Planning Target Volume (PTV) Margin Determination from Marker-Based Setup and The ExacTrac 6D X-ray IGRT System in Prostate Cancer Patients

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ABSTRACT

Background: In radiation therapy, setup uncertainty of patients affect the expected treatment outcome and the addition of PTV margin is able to improve treatment accuracy.

Objective: To evaluate setup variations and calculated optimal PTV margins for prostate VMAT setup using the ExacTrac image guided system with implanted fiducial marker registration and cone beam computed tomography.

Materials and methods: A total number of 923 x-ray pair images and 271 CBCT images from 28 prostate VMAT patients treated with TrueBeamSTx were observed. By daily online localization, the corrections determined from initial laser setup, from the ExacTrac image system, and from CBCT were accumulated. Positioning differences based on fiducial markers registration between Digitally Reconstructed Radiography (DRR) images with the ExacTrac system and internal anatomy matching from CBCT were measured in right-left (RL), supero-inferior (SI) and antero-posterior (AP) directions. The systematic (Σ) and random (σ) errors were calculated and determined PTV margin using van Herk margin formula ($2.5\Sigma + 0.7\sigma$).

Results: The setup uncertainty from laser alignment was 2.65±2.66 mm, 2.96±2.65 mm and 4.83±4.89 mm in right-left (RL), supero-inferior (SI) and antero-posterior (AP) direction, respectively. With marker registration, these uncertainties were reduced to be 0.64±0.77, 0.81±0.95, and 0.90±1.32 mm and the residual error, when rechecked with soft tissue matching from CBCT, was still be 0.65±1.64, 0.80±1.99 and 0.90±2.01 mm in RL, SI and AP directions, respectively. The PTV margins based on implanted markers and ExacTrac daily online correction were calculated to be 1.46, 1.86 and 2.11 mm. in RL, SI and AP directions, respectively.

Conclusion: Frequent CBCT imaging verification presented a limitation in patient dose. Using the ExacTrac x-ray system together with fiducial markers was found to be effective tool for daily setup verification. However, the optimal PTV margin was strongly suggested to assess from both the inter and intrafractional setup deviations.

Keywords: Fiducial marker, Prostate cancer, PTV margin, Systemic error, VMAT

INTRODUCTION

Radiation therapy (RT) aims to deliver a radiation dose to the tumor which is high enough to kill all tumor cells while limiting the radiation received by the normal tissue that surrounds the tumor. Prostate tumor is the most commonly diagnosed male cancer worldwide. Radiation therapy has been shown to allow for good local control and very few side effects with the use of higher radiation doses. With the development of more sophisticated treatment planning software and multileaf collimators, intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) emerged as an advanced form of shaped-field technique. Radiation dose conformity in radiation therapy requires steep dose gradients between planning target volume (PTV) and adjacent organs which indicates some risk for overdosing or underdosing structures in this border region. Thus evaluating the uncertainties related to patient setup is of great interest in defining the optimal Clinical Target Volume (CTV)-PTV margins. As we obtain steep dose gradients with IMRT or VMAT, more delicate image guidance devices is needed to prevent marginal misses and unintentional hot spots in critical organs. There are various image-guided radiation therapy (IGRT) options to correct daily setup uncertain¬ties and the positional variation of the prostate. Patient setup error can be defined as the difference between the actual and the planned position of the patient with respect to the treatment beams during irradiation. To ensure the radiation beam was delivered to the treatment target accurately, it is very important that RT center should assess their setup accuracy.

The IGRT options include kilovoltage (kV) or megavoltage (MV) portal imaging(1), ultrasound(2), in-room computed tomography(3) (CT), various MV and kV cone-beam CT(4) (CBCT) techniques, the ExacTrac system(5) (BrainLAB, Feldkirchen, Germany), and most recently, electromagnetic transponders(6). Currently, there is growing interest in the use of intra-prostate fiducial markers to serve as a surrogate of prostate position. With two-dimensional and three-dimensional image systems, the fiducial-based image guidance has become an effective technique for patient positioning and repositioning. At the present, there was limitation about the investigation of setup error using the ExacTrac x-ray system for prostate VMAT treatment with fiducial markers implanted.

The aim of this study was to investigate of the optimal PTV margin for prostate planning by using the implanted fiducial markers and the ExacTrac stereoscopic kV-imaging system to determine the systematic and random setup uncertainties from prostate cancer patients treated with VMAT technique at the Division of Radiation Oncology, Department of Radiology, Faculty of Medicine Siriraj hospital, Mahidol University.

METHODS AND MATERIALS

Patient Selection

A total number of 28 prostate cancer patients treated with TrueBeam STx linear accelerator were retrospectively studied. Two weeks before the CT simulation, all patients were implanted with 3 fiducial markers in the prostate gland with the guidance of trans-rectal ultrasound. To obtain the 3D dataset for planning, imaging protocol for all patients were given bowel preparative regimen by laxative drugs a few days before CT simulation and day of scanning, all patients drank 600cc of water and recording of full bladder time to control volume of bladder during CT scanning. CT images of each patient from third lumbar spine (L3) down to mid of thigh in 3mm slice thickness was taken in the supine position with knee support immobilization device using Philips BigBore CT scanner (Philips Medical Systems, Cleveland, OH). All scanning images were exported to the Eclipse treatment planning system (Varian Medical System, Palo Alto, CA) for the organ contouring. The structure of prostate gland, seminal vesicles, pelvic lymph node, bladder, rectum, bilateral femoral head and penile bulb in each patient were delineated by responsible physician.

The inverse VMAT planning consisted of 2-3 arcs with 10 MV, 600 MU/min dose rate was generated. Dose optimization and calculation were performed with the Eclipse treatment planning system version 10 with AAA dose calculation algorithm. All patients were treated with Varian TrueBeam STx linear accelerator. The machine is equipped with HD120 MLC that consists of total 60 leaf pairs, 32 leaf pairs of 2.5 mm at central leaves and 28 leaf pairs of 5 mm. at outer leaves. The IGRT is an integrated system between CBCT from On Board Imager (OBI) system and the ExacTrac stereoscopic x-ray system which composed of two infrared cameras for patient positioning, two pairs of KV x-ray sources and detectors for target localization. Both of systems were used for pre-treatment image verification of the patients. At our institution, imaging verification protocol in prostate cancer, started by using in-room laser for initial setup of patient positioning. Then, imaging a patient on treatment couch was undertaken with a radiographic kV x-ray imaging to correct the patient positioning for laser setting up. Positioning deviation was obtained by registration and fusion the implanted fiducial markers seen on the stereoscopic x-ray pair images with the Digital Reconstructed Radiography (DRR) reference images from the planning CT. The information of six-dimensional (6D) positioning deviation allowed the radiation therapists to readjust of patient positioning using 6D couch movement and a second pair of stereoscopic x-ray image was performed to recheck the positioning accuracy. Finally, before the irradiation beam on, the CBCT imaging from on board imager was used to verify the patient positioning again by based on soft tissue contrast.[5] Our IGRT protocol for prostate cancer was daily pre-treatment stereoscopic x-ray pair images for every fraction. CBCT imaging in the first three fractions and weekly was performed to recheck up the accuracy after the x-ray radiograph verification.

Calculation of PTV margins

To determine the PTV margin, treatment preparation (systematic) error and treatment execution (random) error have been evaluated using the x-ray pair images from patients. PTV margin in this study was determined according to the formula proposed by Van Herk et al.(7,8) This margin was provided with a concept that a minimum 95% of prescription dose must cover the CTV with 90% of the patient population and can be calculated from the equation, $2.5\Sigma + 0.7\sigma$. Where, Σ is the treatment preparation (systematic) error and σ is the treatment execution (random) error. The systematic error was calculated from the standard deviation of mean set up error for individual patient and the random error was defined by computing the root mean square of the standard deviation in each individual patient.

RESULTS

Interfractional prostate motion

Table 1. summarizes translational variation in mm. for prostate cancer patients. On 28 patients, the total number of acquired x-ray pairs was 923 images and 271 OBI CBCT images. The mean±standard deviation (SD) of interfractional movement assessed from laser alignment setting up was 2.65±2.66 mm in right-left (RL), 2.96±2.65 mm in supero-inferior (SI), and 4.83±4.89 mm in antero-posterior (AP). Based on a pair of planar stereoscopic x-ray images and the fiducial markers, the displacement was reduced to be 0.64±0.77 mm in RL, 0.81±0.95 mm in SI, and 0.90±1.32 mm in AP. Using the anatomical matching with CBCT, the residual setup error was found to be 0.65±1.64 mm in RL, 0.80±1.99 mm in SI and 0.90±2.01 mm in AP respectively. It was observed that the higher deviation was most likely in AP direction.

Table 1. Interfractional setup variations for prostate cancer patients in different setting-up technique.

Technique	Mean (mm)			SD (mm)		
	RL	SI	AP	RL	SI	AP
Laser setup	2.65	2.96	4.83	2.66	2.65	4.89
Marker	0.64	0.81	0.90	0.77	0.95	1.32
Soft tissue	0.65	0.80	0.90	1.64	1.99	2.01

Notes: RL = right-left, SI = supero-inferior and AP = antero-posterior

Determination of PTV margins

According to Van Herk's formula, PTV margin in different setting-up techniques was determined and presented in Table 2. With laser setting-up, the calculated margins in RL, SI and AP direction was 6.19, 8.08 and 13.79 mm, respectively. If based on the fiducial markers, the PTV margins was reduced to be 1.46, 1.86 and 2.11 mm in the RL, SI and AP directions, respectively. Lastly, setup uncertainty assessed from CBCT images provided the PTV margins to be 3.73, 3.22 and 4.70 mm in the RL, SI and AP directions, respectively. The higher setup deviation was detected in the AP direction. This data resulted in the larger margin in AP direction when compared to the other directions.

DISCUSSION

Setup uncertainty assessed from 3 methods in this study clearly showed that the laser alignment technique provided the highest setup deviation when compared to the others. This is from a fact that laser setup was based on 3 points of intersection on patient's skin which cannot be related to the movable internal organ motion such as prostate gland. For fiducial marker matching, the detection of setup variations was reduced due to the marker seeds was able to track the prostate volume more precisely. About the problem of migration, it was proven by Poggi et al.[9] that the overall migration of all seeds was less than 1 mm.

However, using the ExacTrac system with fiducial marker, the technique provided only 2D x-ray projections and the optimal seed position in prostate gland is highly needed in this technique. Thus, the volumetric soft tissue registration of anatomical organ which was provided from CBCT should be more effective to recheck the setup error which obtained from the marker matching technique only. The results from CBCT presented the similar mean or systematic setup error, while the standard deviation or random error showed a slightly higher in soft tissue matching when compared to marker technique.

Table 2. PTV margin for (assessed from interfraction setup error only) based on laser setup, markers and soft tissue registration.

Technique	PTV margin (mm)		
	RL	SI	AP
Laser setup	6.19	8.08	13.79
Marker	1.46	1.86	2.11
Soft tissue	3.73	3.22	4.70

Notes: PTV = planning target volume, RL = right-left, SI = supero-inferior and AP = antero-posterior

Comparison with other studies which also used the ExacTrac system to define setup uncertainty and margins in prostate cancer. There were studies from Alonso-Arrizabalaga et al.[10] ,Kim et al.[11]and Chi et al.[12]with their results and registration technique were presented and compared with our findings as shown in Table 3. It can be seen that our result was shown in the same direction when compared to the other studies. However, a higher setup deviation in the RL direction was observed, and this may be from our prostate cancer patients in this study including the low risk, intermediate risk and also a high risk that consist of pelvic lymph node, and this might be a cause of increase lateral deviation in this study.

About the PTV margin determined from the marker technique, our results were shown approximately at 2 mm. margin for all directions while margin from the study of Alonso-Arrizabalaga et al. presented in the range of 4.4-6.6 mm. as shown in Table 4. The difference in PTV margin should be the result of different image verification protocol. In our center, patients were performed with online daily imaging verification, while margin was calculated based on offline protocol using the ExacTrac x-ray images in first five fractions in the study of Alonso-Arrizabalaga et al.

Table 3. Interfractional setup uncertainty assessed from ExacTrac system and registration techniques in various studies.

Study	Registration method	Setup uncertainty (mm)		
		RL	SI	AP
Alonso-Arrizabalaga et al[10]	markers	0.00±1.20	-0.60±1.70	-0.20±2.00
Kim et al.[11]	bone	-0.20±0.30	0.60±2.00	-0.80±1.80
Chi et al.[12]	markers	0.20±2.21	-1.09±2.21	0.93±2.70
Our results	markers	0.64±0.77	0.81±0.95	0.90±1.32

Notes: RL = right-left, SI = supero-inferior and AP = antero-posterior

Table 4. Comparison of interfractional PTV margin in prostate cancer using the ExacTrac system studies.

Study	PTV margin (mm)		
	RL	SI	AP
Alonso-Arrizabalaga et al.(10)	4.40	5.90	6.60
Our results	1.46	1.86	2.11

Notes: PTV = planning target volume, RL = right-left, SI = supero-inferior and AP = antero-posterior

Limitation of this study was the calculated PTV margins were based on population systematic error and random error which analyzed from the interfractional data only. Typically, PTV margin should be computed from both of the inter and intrafractional motion. There was a suggestion, even the setup error, mainly found in the interfraction treatment. However, the intrafraction deviation, especially for the prostate cancer[13], should be investigated and will be applied in further study.

CONCLUSION

The ExacTrac x-ray system together with fiducial markers was found to be effective tool for setup verification. However, to determine the optimal PTV margin, the setup deviations should be assessed from both the inter and intrafractional data. In addition, with an appropriate imaging protocol, more detail of 3D anatomical data from CBCT was also an effective method to improve treatment accuracy.

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