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Assessment of three-Dimentional setup error in image-guided radiotherapy for prostate cancer using Kilovoltage cone-beam computed tomography and its effect on planning target volume margins

Abhilasha[1], Nidhi Patni[2], Tejparkash Soni[3], Amrita Rakesh[4*], Sweta soni[5], Dinesh K Singh[6], Naresh Jakhotia[7]
[1] DNB Radiation Oncology, Senior Resident-Department of Radiation Oncology, SMS Medical College, Jaipur, Rajasthan, India
[2, 3, 6, 7] Department of Radiation Oncology, Bhagwan Mahaveer Cancer Hospital & Research Hospital, Jaipur, Rajasthan, India
[4] DNB Radiation Oncology, Senior Resident Department of Radiation Oncology, AIIMS Patna, Bihar, India
[5] DNB Radiation Oncology, Senior Resident Department of Radiation Oncology, AIIMS, Jodhpur, Rajasthan, India

Abstract
Purpose: To achieve the best possible therapeutic ratio using image-guided radiation therapy (IGRT) of external beam radiation therapy in prostate cancer patients using kilo voltage cone-beam computed tomography (Kv-CBCT).
Materials and methods: Thirty patients of carcinoma prostate who were treated with IGRT were included in the study. CBCT was done twice a week in IGRT. These images were registered with the planning CT scan images and translational error were applied and recorded and all 420 CBCT images were studied. The margins of planning target volume were calculated from the variation in setup.
Results: The setup variation was 4.48, 5.18 and 8.03 mm in anteroposterior, mediolateral and superoinferior direction. This allowed adequate dose delivery to the clinical target volume and sparing of organ at risks.
Conclusion: Kv-CBCT is a satisfactory method to accurate patient positioning in treating prostate cancers with high precision technique.

Keywords: Prostate cancer, image-guided radiation therapy (IGRT), Kilovoltage cone-beam computed tomography (Kv-CBCT), setup errors

Introduction

Prostate cancer is the second most common cause of cancer and the sixth leading cause of cancer death among men worldwide with an estimated 899000 new cases and 2,58000 new death in 2008 [1]. However, the patient setup position and anatomy changes daily, particularly in the prostate region, due to rectum and bladder filling. Intensity-modulated radiotherapy (IMRT) for prostate cancer has facilitated the delivery of high radiation doses to the prostate and is associated with excellent biochemical tumor control outcomes for patients with localized disease [2]. It has been well reported that interfraction prostate deformation is common during the course of prostate RT owing to daily bladder and/or rectal filling. The high mobility of the bladder and the rectum causes uncertainty in radiation doses prescribed to patients with prostate cancer who undergo radiotherapy (RT) multifraction treatments [3]. To ensure an adequate coverage CTV, internal organ motion needs to be considered.

The planning target volume (PTV) includes margins for uncertainities in shape and motion of organs, beam geometry, and patient setup [4]. Setup errors though undesirable, Are inherent part of radiation treatment process and are defined as a difference the difference between actual and intended position with respect to radiation delivery [5].

For high therapeutic ratio, setup margins should be reduced to prevent irradiation of adjacent normal tissues. The source of these errors is (a) patient related (skin mark movement) (b) fixation related (patient mobility) (c) mechanical (laser misalignment) (d) experience and competence of treating staff (e) time available with radiotherapy staff. (4) These errors alone or in combination may result in compromised therapeutic ratio.

The goal of this study is to objectively describe the setup error during fractionated external beam radiotherapy for prostate cancers.

Aim

To assess three dimensional setup error in image-guided pelvic radiotherapy for prostate cancer using kilovoltage cone-beam computed tomography (kV-CBCT) and its effect on PTV margins.

Primary objectives

Assessment of systematic errors, random errors, and three-dimentional CTV-PTV margins derived from shifts after 3D-3D matching.

Materials and Methods

This study was prospective observational study conducted in 30 patients of prostate cancer (420 kV-CBCT) from October 2015 to June 2017 in department of Radiation Oncology of Bhagwan Mahaveer Cancer Hospital & Research Hospital, Jaipur.

Inclusion criteria

1. Patients with histology proven carcinoma prostate in whom radical radiation therapy to pelvis indicated.
2. Patients in whom IGRT was delivered.

Immobilization and simulation

Patients were simulated with a comfortably full bladder. According to protocol all the patients were instructed to empty bladder 60 minutes before simulation and then were asked to drink 3 cups (750ml) of liquid during the subsequent 15 minutes, finishing 45 minutes before simulation. They were also advised to take laxative and charcoal tablets on previous night for bowel preparation. Patients were counselled to follow the same practice before each fraction of radiation therapy. Patients were immobilised comfortably in supine position using 4 clamp customized thermoplastic mask of pelvis. External fiducial markers were placed over thermoplastic mask in pelvic region.

Then planning NCCT and CECT scan images were taken using Philips Big Bore CT (64 slice) scanner from the level of L2-L3 to mid thigh with 3 mm cuts in the axial plane. After image acquisition, the data was sent through DICOM (Digital Imaging and Communication in Medicine) format to Eclipse Treatment Planning System (version 10) through local area network (LAN). Then NCCN and CECT images were fused with the inbuilt software in Eclipse Treatment Planning System. Targets were contoured by single radiation oncologist using RTOG guideline as basis.

IMRT plan were generated using 7-9 beams or two full arcs for VMAT treatment. The optimum treatment plan was transferred to ARIA for implementation after doing the required quality assurance (QA) tests.

On board imaging and evaluation

Cone- beam computed tomography acquisition

CBCT scan parameters were 125kVpa and 80 mAs, representing a balance between image quality, patient dose (17.7 mGy), and tube overheating. The device operates in half-fan mode with a half-bowtie filter to reduce scatter and adequately cover patient geometry. The gantry rotation range is 360o , exposure 680mAs, and 2.6 CTDIw (mGy/100 mAs). The images were taken with 655 projections. The typical length of CBCT scan was 15cm in superoinferior (SI) direction and field of view 45 cm.

All patients underwent CT-based RT planning. Then, kV-CBCT was done twice in a week in IMRT, daily in IGRT/VMAT. The setup error was calculated by registration of planning CT with the current CBCT using the bony anatomy. A patient specific alignment box confined the volume for automatic match of the bony anatomy; inside this volume was used as a surrogate for the actual tumor position. After registration, translational errors were recorded. Rotational errors were not recorded. All the translational errors evaluated in this study were determined from the automatic bone match. All translational shifts were applied and recorded in centimetres.

For the purpose of analysis anterior, superior and right-sided shifts were coded as positive shifts and posterior, inferior and left sided shifts as negative shifts. Some of the potential source of errors as laser alignment, display accuracy, and jaw reproducibility were not taken into consideration for the final match results. It was assumed that routine periodic QA employed for the linear accelerator would ensure minimal impact of the aforesaid on daily setup.

Systematic and Random Error

Systematic and random errors were calculated as per conventionally defined norms [6, 7]. The systematic component of the displacement represents displacement that was present during the entire course of treatment. The random error represents day-to-day variation in the setup of the patient.

Mean of individual patient along the respective axes → $\sum_{ind}$ (systemic error [SE] of individual patient).

SD of the mean of each patient → $\sum_{pop}$ (SE of population).

SD of the individual patient along respective axes→ σ_{ind} (Random error [RE] of individual patient).

Root mean square of the random error of each patient (SD)→ σ_{pop} (Random error of population) [8].

Error were calculated separately for all three axes x-axis (left to right),y-axis (SI),and z-axis(anteroposterior; AP).

Using this data, PTV margins were obtained for respective axes (lateral, longitudinal, and vertical) by Van Herk's margin recipe formula

$(2.5 \sum_{pop} + 0.7 \sigma_{pop})$ [9, 10].

Statistical analysis

Data was entered in Microsoft Excel® to prepare Master Chart and was subjected for statistical analysis. Continuous variables were summarized as mean and standard deviation and were analyzed by unpaired 't' test. Nominal or categorical variables were expressed as proportion (%).

The SE of individual patient on particular axis was calculated by arithmetic mean of shifts on particular axes for total days of radiation received by particular patient. The random error of individual patient on particular axis was calculated by SD of shifts on particular axes for total days of radiation. SE of population (Σ_{pop}) was found out by calculation of arithmetic mean of SE of individual patient (Σ_{ind}) while random error of population was calculated as SD of random error of individual patient (σ_{ind}).All statistical calculations were done using Med Calc version 12.2.1.0 software (MedCalc software, Acacialaan 22, B-8400 Ostend , Belgium).

Results

The population systematic error found 1.4, 2.4, and 1.4 mm in AP, SI and RL direction respectively. The population random error ($\sum_{pop}$) in AP, SI and RL was 1.4,2.9, and 2.4 mm respectively. The corresponding CTV-PTV margin calculated by van Herks formulae in AP, SI and RL direction were 4.48mm, 8.03mm, and 5.18 mm respectively.

Discussion

Accounting accurately for daily uncertainties in target positioning is an important goal in treating prostate cancer. Uncertainties can arise due to setup variation caused by both, interfraction and intrafraction motion, former being the greater of two components. All these uncertainties can results in compromised local tumor control rate and an increased risk of side effects. IGRT enhance the precision of patient positioning, allowing for improved sparing for normal tissue through a reduction in treatment margin. Using tight margins, however, require technique to ensure precise target localization.

In present study we calculated patient setup errors (translational shifts) using kV CBCT before delivering treatment fraction. Rotational errors were not recorded. For adequate volume coverage, while increasing organ at risk sparing, individualized a wide range of different margin of PTV (M_{PTV}) were calculated.

In recent study done by Patni *et al.* [5] M_{PTV} obtained from initial inter fraction error were 5.8, 10.3, 5.6 mm along AP, SI and ML direction in gynaecological malignancy. Another study done by Yao L *et al.* [11] calculated margin of 5.6 , 8.3 and 7.6 mm along AP , SI and ML direction in gynaecological malignancy. Lauren *et al.* [10] calculated margins of 11.6 AP, 8.2 SI, 9.6 mm ML respectively in gynaecological malignancy.

Perez-Romasanta LA *et al.* [12] M_{PTV} obtained 9-10.5 mm (X), 15.2-17.8 mm (Y) , and 10.6-12.4 (Z) direction in prostate malignancy with conventional conformal radiotherapy.

McNair HA *et al.* [13] obtained systematic error in RL, SI, and AP direction 1.3, 1.9 and 2.5 mm and random error 2.2, 2.2, 3.1 mm respectively. They found PTV margin 4.7, 6.3 and 8.4mm in RL, SI, and AP direction respectively.

Jeong *et al.* [14] obtained systematic error 2.21± 3.42, -0.67± 2.27,and 1.05± 2.28 in RL, AP and SI direction respectively, random error 1.95± 1.60, 1.02± 0.50 and 1.01± 0.48 mm in RL, AP and SI direction respectively. They found PTV margin 8.20, 5.25, and 6.45 mm in RL, AP and SI direction respectively.

In our study systematic error found 1.4, 2.4, and 1.4 mm in AP, SI and RL direction respectively. The corresponding CTV-PTV margin derived in our study were 4.48mm, 8.03mm and 5.18 mm in AP, SI and RL direction respectively. The systematic and random errors yielded asymmetric margins for the CTV-PTV for prostate malignancy patients treated by IGRT using kV-CBCT. Our results suggested larger setup errors in longitudinal (SI) direction (8.03 mm).

In due course of time from 2015 to 2018 in our institution, patient treatment with orfit had changed to skin marking. This reduced the mean shifts in all three directions.

Mean, Standard deviation, (Σ_{pop}) & (σ_{pop}) in respective axes (anteroposterior, superoinferior, & right-left)

Table 1

	Mean	SD	Min	Max	SE of population (Σpop)	Random error of population (σpop)
Vertical	-0.07	0.14	-1.2	0.4	0.14	0.14
Longitudinal	-0.01	0.24	-1.1	1.4	0.24	0.29
Lateral	-0.05	0.14	-1	2.4	0.14	0.24

Daily kV-CBCT is a satisfactory method of accurate patient positioning in treating prostate cancers with high precision techniques. This resulted in avoiding geographic miss. One could use the available daily imaging techniques for patient setup and retrospective use the setup error to estimate site-specific margins. Establishing online correction protocols could help in improving treatment positioning accuracy.

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