ORIGINAL ARTICLE

Isocentre shift during radiotherapy to the prostate in overweight and obese patients

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Abstract

Background: The ability to escalate the dose to the prostate without causing normal tissue complications (e.g., rectal bleeding) may be compromised by a variety of geometric uncertainties including true target definition, inter- and intrafractional patient motion, and daily setup error. Organ motion and patient setup variation are two major concerns during radiation delivery for prostate cancer because they lead to shift of the target from its reference frame in the treatment-planning CT. Depending on the treatment margins, uncorrected target shifts may lead to under-dosage of the prostate, thus decreasing local tumor control, or over-dosage the rectum, thus increasing rectal complications. Understanding the interfractional target shifts due to interfractional target motion and daily setup error and their management becomes a critical issue for prostate cancer radiotherapy. Image-guided radiotherapy is used for correcting interfractional organ shifts before radiation delivery with image guidance.

Purpose: To confirm the accuracy of the location of the skin markings in relation to the actual isocentre of the irradiated volume in overweight and obese patients.

Materials/Methods: In this study, radio-opaque markers are placed on the patient's anterior and lateral skin marks to define the central axis plane of the prostate gland; the planning isocenter can be triangulated from the three positions. CT studies of 10 high risk locally advanced prostate cancer patients are transferred to planning system. The target volume, rectum, and bladder are contoured. Whole pelvis irradiation is carried out using box technique. The dose of whole pelvis irradiation was 45Gy in 25 fractions to the isocenter.

Then after its delivery the patient is prepared for the CT scan of the boost dose delivery. The dose of 10Gy in 5 fractions to the prostate and seminal vesicle was prescribed also to the isocenter which is placed at the center of the prostate. Then 2400 cGy are delivered in 12 fractions to the prostate (CTV).

The patient is set up in the treatment position, and the radio-opaque markers are again placed on the anterior and lateral skin marks that are assumed to best define the axial plane of the prostate gland containing the planning isocenter. Then the distance between the initial planning isocenter and the boost isocenter (target shift) is calculated for three axes. All patients gave informed consent that we can study their computerized plan and do research on it.

Statistical analysis: The isocentre position was listed for each patient in the three axes for whole pelvis plan and the boost plan. Then target shift between the two isocentres in the x, y and z directions for all patients was calculated and listed. The minimum, maximum and average shift for each patient were calculated using excel sheet**.** To check if there is any correlation between target shifts in x & z axes and body weight a simple correlation test was done. The R-value is taken as an indicator for the correlation. A *P* value of less than 0.05 is taken to indicate whether the correlation is significant or not.

Results: 10 patients included in this study, their weight ranges from 88-130kg (the average is 101.7 before whole pelvis treatment and 104.8kg before boost). The calculated minimum shift was -2.33cm & -0.93cm, the maximum shift was 2.77cm & 1.05cm and the average was -0.31cm & 0.39cm in lateral direction (x) and superior inferior direction (z) respectively. So the minimum and maximum shifts in x axis are larger than that for z axis. There was a weak positive correlation between target shift and body weight in x axis (R value= 0.39) but this correlation was not statistically significant (P=0.15). On the other hand there was not any correlation between target shift and body weight in z axis (R value= 0.009).

Conclusion: Correction of the target shift is mandatory with 3DCRT in overweight and obese patients using IGRT otherwise a generous non-uniform treatment margin is required in the lateral direction compared to that commonly used. This may result in either local control failure or high dose to the rectum with sever rectal complications.

Introduction

Margins around clinical target volume (CTV) to create planning target volume (PTV) play an important role in radiotherapy. This is to ensure that all parts of the CTV received the prescribed dose. These margins include internal and set-up margins. Internal margin (IM) takes into account the expected physiological movements and change in the size, shape, and the position of the CTV in relation to an internal reference point and its corresponding coordinate system. Filling of rectum and bladder is an example for target movement in prostate cancer. [(1)]

The set-up margin (SM) considers any beam size variation and set-up inaccuracy due to misalignment of the therapeutic beams during treatment planning and beam delivery (e.g., misalignment of the skin markers and in room lasers). [(2-4)]

Organ motion and patient setup variation are two major concerns during radiation delivery for prostate cancer because they lead to shift of the target from its reference frame in the treatment-planning CT [(3)]. So accurate and reproducible patient setup is a pre-requisite for radiotherapy in order to limit the margin around the clinical target volume (CTV) to form PTV, and consequently minimize irradiation of healthy tissues responsible for early and late side effects. This margin depends not only on the interfractional prostate shift but also on different treatment techniques, such as three-dimensional conformal radiotherapy, IMRT, or image guided radiotherapy (IGRT).[10]

Uncorrected target shift may lead to under-dosage of the prostate, thus decreasing local tumor control, or over-dosage of the rectum, thus increasing rectal complications. This will also limit dose escalation to the prostate. [5-7] So understanding and correction of the interfractional target shifts becomes a critical issue for prostate cancer radiotherapy. [8,9, 10]

IGRT modalities include CT scanner, megavoltage and kilovoltage cone beam CT. With IGRT the treatment margin will be small because the interfractional target shifts can be corrected before radiation delivery in each fraction. As IGRT overcomes the problem of using large margin around the prostate so the prostate could be irradiated to the prescribed dose and the dose could be escalated while rectum receives acceptable dose. [10]Because error in target shifts may lead to serous problems so this study **aims** to confirm the accuracy of the location of the skin markings in relation to the actual isocentre of the irradiated volume in overweight and obese patients.

Materials/Methods

10 consecutive patients aged from 60 to 78 years treated from August 2010 to June 2011 in Ayady Almostakbal Oncology centre were included in the present study. CT simulation was done for all patients with fixation using alpha cradle, then radio-opaque markers were placed on the patient's anterior and lateral skin to define the central axis plane of the prostate gland; the planning isocenter can be triangulated from the three positions. These patients were assessed as moderate to high risk therefore received whole pelvis radiotherapy prior to prostate irradiation.

All patients were planned on XiO® (CMS Inc) radiotherapy planning system. The PTV, rectum, and bladder were contoured by radiation oncologists. The PTV included the prostate and any local tumor extensions, with a margin of 10 mm circumferentially except 7 mm posteriorly. All CT scans were planned, calculated and treated with a 15 MV photon beam on a Primus linear accelerator (Siemens, Germany). The plan was carried out using box technique. The dose of 45Gy in 25 fractions was prescribed to the isocenter which is placed at the center of the prostate.

After the delivery of the whole pelvis irradiation (25 fractions), the patient is prepared for the CT scan of the boost dose delivery. The patient is set up in the treatment position, and the radio-opaque markers are again placed on the anterior and lateral skin marks that are assumed to best define the axial plane of the prostate gland containing the planning isocenter.

After the prostate gland is aligned on both scans, CT scan is then compared with the initial planning CT scan (for whole pelvis irradiation). The location of the isocentre on the second CT scan (for boost irradiation) is compared to the skin marks which were placed at the beginning of the whole pelvis radiotherapy. Then the isocenter shift is measured as the distance between the initial planning isocenter and the boost isocenter. The treatment couch is then adjusted to the original position in anterior posterior axis (Y) and the distance between the two isocentres is calculated in the other two orthogonal directions (left to right & superior to inferior).

After adjusting the position of the treatment table and so the placement of the isocenter inside the patient and the target shifts the treatment is delivered. The plan was carried out using 6 fields. The dose of 10Gy in 5 fractions to the prostate and seminal vesicle was prescribed to the isocenter which is placed at the center of the prostate. Then 2400 cGy are delivered in 12 fractions to the prostate (CTV). The weight of all patients was measured at the beginning of radiotherapy and before boost irradiation **(Table 1).**

Patients were treated on The ARTISTE™ from Siemens linear accelerator, aligning the anterior and lateral tattoos and setting the isocentre relative to the anterior tattoo with a fixed couch height. Weekly isocentre portal verification images acquired and assessed online in relation to bony anatomy. In addition, daily treatment "capture" images of the anterior and most lateral aspects were acquired for assessment offline in relation to fiducial markers and bony anatomy.

Statistical analysis

The isocentre position was listed for each patient in the three axes for whole pelvis plan and the boost plan. Then target shift between the two isocentres in the x, y and z directions for the patients is calculated and summarized in **Table 2**. The minimum, maximum and average shift for each patient are calculated using excel sheet**.** To check if there is any correlation between target shifts in x & z axes and body weight a simple correlation test is done. The R-value is taken as an indicator for the correlation. A *P* value of less than 0.05 was taken to indicate whether the correlation is significant or not.

Table 1. Weight of patients before whole pelvis and boost irradiation.

Pt number	Weight before whole pelvis	Weight before boost
1	99	102
2	104	110
3	96	98
4	89	92
5	95	101
6	111	111
7	130	130
8	88	88
9	110	115
10	95	101

Results

Table 1 shows the weight of all patients included in this study. It ranges from 88-130kg (average 101.7 before whole pelvis treatment and 104.8kg before boost).

Isocentre position was recorded for each patient in the three axes before whole pelvis plan and before boost plan. Then prostate movement (target shift) between the two isocentres in the x, y and z directions for the patients is calculated and summarized in **Table 2**. The minimum shift in cm was -2.33, 0 & -0.93 in the three axes respectively and the maximum shift in cm was 2.77, 0 & 1.05 respectively. The average shift was -0.31, 0.00& 0.39 in the three axes respectively.

In 4 patients out of 10 the shift in lateral direction was around 3 mm so the setup adjustment was not required before delivery. On the other hand set up adjustment was required for other patients in this direction and for all patients in superior inferior direction (z) as the shift was > 3mm. In extreme case the shift was 2.77 & 1.05cm in lateral and superior inferior directions respectively.

Summary of the average, minimum and maximum shift among the patients and so the setup adjustments in the 3 directions are listed in **table 3**.

The minimum shift was -2.33cm & -0.93cm, the maximum was 2.77cm & 1.05cm and the average was -0.31cm & 0.39cm in lateral direction (x) and superior inferior direction (z) respectively. So the minimum and maximum prostate shifts in the lateral direction are larger than that for superior- inferior axis.

There was a weak positive correlation between target shift and body weight in x axis (R value= 0.39) but this correlation was not significant (P=0.15). On the other hand there was not any correlation between target shift and body weight in z axis (R value= 0.009).

Table 2. Isocentre position shift in cm in the three axes for whole pelvis plan and the boost plan

Axis	Pt. 1	Pt. 2	Pt. 3	Pt. 4	Pt. 5	Pt. 6	Pt. 7	Pt. 8	Pt. 9	Pt. 10
Rt-lt (x)	-1.36	-0.33	2.77	0.11	0.08	-2.33	-1.47	-0.97	0.42	0.08
A-p (y)	0	0.0	0	0	0	0	0	0.0	0	0
S-i (z)	1.05	-0.93	-0.51	0.84	0.56	1.01	0.45	0.39	0.5	0.56

Table 3. Summary of isocentre position shift in cm in the three axes for whole pelvis plan and the boost plan

Axis	Average	Min	Max
Lateral. RT-LT (X)	-0.31	-2.33	2.77
Anterior-posterior (Y)	-0.00	0.00	0.00
Superior-inferior (Z)	0.39	-0.93	1.05

Discussion

This study helps in the determination of an appropriate tumor margin for prostate irradiation to form a PTV from the clinical target volume. The margin depends on the inter-fractional prostate shift and the technique used such as three-dimensional conformal RT and IGRT. Target shift could be due to target movement caused by day-to- day filling status of the rectum and bladder or it could be related to daily setup error caused by different patient body characteristics or misalignment of the skin markers and in room lasers. [10-13]

This study shows that there is prostate shift in the isocentre between the whole pelvis irradiation and the boost irradiation of the prostate. So we could not relay on the adjustment done for the patients during whole pelvis irradiation for boost irradiation delivery.

This shift is up to 2.77 & 1.05cm in lateral and superior inferior direction respectively. As the shift is more than 1cm in both directions so the current treatment margin of 1cm around CTV is not sufficient to compensate for such large shifts especially in the lateral direction. This could lead to under-dosage of the target with an increase of the dose to the normal tissue involved mostly the rectum. Also as the shift is different in both axes so we should not use uniform margin around the CTV. Using our prostate shift data, treatment margins of about 3cm and > 1cm are required in the lateral and superior inferior directions respectively. As it is very aggressive to use 3cm margin so to compensate for this shift, accurate measurement and correction of prostate shifts throughout the treatment should be done. This could be achieved using any of image guided radiotherapy modalities. So IGRT is mandatory in prostate irradiation especially among obese patients. By IGRT we can use small treatment margin because inter-fractional shift with the help of image guidance from localization CT can be corrected.

As the patients included in this study all are overweight and obese with no variation in body weight the difference of the shift isocenter shows no correlation with patient weight in z axis and although it is weakly correlated in lateral direction but the correlation was not significant.

We compared our results with Millender et al [14] and Wong et al [10]. Millender et al studied the magnitude and the direction of patient positioning error for each fraction for 3 obese prostate men. They found that the absolute magnitude of positioning error was greatest in the left-right direction with a mean of 11.4 mm/ fraction (median, 8 mm; range, 0-42 mm). Mean error in the superior-inferior direction was calculated as 7.2 mm/fraction (median, 5 mm; range, 0-47 mm) and the anteroposterior error was 2.6 mm/fraction (median, 2.5 mm; range, 0-8 mm). So they concluded as we did in our study that obese patients tended to have the largest shifts in the lateral direction, they also concluded that the shift is due to setup variation rather than prostate motion.

In the study done by Wong et al, the minimum shift in cm was -2.7, -2.0 & -1.0 in x, y & z axes respectively and the maximum shift in cm was 2.5, 2.3 & 1.5 respectively. A part from the shift they calculated in y axis, the shift in x & z axes agreed with the shift calculated in our study. They also found that the interfractional prostate shift in the AP direction for the overweight subgroup was statistically larger than those for the control and obese patient subgroups. On the other hand, the interfractional prostate shift in the lateral direction for the obese patient subgroup was significantly larger than for the overweight and control subgroups. So they concluded that overweight and obese patient groups showed a significant difference from the control group in terms of prostate shift. In our study we also found that there is a greater shift in lateral direction than in superior inferior direction however we could not correlate this to the patient weight as we did not have variations in patients' weight (The variation is less than 5% which is not considered variation) as in Wong's study.

Conclusions

The treatment of prostate cancer with three dimensional conformal radiotherapy (3DCRT) in overweight and obese patients requires either generous non-uniform treatment margin in the lateral direction compared to that commonly used. As this margin will cause very high dose to the rectum so the use of IGRT to correct for prostate motion is mandatory otherwise without this correction local control failure or high dose to the rectum with sever rectal complications will be the results.

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