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Predicting Isocenter Shift due to Prostate Motion and Selecting Patient Specific Posterior Margin for IGRT of Prostate

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Abstract

Purposes/Objective: Image-Guided Radiation Therapy has been shown to significantly decrease setup errors and correct for organ motions (by patient repositioning, referred to as shift here), thus allowing the use of a tight treatment margin. The objective of the present work is to show that our evidenced-based patient positioning technique (isocenter shift) can effectively reduce the overall setup error for the majority of prostate patients.

Methods and Materials: We reviewed and analyzed the pre-treatment CT scans of 87 prostate patients treated from 2005-2007. Each patient received 10-15 image-guided fractions in the first phase of the treatment course. By systematically analyzed the imaging data and comparing to the planning CT, the isocenter positioning in both the left-right and anterior-posterior directions in the second phase of the treatment course can be predicted, along with the selection of a patient specific posterior margin.

Results: For 90% of the patients, the isocenter correction can be predicted to within 95% confidence. 90% of the patients in the study have a posterior margin in the range 5-8 mm for the second phase of treatment. The outliers in the frequency distributions of the iso-shifts for both the left-right and anterior-posterior directions seems to indicate that more frequent image-guided sessions are required in order to improve the setup accuracy.

Conclusions: An adequate number of image-guided treatments provide a semi-pattern recognition approach for patient repositioning. This, together with the inclusion of a quasi-adaptive margin can accommodate the daily variance of the prostate positions and affords a 95% confidence limit for tumor coverage. Our evidence-based method can effectively reduce the systematic setup error which potentially could modify the cumulative dose distribution. The use of adaptive strategy as proposed in this work reduces the overall setup error.

Keywords: Image-guided IMRT, IGRT, Adaptive targeting, Prostate, Organ motion, CT-on-rails

Introduction

The varying filling states of the rectum and the bladder manifested as an inter-fractional motion of the prostate gland is a well known problem in external beam radiation therapy of prostate cancer [1-16]. A wide range of movement of the prostate gland has been reported in all three orthogonal directions: superior/inferior (S-I), left-right (L-R) and anterior-posterior (A-P), and movements as much as 2 cm or more have been observed in the A-P direction. A direct consequence of prostate motion is a shift of the target from its reference frame (as delineated in the treatment planning CT). Depending on the treatment margins employed, these uncorrected target shifts may lead to under dosage of the prostate, thus potentially decreasing the local tumor control, or over dosage to the rectum, thus increasing rectal complications. Various targeting solutions (better known as image-guided radiation therapy, IGRT) have been developed and implemented in the clinics to determine and correct for the positional variation of the prostate gland prior to the external beam irradiation. The goal in IGRT is to localize the prostate gland prior to delivery of radiation, whereby any change of the prostate location relative to the patient's anatomy may be corrected. This is done either directly by imaging the anatomical sites of interest with ultrasound [17-20], serial CT scans [21], cone beam CT [22-24], CT-on-rails [25,26], or indirectly by using implanted markers [27-30] as surrogates to infer the location of the prostate gland. Deviation of the treatment isocenter from its reference location obtained in the treatment planning process can be corrected by adjusting the couch position in the three orthogonal directions (referred to as iso-shift in this paper for convenience) thus returning the isocenter to its 'planned' location. Due to the apparent random nature of the motion of the prostate, predicting the iso-shift appears to be a futile exercise. Thus IGRT of prostate cancer is generally performed for the entire treatment course, requiring significant resources.

Another problem in prostate irradiation is the choice of treatment margin for the target volume. The concepts of gross target volume (GTV), clinical target volume (CTV) and planning target volume (PTV), introduced by ICRU50 [31] in 1993 have since been accepted in external beam radiation therapy, but the generation of an appropriate margin for CTV (which forms the PTV) to account for the inter-fractional and intra-fractional prostate motion is not a trivial problem. Several studies have been reported on the determination of target margin [32-39]. Regardless of the methodology used in the various studies, it is important to point out that there is no unique solution to define the tumor margin. Rather, the selection of a tumor margin (either isotropic or anisotropic) is dependent on individual institutions since each has its own protocol for dose constraints.

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We have developed a simple technique in which accurate patient repositioning coupled with a 'quasi-adaptive margin' can be generated for a limited number of IGRT treatments to accommodate the daily variance of the prostate positions. In this study, we present our clinical data on prostate IGRT for patients treated between 2005- 2007. The objective of the present work is to show that our evidenced-based isocenter shift technique can effectively reduce the overall setup error for the majority of prostate patients, and that it is possible to design a patient specific treatment margin with 95% confidence limit for more than 90% of the patients.

Materials and Methods

Our technique utilizes the concept that, for a certain group of patients, the pattern of setup variation can be learned over a finite number of IGRT treatments, from which the direction and magnitude of shift (shift vector) to restore the patient positioning can be predicted. IGRT for prostate irradiation in our department is performed on a Siemens Primatom by image fusion of the Primatom CT images with the planning CT study for each patient. A detailed description of the IGRT procedure has been reported in previous publications [25,26,40]. Based on our previous studies, shifts in the S-I direction are within the slice thickness of the CT scan. Thus only shifts in the L-R and A-P directions are considered.

For prostate irradiation in our department, the first phase of treatment irradiates only the prostate gland. Since smaller fields and tighter posterior tumor margin (typically 5mm) are used for the prostate gland irradiation, which traditionally corresponds to the cone down phase in prostate irradiation, image guidance is performed to improve the setup and dose delivery accuracy. Each patient receives 10-15 fractions in the first phase at 1.8 Gy/fraction. In our image guidance protocol, deviations between the pre-treatment CT isocenter and the planning CT isocenter is > 3mm in any one of the three orthogonal directions will require a shift correction in that particular direction. The 10-15 IGRT fractions is divided into groups of fives in which the iso-shift results are reviewed every 5 fractions and an 'average' iso-shift is determined for setting up the patient in the next 5 IGRT fractions. After all 10-15 IGRT fractions had been delivered, a final iso-shift is determined from all previous 15 fractions. This knowledge of the isocenter shift is then used to set up the patient in the next phase of treatment. In addition, depending on the magnitude of the A-P shift, a patient specific posterior margin is also determined for treatment planning of the second phase. Since the minimum posterior margin is 5mm in our prostate IG-IMRT protocol, a shift-margin table is constructed [Table 1] to facilitate the determination of the posterior margin for treatment planning of the second irradiation phase.

In the second phase of the treatment, the treatment field sizes are expanded to include both the prostate gland and seminal vesicles. The 'average' iso-shift is used to set up the patient, whereby the systematic setup error may be reduced and a smaller treatment margin can be used. Each patient receives 28-33 fractions, depending on whether the first IGRT phase is 15 or 10 fractions. The total dose delivered is 77.4 Gy. The accuracy of the iso-shift for patient setup is then verified weekly by a pre-treatment CT scan (referred to as iso-check) instead of the weekly portal imaging. Should the weekly iso-checks reveal discrepancy between treatment and planning isocenter positioning that is beyond the tolerance (namely, the patient specific margin employed in the second phase of treatment), the patient positioning will be adjusted accordingly based on the iso-shifts obtained in the pre-treatment CT. In the subsequent fraction, a pre-treatment CT will be performed (the patient is still set up based on the averaged iso-shifts). If the shifts of the isocenter are within tolerance, nothing will be changed and the patient will be setup with the average isoshifts in all subsequent fractions. However, if discrepancy between treatment and planning isocenter is still beyond the tolerance, the new shift coordinates will be used for the subsequent treatments. In either case, the weekly iso-check continues.

In this study, we have reviewed and analyzed the pre-treatment CT scans of 87 prostate patients treated at the Department of Radiation Oncology, Morristown Memorial Hospital from 2005-2007. A total of 1050 pre-treatment CT scans are examined and image fusions are performed, from which 2100 isocenter shift measurements (1050 each in the L-R and A-P directions) are determined.

To show the effect of the patient's positioning adjustment as a result of IGRT, the shift data in the first 10-15 IGRT fractions for each patient is 'un-shifted' relative to the initial treatment isocenter to represent the original isocenter positions. Frequency distributions (FD) of the 'un-shifted' and shifted data sets (iso-shifts) in the LR and AP directions are compared. The shift data from iso-checks is also compared. Of the 87 patients included in the study, 51 patients received 10 IGRT sessions (510 pre-treatment CT + 306 iso-checks =total of 816 CT scans) and 36 patients received 15 IGRT fractions (total of 720 CT scans). A comparison is made between the iso-shift distributions of these two

A-P Shift (mm)	Posterior margin (mm)
3	5
4	6
5	7
6	8
7	9
8	10

Table 1: Final A-P shift estimated from 15 consecutive IGRT fractions and the posterior margin used for PTV in treatment planning.

Fraction # with CT	L-R shift (mm)	Av. L-R shift (mm)	A-P shift (mm)	Av. A-P Shift (mm)
1	4.1R		8.4P	
2	2.3R		8.3P	
3	1.9R		5.4P	
4	4.0R		4.5P	
5	1.9R	0	7.1P	7P
6	0.8R		4.1P	
7	5.7R		7.0P	
8	6.1R		0.93P	
9	3.1R		5.5P	
10	5.5R	4R	9.4P	5P
11	0.9L		0.33P	
12	3.2R		0.56A	
13	2.6R		1.5A	
14	0.7R		0.5A	
15	0.7R	4R	1.9P	5P
16	1.9R		0.3A	
17	1.3R		0	
18	1.2L		0.9P	
19	0		1.1P	
20	1.2R		0.3A	

Table 2: Isoshift in the L-R and A-P directions in 15 consecutive treatment sessions. Each entry represents the magnitude and direction of shift required in order to match the pre-treatment CT scans with the corresponding planning CT image set. Fractions 1-15 are treatments with image guidance. Fractions 16-20 represent the weekly isochecks. The numbers in the columns labeled 'av. L-R and Av. A-P shifts are used to set up the patient for the five subsequent fractions.

groups of patients to examine if there is an improvement in setup accuracy with 15 IGRT fractions.

Results

(1) Predicting iso-shifts

An example of the iso-shifts is shown in [Table 2] for a prostate patient. To illustrate how the iso-shifts are used to determine the final 'average' shifts in the L-R and A-P directions for the second phase of the treatment, the variations in the L-R and A-P directions of the isocenter positions in [Table 2] are plotted in [Figure 1a and 1b] respectively.

In the first five fractions, the 'average' variation of the isocenter position in the L-R direction is about 2.8 mm, indicating that the variation in the L-R direction is within our criterion for no shift (≤3mm). Thus in fractions 6-10 the initial patient setup in the L-R direction remains the same as obtained from the plan. In fractions 6-10, image guidance with the Primatom shows that adjustment of the order of >6 mm towards the right are needed to correct for the deviation between the treatment isocenter (as shown in the pre-treatment CT scan) and the planning isocenter. The 'average' shift after the 10th fraction is 4mm towards the right, which is simply the mathematical average of the shifts from fractions 6-10. The small L-R shifts in the first five fractions are not used in the determination of the average shift since no shifts are made in the first five fractions. Thus the patient positioning is adjusted 4 mm to the right in the initial setup to 'anticipate' the change in the L-R direction of the prostate gland. The resulting L-R shifts in fractions 11-15 based on image fusion are within the tolerance of 3mm (except for fraction #11, which is 3.3mm, and the patient positioning is corrected in the L-R direction accordingly), indicating that the '4mm shift towards the right' is the correct adjustment to account for the systematic error, and will be used for patient setup in the L-R direction in the second phase of prostate irradiation (the 3.3mm shift in fraction #11 does not affect the average of the L-R shift). Five weekly iso-checks are performed to verify the accuracy of the patient positioning and the 'correctness' of the shift. As can be seen from [Figure 1a], the isocenter position in the L-R direction in these five iso-checks (fraction #16-20) are well within the 3mm tolerance, verifying that the 'average' L-R shift determined from the 15 IGRT fractions correctly predicts the change of the isocenter position in the lateral direction.

In the A-P direction as shown in [Figure 1b], the large posterior shifts in fractions 1-5 resulted in an 'average' shift of 6.7 mm in that direction. Thus the patient positioning is shifted 6.7mm posteriorly in the initial setup for the next five fractions. The A-P shifts for fractions 6-10 show smaller posterior shifts, and an 'average' shift of 3.5 mm in the posterior direction is used for fractions 11-15. The subsequent A-P shifts as determined in those five fractions are in the range 3-6 mm. The final shift of 4.9 mm obtained from the average of the shifts in fractions 11-15 is used to set up the patient in the A-P direction for the second phase of treatment. As shown in [Figure 1b], the isocenter position in the A-P direction in the five iso-checks are well within the 3mm tolerance, verifying that the 'average' A-P shift determined from the 15 IGRT fractions correctly predicts the change of the isocenter position in the anterior-posterior direction. The AP shifts of this patient in the first 15 fractions illustrate a trend of an oscillating average with diminishing amplitudes. The fact that the final shift resulted in less than 2mm AP shifts in the second phase of the treatment is proof that it is possible to estimate a shift vector from a limited number of pre-treatment CT scans.

Furthermore, the 4.7 mm posterior shift requires a posterior margin of 6 mm in treatment planning to account for the random error that may arise due to organ motion, setup uncertainty, etc.

(2) Frequent distributions (FD) of iso-shifts in the L-R and A-P directions

To show the effect of IGRT on patient positioning, the iso-shift data in the L-R and A-P directions are 'unshifted' for all the patients to obtain the original isocenter positions. The FD of the 'unshifted' (original) isocenter positions in the L-R and A-P directions are shown in [Figure 2a and 2b] respectively.

Ideally, histograms of the isocenter positions in the L-R and A-P directions are delta functions at the origin. In reality, setup errors, organ motions, breathing, laser calibration errors, and various other factors contribute to the displacements of the L-R and A-P components of the isocenter from the origin as shown in [Figure 2a and 2b]. The objective of IGRT is to reduce the displacements of the treatment isocenter from its planning position as much as possible. [Table 3] shows the mean and standard deviation of the iso-shifts in the L-R and A-P directions in the three successive 'groups of five IGRT fractions'. Also included are the mean and SD for the 'unshifted' distributions in [Figure 2] for

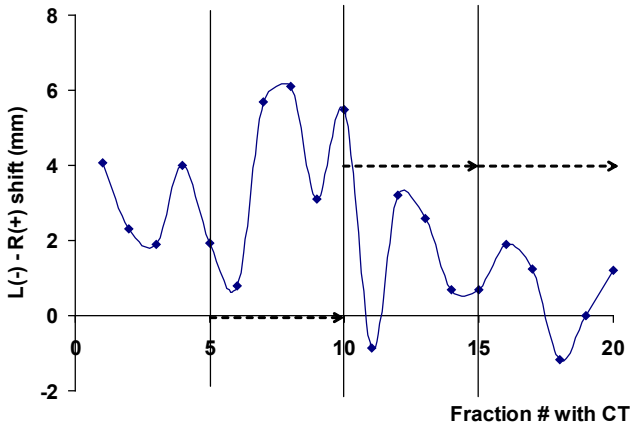

Figure 1a: Variation of the isocenter shift in the L-R direction. All shifts are measured relative to the planning position. The dashed lines indicate the 'average' shifts used to set up the patient in the next five IGRT fractions. Also shown are the five iso-checks in the L-R direction (fraction # 16-20).

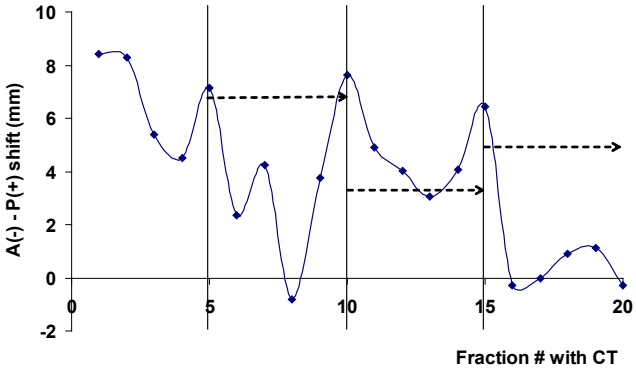

Figure 1b: Variation of the shifted isocenter position in the A-P direction. The dashed lines indicate the 'average' shifts used to set up the patient in the next five IGRT fractions. Also shown are the five iso-checks in the A-P direction.

comparison. With each five IGRT sessions, the SD of the iso-shifts in the three successive groups become progressively narrower, indicating improvement in the setup accuracy, especially in the A-P direction. It should be pointed out that in the L-R direction the difference between the 'unshifted' and each of the three groups is more significant than it appears numerically since the sample size for the unshifted data set is three times more than each of the three groups.

The improvement in the setup accuracy can be further demonstrated by comparing the mean and SD of the isocenter displacements from the planning position for the three data sets (unshifted, shifted and iso-check) for the entire patient population in the study. This collection of iso-shift values can be considered as a random data set. As shown in [Table 4], there is little variation in the SD of the isocenter displacement for the three data sets in the L-R direction, indicating that the isocenter shift in the lateral direction is usually small. On the other hand, a more dramatic change in the SD of the isocenter displacement in the A-P direction can be observed. The progressively smaller SD in the A-P direction indicates that we have 'learned' the behavior of the systematic component of the iso-shift in the A-P direction from the IGRT sessions. By applying the predicted A-P iso-shift in the patient setup in the second phase of the treatment, we are able to reduce the variation of isocenter displacement in the A-P direction, from an initial value of 6.1 mm to 3.4 mm.

There is a subpopulation of patients whose iso-shifts are more than 2SD away from the planning position, as shown in [Figure 3] for the A-P direction. For this subset of patients, more IGRT sessions may be warranted.

(3) Selection of patient specific posterior margin

The selection of posterior margin for each patient is based on the final A-P iso-shift value after 15 IGRT fractions. The minimum posterior margin for the CTV is 5mm, which corresponds to iso-shifts ≤ 3mm. For each millimeter increment in the A-P iso-shift, an additional millimeter is added to the posterior margin to account for the increased movement. Thus for our example above, the posterior margin that is used for the second phase of treatment is 6 mm, given that the A-P iso-shift estimated after 15 IGRT sessions is 4.7 mm. Note that this 6mm adaptive margin is to account for the random setup error as well as any residual systematic error. About 90% of the patients in this study have a posterior margin in the range 5-8 mm, covering roughly 2SD of the average shifts in the A-P direction.

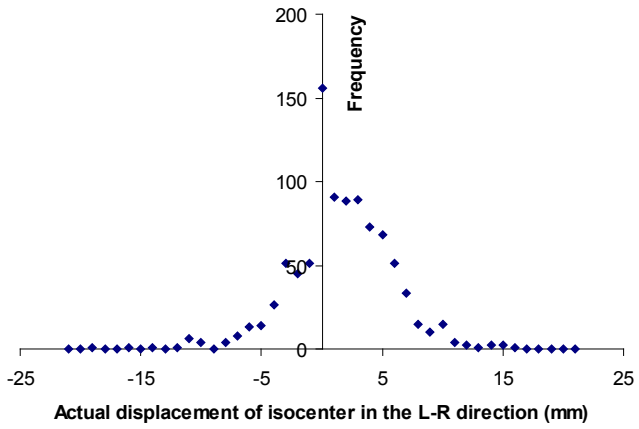

Figure 2a: The frequency distribution of the 'unshifted' isocenter position in the L-R direction for all the patients in this study, with a mean of 1.5 mm and a standard deviation of 4.1 mm.

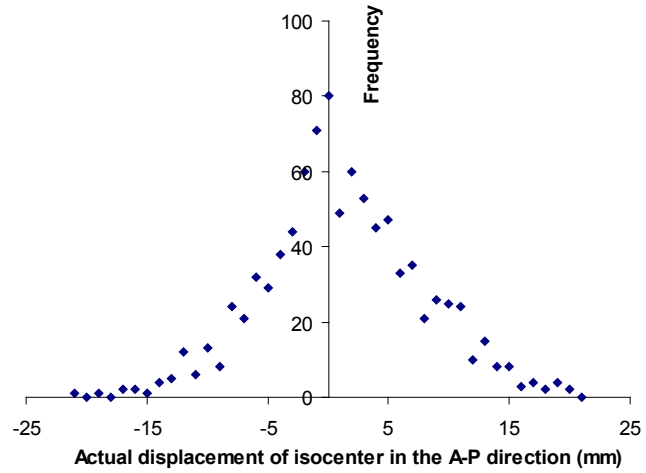

Figure 2b: The frequency distribution of the 'unshifted' isocenter position in the A-P direction for all the patients in this study, with a mean of 1.2 mm and a standard deviation of 6.1 mm.

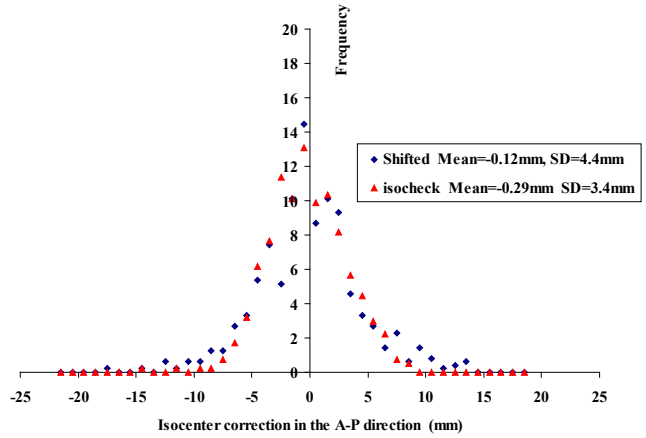

Figure 3: Frequency distributions of the isocenter displacements from the planning position in the A-P direction for the shifted and the iso-check data set. The SD for the iso-check curve is narrower than that of the shifted curve, indicative of our ability to predict the A-P shift.

(4) Iso-shift comparison between patients with 10 IGRT fractions and 15 IGRT fractions

For the group of patients receiving 10 IGRT fractions, 44, 38, 14 and 3.7% of the 510 samples yield a resultant shift vector in the ranges ≤2mm, 2-5mm, 5-10 mm and ≥10 mm, respectively. For the group of patients receiving 15 IGRT fractions, the corresponding % of shifts are 54, 32, 13, and 0.7% respectively. The daily setup uncertainties for these two groups are summarized in Table 5. There is no statistical difference in the daily set up variation between the two groups after the first five IGRT fractions. The second shift vectors are also very similar at 4.36 mm and 4.48mm between the two groups. However, the third five IGRT fractions effectively reduce the setup variation compared to those with 10 sessions.

		L-R				A-P		
	1st five IGRT	2nd five IGRT	3rd five IGRT	Unshifted	1st five IGRT	2nd five IGRT	3rd five IGRT	Unshifted
Mean (mm)	1.1	0.67	0.48	1.5	0.5	0.1	0.13	1.2
SD (mm)	3.8	3.8	3.6	4.1	6.1	4.6	3.9	6.5

Table 3: Comparison of isoshifts in the L-R and A-P directions in the three successive 'groups of five' IGRT fractions.

		L-R (mm)			A-P (mm)	
	Unshifted	Shifted	Isocheck	Unshifted	Shifted	Isocheck
Mean	1.1	0.7	0.5	0.18	-0.12	-0.29
SD	3.8	3.8	3.6	6.1	4.4	3.4

Table 4: Comparison of mean and standard deviations of the displacements of the treatment isocenter from the planning position in the L-R and A-P directions for the 'unshifted', shifted and isochecks data sets.

Conclusion

Each iso-shift such as those shown in Figure 1 invariably consists of two components: systematic and random. Example of systematic errors include misalignment of room lasers used for patient setup, skin marks not placed correctly to find patient positioning, etc. while random errors are misplacement of 'bbs' on skin marks, patient movement, etc. In general, there are two approaches to correct for the systematic and the random errors. A direct approach is to perform IGRT for every treatment. This method is straightforward, but is time consuming and requires a lot of resources. Another approach is the so-called 'No Action Level' (NAL) protocol [41]. In NAL, measurements are made in N treatment fractions to determine the systematic errors, which are then applied to all subsequent fractions unconditionally. The question to answer is: how many IGRT fractions is required to provide a reliable estimate of the systematic errors? De Boer et al. reported in their proposal of the NAL protocol, that all patients have their setup corrected based on the average of three measurements. Bortfeld et al. estimated theoretically that the optimal number of treatment fractions to perform IGRT for setup correction is 4, for the NAL protocol [42]. In another study using daily electronic portal images for prostate irradiation with the four-field technique, the number of portal images required to improve the setup accuracy was reported to be 5, taken in the first week of treatment [43].

In the present study, we have used a simple method to estimate systematically the magnitude and direction of the iso-shifts in the L-R and A-P directions based on 10-15 IGRT sessions. The average shift calculated every 5 pre-treatment CT scans reduces the systematic error in the iso-shift in the next 5 IGRT treatments. Thus after 15 IGRT fractions, the final average shift would reduce the systematic error to a minimum. The margin chosen for the posterior aspect accounts for the random error in the patient setup.

We have shown that the predicted iso-shifts reduce the isocenter correction in the second phase of the treatment for 95% of the patients. In addition, the predicted A-P shift also allows the selection of a patient specific margin to account for the random errors. Thus Instead of performing a full fledged IGRT treatment for 43 fractions, which would require significant resources, we have shown that it is only necessary to perform IGRT for about 35% of the treatments for 90% of the patients with 95% confidence (2SD). The time saved is about one hour per day per machine, based on our patient schedule for prostate IGRT, which adds 10 extra minutes to a normal treatment slot, and assuming that there are 6 prostate patients on the machine. This is a significant saving in time, which in turn, implies less stress on the staff and no extended hours. The patient subgroup that lies outside of the 2SD range indicates that a daily IGRT may be needed for these patients. Indeed, a detailed study on the physical characteristics of patients with respect to the frequency of IGRT sessions published recently by us has specifically answered the very question [44].

In the present study, we have shown that 15 IGRT sessions allow more accurate prediction of isocenter shift compared to 10 IGRT sessions. While the number of IGRT fractions performed in this study is vastly different from the other published work mentioned above, it is beyond the scope of this work to determine the optimal number of pre-treatment CT scans for precise iso-shift prediction. On the other hand, our approach is different from the NAL protocol in that the corrections applied to the second phase of the treatment are still subject to verification with image guidance on a weekly basis and new shift parameters may be necessitated for further treatment fractions.

A major advantage of using CT for image guidance is its superior image quality which allows easy and accurate identification of patient anatomy and soft tissues. This would not be possible with electronic portal images, or other imaging modalities which are not of diagnostic quality. Our ability to successfully predict the isocenter shift can be attributed at least partially to the superb image quality that we obtained with the Primatom CT scanner. The fact that we are comparing two CT data sets in image fusion allows precise determination of the iso-shifts to sub-millimeter accuracy. We can only speculate that with suboptimal image quality in IGRT, there is a limitation in the accuracy of setup error measurements, which depend on how well anatomical structures and soft tissues can be identified. Thus it may well be true that there is an upper limit on the number of such images that are needed for error estimation, beyond which no improvement in setup accuracy can be achieved.

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