Analysis of Intrafractional Organ Motion for Patients with Prostate Cancer Using Soft Tissue Matching Image-guided Intensity-modulated Radiation Therapy by Helical Tomotherapy

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Abstract. *Aim: To analyze an intrafractional organ motion for patients with prostate cancer using soft tissue matching by megavolt computed tomography (MVCT) images during the course of image-guided intensity-modulated radiotherapy (IGRT–IMRT) using helical tomotherapy. Patients and Methods: Data from a total of 10 patients with prostate cancer who received IGRT–IMRT were analyzed, and MVCT images were acquired before and after radiation therapy. Intrafractional movement and PTV margins for soft tissue matching were calculated by comparing treatment planning images with 740 MVCT images for right–left (RL), superior–inferior (SI), and anteroposterior (AP) dimensions. A total of 74 Gy/37 fractions were administered. A margin to compensate for these variations was calculated using the van Herk's equation. Results: The intrafractional motion was 0.03 (−1.3 to 1.4) ±0.39 mm in the RL dimension, 0.08 (−1.8 to 0.28) ±0.73 mm in the SI dimension, and 0.52 (−1.8 to 1.8) ±0.63 mm in the AP dimension. The required PTV margin was 0.60 mm, 1.10 mm, and 0.78 mm in the RL, SI, and AP dimensions, respectively. Only one patient exhibited a deviation greater than 5 mm only once in 37 fractions (1/370=0.2%) caused by anal contraction. Conclusion: The PTV margin in soft tissue matching IGRT–IMRT by helical tomotherapy for a patient with prostate cancer was 3 mm or less, and our tentative PTV margin of 3-5 mm is sufficient for most patients, if adequate instruction for avoiding anal contraction is given.*

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Radiation therapy is one of the major treatments for localized prostate cancer. With the advent of radiation technique, we have been able to deliver higher prescribed doses without severe adverse reactions. Intensity-modulated radiation therapy (IMRT) approach allowed the administration of higher doses of radiation to the prostate while limiting the doses to the surrounding normal organs (1). Image-guided radiation therapy (IGRT) is the process of frequent two and three-dimensional imaging, during a course of radiation treatment, used to direct radiation therapy utilizing the imaging coordinates of the actual radiation treatment plan, which enables us to deliver accurate radiation therapy with reduction of set-up margin, therefore to allow the reduced planned target volume (PTV) for prostate cancer (2). Helical tomotherapy is a form of IMRT, and has the ability to acquire megavoltage computed tomographic (MVCT) images of a patient in the treatment position before therapy. As this precise positioning using CT images allows not only for correct bone position (bone matching) used in conventional radiation therapy and suitable for bone lesion (3) but also visualize and identify the precise prostate location (soft tissue matching). Therefore we have explored intrafractional organ motion using repeated MVCT before and after treatment and calculated required margins for each treatment for soft-tissue matching.

Patients and Methods

We evaluated 10 male patients with prostate cancer who received IGRT–IMRT using helical tomotherapy (HI-ART TomoTherapy Inc., Madison, WI, USA) between April 2012 and June 2012. The ages of the patients ranged from 59–80 years (median 71 years). All

patients were categorized into intermediate- or high-risk groups and were initially treated by androgen ablation therapy. For imaging, vacuum cushions (Blue Bag, Medical Intelligence, Schwabműenchen, Germany) were used to immobilize the patients in the supine position, and kilovoltage CT images were acquired for each patient (2-mm slice thickness), with a minimum of 5 cm above and below the level of PTV. The prostate gland and seminal vesicle were contoured as the clinical target volume (CTV). The primary planning target volume (PTV), 74 Gy in 37 fractions (2 Gy/fraction), was defined by margins of 3 mm posteriorly and 5 mm in all other dimensions around the prostate gland and seminal vesicles. The dose was set as D95 i.e., 95% of the PTV received the prescribed dose. The bladder and rectum were defined as the risk organs, and the major constraints during inverse planning were that no more than 35% and 50% or the rectal and bladder volume, respectively, would receive 40 Gy radiation.

MVCT, using 3.5-MV energy images, were acquired through the PTV before treatment delivery, with a minimum slice thickness of 4 mm and a field of view of 35 cm. The first MVCT images were taken and autofused with the kilovolt CT treatment planning images, and the superior–inferior (SI), anterior–posterior (AP), and right–left (RL) shifts were then calculated by automatic image fusion for bone matching. Images were then manually inspected for prostate soft tissue matching, and verified and corrected by two clinicians (rotational corrections were not implemented at the time of this study). The patients were then shifted along calculated translating couches. For the first six patients, a second set of MVCT images were acquired to verify that the shifts had been applied correctly. Two clinicians then manually inspected the images, and the patients were then re-adjusted, if necessary, and treated. The distance between bone and prostate matching were identified as inter-fractional movements. The third MVCT images were then obtained to assess intrafractional organ motion after radiation therapy (3). The total time between image acquisition and treatment delivery was typically less than 10 min. Intrafractional movement was initially calculated by comparing the second and third MVCT images. However, the second MVCT images were omitted because little displacement (<1 mm) occurred in the location between the second MVCT image and the expected location. Thereafter, the first and third MVCT images were used to calculate intrafractional organ motion in the subsequent 13 lesions in 13 patients. Intrafractional movement was calculated by comparing the expected location with the shifts applied to the locations in the first and third MVCT images. van Herk's formula ($2.5\Sigma + 0.7\sigma$, where Σ and σ are systematic and random positioning errors, respectively) was used to calculate the PTV margin to compensate for these variations (4). This method should ensure that 90% of the patients receive a minimum cumulative CTV dose of at least 95% of the prescribed dose.

Results

Ten patients were treated with 74 Gy/37 fractions. Thirty-seven fractions were examined by repeated MVCT for each patient, and the 740 MVCT images were analyzed for deviations of prostate soft tissue matching. Intrafractional motion was 0.03 mm (−1.3 to 1.4 mm) ± 0.37 mm (mean ± standard deviation) in the RL dimension (right dimension regarded as positive), 0.08 mm (−1.8 mm to 0.28 mm) ±0.13 mm in the SI dimension (superior dimension considered positive), 0.52 mm (−1.8 mm to 1.8 mm) ±0.63 mm in the AP dimension (anterior dimension regarded as positive) (Figure 1). The required PTV margin was therefore 0.60 mm, 1.10 mm, and 0.78 mm in the RL, SI and AP dimensions, respectively. The distributions of movement are shown in Figure 1. One patient exhibited a deviation of greater than 5 mm in the inferior dimension only in one image (1/370=0.2%) with deviations of 5.2 mm superior and 2.8 mm anterior from the expected position. His prostate was moved by anal contraction during radiation therapy (Figure 2).

Discussion

Interest in IGRT arose from the need to account for daily anatomical variations in the delivery of fractionated radiation therapy. This is particularly relevant in the treatment of prostate cancer, since the position of the prostate gland varies as a result of bladder and rectal filling and emptying (5, 6). A number of correctional strategies, including implanted fiducials (7) and online three-dimensional CT imaging (8), have been developed and clinically-implemented. For example, Pinkawa *et al*. reported that initial rectal distension and the superior–inferior CTV level should be considered when defining the posterior margins for radiation therapy to the prostate (9).

To ensure that the target is situated in the same geometric location on a daily basis, registration should result in the overlap of prostate volumes based on MVCT and planning CT images. This varies from traditional treatment protocols for prostate cancer, where the lack of soft tissue contrast in portal images made prostate matching impossible, and patient re-positioning was based on the matching of bone structures (10-16). Previous studies showed that bone matching required PTV margins of 4.7-10.5 mm, 7.4-12 mm, and 1.4-4.4 mm in the AP, SI, and LR dimensions, respectively (16). IGRT–IMRT can reduce these values, and prostate soft tissue matching using IG-IMRT also enables the use of smaller PTV margins compared with IMRT. Melancon *et al*. reported that a 3-mm intrafractional margin was adequate for prostate dose coverage (18). However, a significant number of patients lost seminal vesicle dose coverage, since the rectal volume change significantly affected seminal vesicle dose coverage. Mutanga *et al*. developed a system for margin validation in the presence of deformations (19). Here a 5-mm margin provided sufficient dose coverage for the prostate. However, an 8-mm seminal vesilcle margin was still insufficient due to deformations. One of the limitations of our study was that we only checked PTV movement in three dimensions, and alterations in dose coverage could have been caused by deformation in other dimensions.

The ambiguity of MVCT is also an important consideration. Mahan *et al*. carried out anthropomorphic phantom studies which indicated that MVCT images in

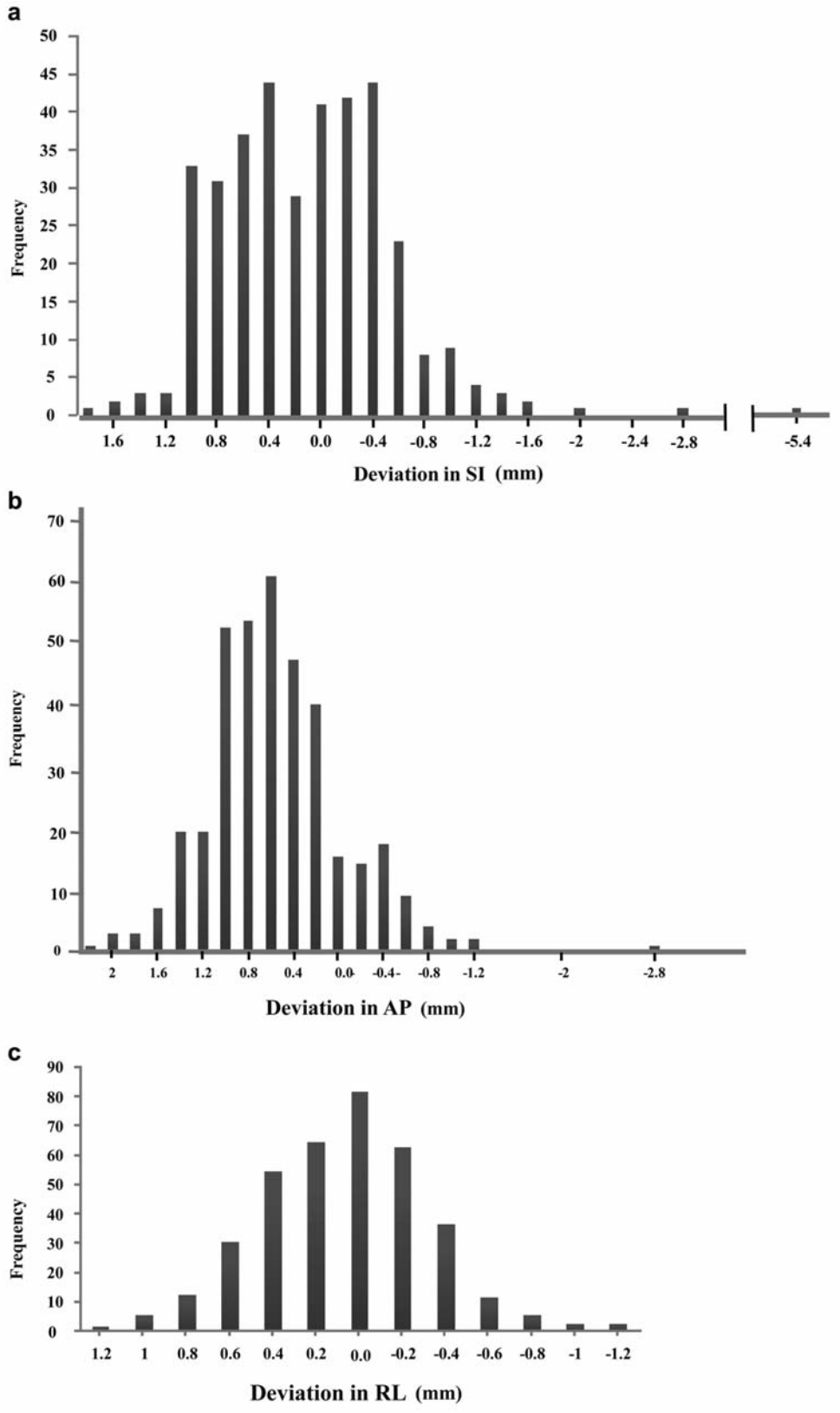

Figure 1. *Distribution of intra-fractional motion. Only one session revealed a deviation larger than 5 mm in the superior–inferior (SI) direction (1/370=0.2%). AP: Anterior–posterior; RL: right–left.*

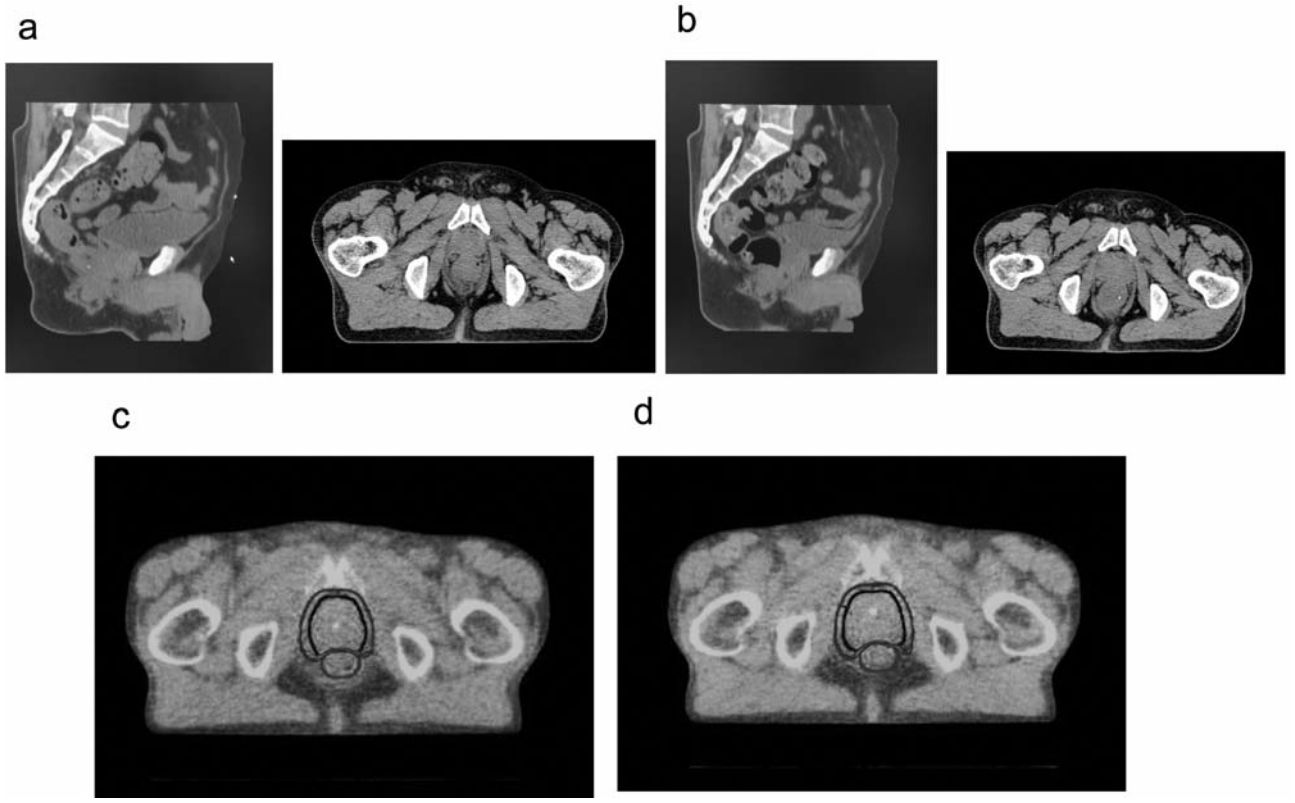

Figure 2. *Prostate movement caused by anal contraction: a) Image without contraction, b) image with contraction, c) Megavolt computed tomography (MVCT) before treatment, d) MVCT after treatment revealed contraction. Contraction made the prostate move in anterior and superior directions.*

tomotherapy were capable of imaging with sufficient accuracy to place the isocenter within 1 mm of the desired position (20). Our results showed that the required maximal PTV margin was 1.10 mm in the SI dimension, suggesting that a 2.16-mm margin (1.16+1 mm) for the PTV may be sufficient to compensate for image ambiguity if clear images can be obtained.

Onishi *et al*. reported that the mean (±standard deviation) overall displacement of the prostate due to anal contraction was 0.3±1.4 mm to the right, 9.3±7.8 mm to the anterior, and 5±4 mm in the cranial dimension (21). They concluded that voluntary anal contraction within an experimental setting caused significant movement of the large prostate and bone, predominantly in the anterior and cranial dimensions (21). Anal contraction is, therefore, an important consideration during radiation therapy, and routinely instructing the patient to avoid anal contraction may be a simple solution.

In conclusion, the PTV margin in soft tissue matching IGRT–IMRT using helical tomotherapy for prostate cancer was found to be 3 mm or less. Our tentative PTV margin of 3-5 mm was sufficient, if adequate instruction for avoiding anal contraction is made.

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