clinical target volume [CTV]. The OARs were defined according to the guidelines provided by our institutional protocol. All patients received a total prescribed dose of 70 to 74 Gy, with 2 Gy per fraction for the dose to be delivered at 95% of the PTV using 7 to 9 fields of IMRT. Dose constraints of the OARs were evaluated base on the Radiation Therapy Oncology Group [RTOG] 0415[9] and Quantitative Analyses of Normal Tissue Effects in the Clinic [QUANTEC] protocols[10]. Patients were then treated on Trilogy linear accelerator (Varian, Palo Alto, USA).

Image acquisition

On treatment days, the patients were fixed to the same position and full bladder protocol as the simulation by aligning the skin marks with the laser coordinate system in the treatment room. A volume metric image was acquired using the Varian OBI system version 1.4as CBCT mode in 45x45x16 cm for lateral, vertical and longitudinal FOV directions, respectively. The pelvis protocols (125 kV, 80 mA and 13 ms) and a half-fan bow tie filter mode were used in all scans. The slice thickness of 3 mm and matrix sizes of 512x512 pixels were used for CBCT image reconstruction.

The CBCT images and the planning CT images were performed with two different methods. First, they were manually matched using prostate soft-tissue during the online image registration for total positioning error (tumor motion and setup error), then shifted to apply the couch before treatment delivery. Second, the bony anatomy region of interest around prostate was matched for only setup error in offline review of eclipse treatment planning system (Figure 1).

Statistical analysis

We analyzed 14 patients, who collectively underwent 395 sessions of image matching in total. The setup errors and total errors for each patient were obtained from matching in three directions: anterior-posterior (Vertical: Vrt), cranio-caudal (longitudinal: Lng) and left-right (lateral: Lat). Target motion values were estimated by subtracting the setup error from the total error. Mean error (Σ_i) and standard deviation [SD] of each patient were calculated from the report data. Systematic error (Σ_{pop}) and random error (σ_{pop}) of the total positioning error, setup error, and target motion were calculated. The systematic error of population (Σ_{pop}) was defined by the standard deviation of mean for each patient (Σ_i), whereas the random error of

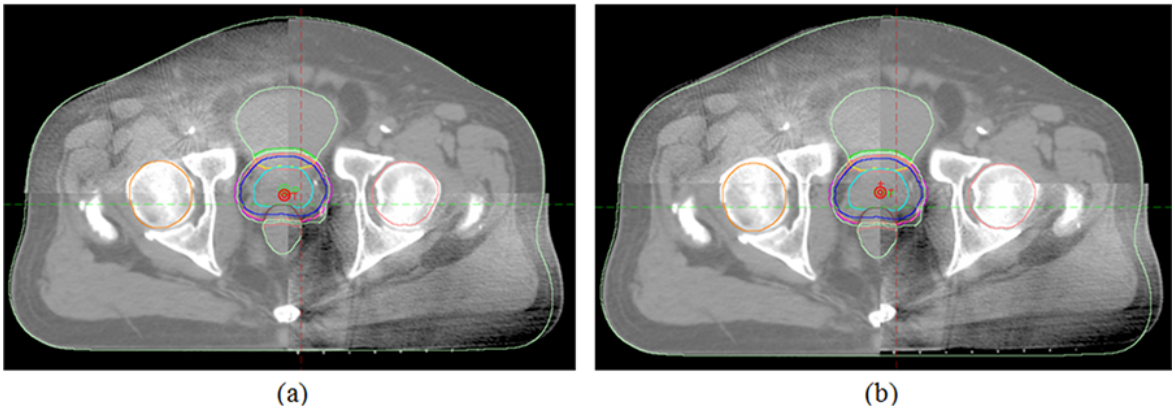

Figure 1. Offline review showing overlaid images for bony anatomy (a) and soft tissue prostate (b) matching between reference and CBCT images.

population was represented by the root mean-square of the SD's of all patients.

We also estimated CTV to PTV margin as $2.50\Sigma_{pop} + 0.7\sigma_{pop}$ to ensure 90% of the patients were covered by 95% of prescribed dose according to the Van Herk's formula[11,12] (Equation 1). Additionally, couch shift percentage was calculated with threshold levels > 5 mm.

Equation 1: $m_{PTV} = 2.5\,\Sigma_{pop} + 0.7\,\sigma_{pop}$

The protocol of this research was reviewed and approved by the Ethics committee for Human Research of Chulabhorn Research Institute (EC No. 20/2554).

Results

In the cohort of 14 patients (with 395 image sessions), mean error of individual and mean error of population (M_{pop}) couch shift, systematic errors (Σ_{pop}), and random errors (σ_{pop}) are shown in Table 1. Deviations in matching are illustrated in Figure 2.

Mean values for all total positioning errors were 3.0±1.1 mm, 1.9±1.1 mm (0 to 9 mm) and 2.8±1.8 mm (0 to 14 mm) for Vrt, Lng and Lat directions, respectively. The mean values for all setup errors were 2.7±1.2 mm (0 to 13 mm) for Vrt, 2.2±1.0 mm (0 to 8 mm) for Lng, and 2.8±1.6 mm (0 to 14 mm) for Lat directions. The mean values for error in target motion were 0.9±0.6 mm (0 to 8 mm), 0.7±0.5 mm (0 to 0.6 mm), and 0.5±0.3 mm (0 to 6 mm) for Vrt, Lng, and Lat directions, respectively.

Table 2 shows the PTV margins of the total positioning error, setup error, and target motion. From Van Herk's formula, the margins of total positioning error were 4.2 mm, 3.9 mm, and 5.8 mm for Vrt, Lng, and Lat directions, respectively.

Figure 3 shows the distributions of the shift range for matching both bony anatomy and prostate soft tissue in vertical (a), longitudinal (b) and lateral (c) direction of all session images.

As a result, the offline bone matching values appeared to be similar pattern to the prostate online

Table 1. Mean couch shift of individual patients, systematic and random errors in total positioning, setup error, and target motion in vertical, longitudinal and lateral directions

Patient number	Mean of individual couch shift (mm)									Number of CBCT
	Vrt			Lng			Lat			
	Prostate	Bone	Target motion	Prostate	Bone motion	Target	Prostate	Bone	Target motion	
1	2.6	2.6	0.0	1.0	1.0	0.0	0.7	0.7	0.0	15
2	3.0	2.0	1.6	2.6	2.6	0.3	3.7	3.5	0.2	34
3	3.7	4.1	1.1	2.7	2.6	0.6		5.4	5.4	0.7
34										
4	2.4	1.0	1.6	3.9	4.2	0.5	3.8	3.6	0.4	38
5	2.9	2.7	1.1	3.6	3.5	0.2	1.3	1.1	0.5	37
6	2.6	2.6	0.1	1.3	1.3	0.0	1.8	1.8	0.0	33
7	1.7	1.6	0.1	1.9	1.8	0.2		1.4	1.5	0.4
11										
8	4.1	3.9	0.3	3.6	3.3	0.8	1.3	1.6	0.9	13
9	1.8	2.1	0.4	1.1	1.2	1.7	2.4	2.1	0.3	15
10	3.2	2.4	0.2	1.3	2.0	1.6	1.7	1.9	0.6	36
11	1.9	2.1	1.4	1.1	2.0	1.1	3.6	4.1	0.8	34
12	4.9	4.1	1.0	1.7	2.7	1.3	7.2	6.3	1.2	37
13	1.8	1.7	0.6	0.6	1.2	0.7	3.1	3.0	0.6	29
14	5.2	5.1	0.8	0.8	1.2	0.8	1.8	2.2	0.5	29
≤5 mm (%)	88.9	85.1	98.0	93.4	94.9	99.5	85.6	84.3	99.5	395
>5 mm (%)	11.1	14.9	2.0	6.6	5.1	0.5	14.1	15.7	0.5	
>8 mm (%)	0.8	2.2	0.7	0.0	0.3	0.0	4.1	4.8	0.0	
M_{pop}	3.0	2.7	0.9	1.9	2.2	0.7	2.8	2.8	0.5	
Σ_{pop}	1.1	1.2	0.6	1.1	1.0	0.5	1.8	1.6	0.3	
σ_{pop}	2.0	1.7	1.3	1.5	1.6	0.9	1.8	1.8	0.7	

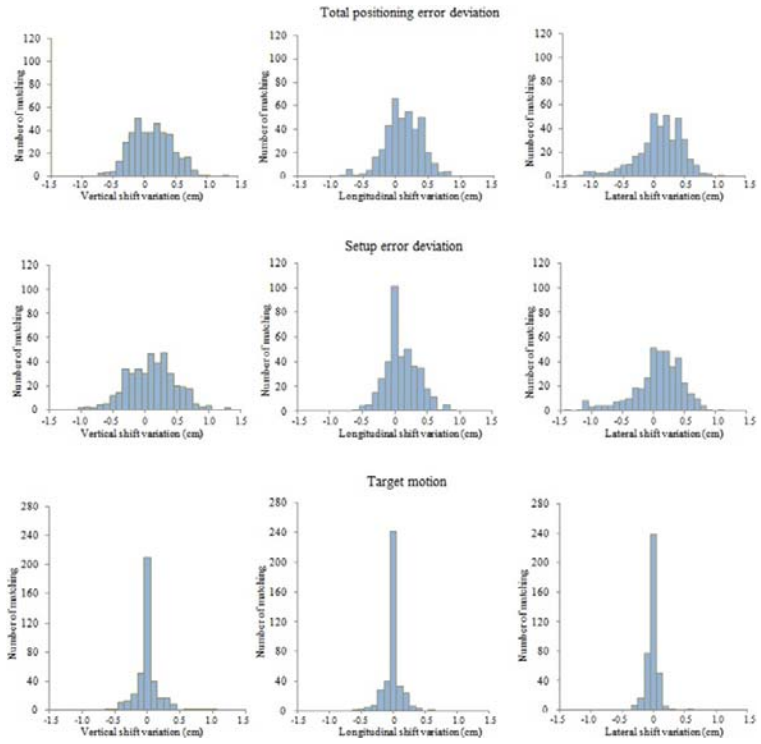

Figure 2. The deviations of the total positioning error, setup error, and target motion representing the corresponding Gaussian distribution.

Table 2. PTV margin for the total positioning, setup error and target motion

Margin	Vrt (mm)	Lng (mm)	Lat (mm)
Total positioning error	4.2	3.9	5.8
Setup error	4.1	3.6	5.3
Target motion	2.5	2.0	1.3

matching in all directions. The shift values of bone matching within 0.5 cm were 85.1%, 94.9%, and 84.3%, which corresponds to the shift values of prostate matching of 88.9%, 93.4%, and 85.6% in Vrt, Lng, and Lat directions, respectively. In Lat direction, the shift show large deviation in image session No. 301 to 338 (patient No. 12).

Discussion

The couch shift error of bony anatomy and soft tissue matching were good and acceptable within 8 mm by our institutional margin protocol. The small variation in the error found in Lng direction, which is related to prostate, rarely moves in craniocaudal direction. For lateral direction, we found that patient No. 12 had the shift values higher than 8 mm. The cause for this may be that the patient had the fatty skin that made more errors from the skin marker for setup positioning inconsistencies with the internal organs.

There are good agreements of shift deviations greater than 5 and 10 mm in our study with Volker et al[13] on average of 0.5 to 14.7% and 0 to 4%, respectively. The systematic error in this observation was in agreement with McNair et al[14] which used fiducial marker. In case of not using IGRT, a posterior direction should be careful and may add the PTV margin more than 5 mm. Based on our results, we recommend the PTV margin be within 6 mm in all directions for inter-fraction motion in prostate cancer. That includes both setup error and target motion by soft tissue matching using CBCT images. Additionally, institutional full bladder protocol may reduce the movement of cancerous tumors in anterior-posterior direction.

The present study has some limitations. First, it had a small sample size of 14 patients; however, our

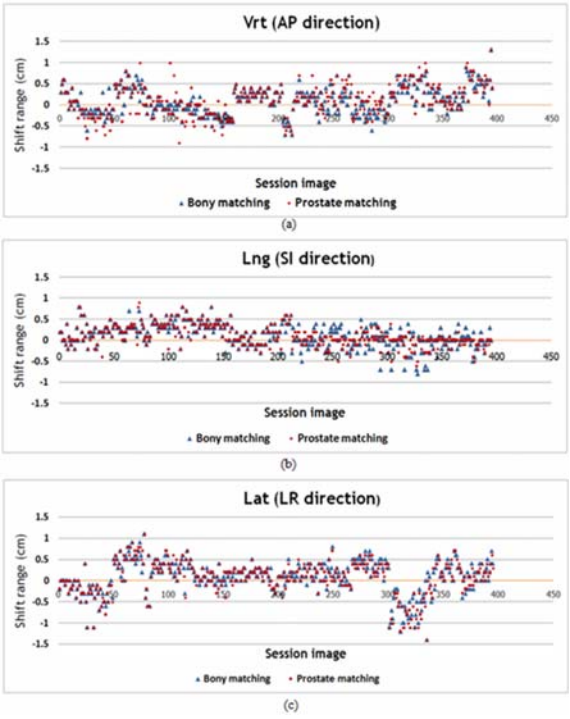

Figure 3. Distribution plots of the shift range in both bony anatomy and soft tissue prostate in vertical (a), longitudinal (b) and lateral (c) direction of all session's image.

data came from many image sessions from this group of patients. Second, intra-fraction error that occurred between treatment deliveries was not included in this study. Third, strategies for IGRT verification that used soft tissue matching by CBCT without implanted fiducial markers are a non-invasive procedure. Nevertheless, CBCT has inferior image quality compared with planning CT. Therefore, it is difficult to confine the prostate boundary from other soft tissues because it has similar CT numbers as muscle, rectum, and bladder wall. For this reason, it requires an experienced operator to match the soft tissue images rather than the bone matching.

Conclusion

The total systematic errors were within 5 mm in all directions. However, PTV margin of 4 to 6 mm is still needed to correct inter-fraction motion. From our study, the set-up error component was larger than the internal organ component. Although using image comparison with bone matching can reduce the PTV margins, the margins need to be compensated for intra-fraction organ motion with CBCT images.

What is already known on this topic?

In radiotherapy of prostate cancer, IGRT verification has widely been studied. Most techniques involved invasive strategies such as fiducial implantation. Although the international standards for radiation units & measurement [ICRU] guideline exist for PTV margin. The variation of PTV margin depends on positioning, immobilization, systematic error, target motion and modality of verification.

What this study adds?

This study adds information that can improve PTV margin and also create an imaging protocol to verify positioning before treatment of prostate cancer patients.

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Potential conflicts of Interest

The authors declare no conflict of interest.

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