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Inferences about Prostate Intrafraction Motion from Pre- and Post-Treatment Volumetric Imaging

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Abstract

Purpose—To evaluate the ability of rectal filling, bladder filling, and prostate localization from pre- and post-treatment volumetric imaging to predict prostate intrafraction motion.

Methods and Materials—Pre- and post-treatment Cone Beam CTs (CBCTs) and intrafractional kV fluoroscopy were acquired at each fraction for 20 prostate patients in supine position, totaling 374 fractions available for analysis. Rectal and bladder filling status were evaluated for each CBCT and the correlation with prostate intrafraction motion measured from kV fluoroscopy was performed. The accuracy of pre and post-treatment prostate localization to predict intrafraction motion was evaluated.

Results—Rectal filling status was a significant predictor of prostate intrafraction motion ($p < 0.001$), and gas volume was correlated with the maximum vector displacement at MV delivery with a correlation coefficient (cc) of 0.37 and $p < 0.001$. Prostate motion was greater for patients who consistently had gas volume $> 0.5 \text{ cm}^3$ within the imaged region (cc=0.52, $p=0.028$). A weak relationship was found between bladder filling and posterior prostate drift for fractions with gas volume $\leq 0.5 \text{ cm}^3$ (cc=-0.17, $p=0.046$). The sensitivity of detecting a 3, 5, and 7 mm excursion at MV delivery using post-treatment imaging was 76%, 75%, and 81% respectively.

Conclusions—Rectal filling is a significant predictor of prostate intrafraction motion, while bladder filling is of limited usefulness. Pre- and post-treatment localization can provide a reasonable estimate of prostate motion during MV delivery when intrafraction localization is not available, with an error of 95% within 3.1 mm.

Keywords

Prostate cancer; Intrafraction; Organ Motion; Radiation Therapy; CBCT

Introduction

Efforts to improve the outcome of radiation therapy have lead to the development of guidance techniques which minimize dose discrepancies caused by inter- and intrafraction motion. Intrafraction motion of the prostate can now be monitored in real time during treatment delivery using implanted electromagnetic transponders (1) or x-ray imaging of implanted fiducial markers (2). With this capability, dose discrepancies from intrafractional motion can be

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minimized, in principle, by target tracking or by stopping the radiation when the target displacement exceeds an action limit. However, for the majority of clinics image guidance is currently limited to pre-treatment imaging, or preand post-treatment imaging for target alignment and verification. Intrafraction motion is then compensated using treatment margins.

The effectiveness of pre- and post-treatment imaging to determine prostate intrafraction motion has been recently investigated by Noel *et al.* (3). This study monitored the position of the prostate throughout each treatment fraction at 10 Hz using implanted electromagnetic transponders, and concluded that pre- and post-treatment imaging is not a sensitive method of assessing intrafraction prostate motion. Because the measurement was not synchronized with treatment delivery, the duration spent outside a threshold was added up throughout the entire measurement period. Also, volumetric images were not acquired.

Information that is supplemental to prostate localization such as rectal and bladder filling status is often available from volumetric image guidance modalities used for pre and post imaging, such as Cone Beam Computed Tomography (CBCT), Ultrasound, CT on rails, etc. Many studies have shown that anatomical information from volumetric imaging is indicative of prostate motion (4-7) and may be valuable to evaluate prostate intrafraction motion. Ghilezan *et al.* measured prostate motion with cine-MRI and showed that rectal filling status is a significant predictor of prostate motion (7). However motion was measured only in two dimensions, lacking full three-dimensional (3D) localization.

At our clinic, an image-guided prostate radiotherapy protocol is underway which includes pre- and post-treatment volumetric imaging as well as intrafractional positional measurements of the prostate. Pre- and post-treatment CBCTs are acquired at each fraction which include bladder and rectal filling information as well as the position of fiducial markers implanted into the prostate gland. The 3D position of the prostate at the time of each Mega-Voltage (MV) beam delivery is estimated using kV fluoroscopy images of the fiducials (8,9). The purpose of this study is to use this data set to investigate the ability of pre and post volumetric imaging to predict prostate intrafraction motion. We evaluate what inferences can be made about prostate intrafraction motion from rectal and bladder filling status in pre and post-treatment CBCTs, and we evaluate the ability to predict prostate motion during treatment from pre and post-treatment localization.

Methods and Materials

Treatment Protocol

Twenty patients with biopsy proven prostate adenocarcinoma underwent hypofractionated radiotherapy as part of an institutional review board approved study. All patients had 3 radiopaque gold coils (Visicoil, Radiomed) implanted into the prostate gland under ultrasound guidance. Each coil is 3-4 cm long with a 0.35 mm diameter, and can be visualized in kilo-Voltage (kV) projection, CT, and CBCT images without noticeable artifacts. Patients were given dieting instructions and were provided Gas-X to reduce gas, but were not given instructions to empty bladder or rectum before treatment.

Treatment consisted of 20 radiotherapy fractions at 3.2 Gy per fraction and included image guidance using a gantry mounted kV imager which has been described elsewhere (10). At each fraction, the patient was set up to skin marks in supine orientation and a CBCT (CBCT₁) was acquired of the prostate region. The CBCT image was reconstructed and a rigid 3D registration to the planning CT was performed for a region of interest containing the prostate and implanted coils (11). A couch translation was then applied based on the registration, after which step-and-shoot Intensity-Modulated Radiation Therapy (IMRT) was delivered at 5-7 gantry angles using either 6 or 15 MV photons. The kV fluoroscopy images were acquired at each beam

angle simultaneously throughout each beam delivery and were used to evaluate the intrafraction motion. Finally after treatment delivery, a post treatment CBCT (CBCT₂) was acquired with the patient still in the treatment position and was used for treatment verification. The time from the beginning of CBCT₁ acquisition to the end of the MV delivery was 15.5±4.2 minutes (mean ±standard deviation), and from the beginning of CBCT₁ acquisition to the ending of the CBCT₂ acquisition was 18.8±5.2 minutes.

Data Set & Analysis

Each CBCT has a reconstructed volume of 41×41×12 cm³ with a resolution of 1×1×1 mm³ centered at the treatment isocenter. Visible in each CBCT is the prostate, rectum, the majority or entire bladder, and some of the small and large intestines. An intrafraction motion evaluation was carried out for each fraction and has been described in detail elsewhere (8). For each beam angle, the kV projection images acquired with no MV beam contamination (between segments) were averaged together and registered to a template image which consists of a digitally reconstructed radiograph of the coils only, and was derived from one of the daily CBCTs. A 3D estimate of the prostate position throughout the treatment fraction was obtained from the kV image registrations using an algorithm developed by Kotte *et al.* (9). This method assumes the shortest path that satisfies all 2D localizations, the accuracy of which has been previously investigated in detail for prostate (12). From all 20 patients combined, pre and post CBCTs and intrafraction fluoroscopy were recorded for a total of 374 fractions.

Rectal and bladder filling status were analyzed in all CBCT images. For each CBCT the rectum was classified *subjectively* by visual inspection as being either “full” or “empty”. The rectum was classified as “full” when either feces or gas was visibly present anywhere in the portion of the rectum imaged in the CBCT, extending from the sigmoid colon down to the anorectal junction. Figure 1 shows CBCT images from various patients with the corresponding classification of rectal filling status.

The volume of gas in the rectum and surrounding digestive track was *quantitatively* measured by automatically summing the number of voxels with gray values below a threshold within the patient interior. For each CBCT, a threshold was chosen automatically to separate tissue from air. Morphological operators were then used to sum the voxels with gray values below the threshold. Gas volume was measured from the entire imaged volume within the patient, which included ±6 cm superior and inferior of the treatment isocenter. CBCT gas volume was not measured for 2 of the 20 patients because of reconstruction artifacts caused by hip prosthesis.

The bladder volume on each CBCT was estimated by measuring the maximum length in each axis as shown in Figure 2. The bladder was assumed to be ellipsoidal with a volume of:

$$V = \frac{4\pi}{3}xyz \quad 1$$

where x , y , and z are the measured radii of bladder in the right-left (RL), posterior-anterior (PA), and superior-inferior (SI) axes. Bladder contours were available on 415 CBCT images to compare with the estimated volume from equation 1.

Statistical analysis included descriptive analysis and tests of correlation of pre- and post-treatment gas volume and change in gas volume with intrafraction motion. For normally distributed data the Pearson correlation coefficient (cc) and Student's t -test were used. The Spearman's Rank Correlation Coefficient (CC) and the Wilcoxon Rank Sum Test were used on data with highly skewed non-normal distributions.

The sensitivity and specificity were calculated when using rectal filling status to predict prostate displacement above a threshold relative to the planned position in the planning CT. They are defined as:

$$\text{sensitivity} = \frac{TP}{TP + FN} \quad 2$$

and

$$\text{specificity} = \frac{TN}{TN + FP} \quad 3$$

TP, TN, FP, and FN are the number of true-positive, true-negative, false-positive, and false-negative cases, respectively. In this situation, a true-positive is a full rectum fraction where the prostate was displaced greater than the threshold. A true-negative is an empty rectum fraction where displacement greater than the threshold did not occur. A false-positive is a full rectum fraction with no motion greater than the threshold, and a false-negative is an empty rectum fraction for which the prostate was displaced above the threshold. The sensitivity and specificity were calculated for the entire range of possible thresholds of prostate motion, and were used to perform receiver operator characteristic (ROC) analysis (13).

We evaluated the accuracy of using CBCT₁, CBCT₂, and the combination of CBCT₁ and CBCT₂ to estimate the intrafraction motion. When only CBCT₁ is used, residual setup error and intrafraction motion are assumed to be zero. When only CBCT₂ is used, the prostate is assumed to reside at the CBCT₂ localization throughout treatment delivery, i.e., the prostate stays at the same position during the treatment, the displacement shown by CBCT₂ is from residual setup error. When CBCT₁ and CBCT₂ are both used we assume a linear drift between pre- and post-treatment prostate localization, as illustrated in Figure 3. The prostate is first localized using CBCT₁, after which a constant drift is assumed in each axis (dashed lines in Figure 3), ending at the CBCT₂. Any setup error measured by CBCT₁ is assumed to be corrected and is therefore ignored. The error from each prediction was calculated by comparing the prediction with the position measured using kV fluoroscopy.

One purpose of image guidance is to monitor the maximum deviation of the target from the treatment plan. Often an action limit for target displacement is defined, above which treatment intervention may be required. We evaluated the ability of the CBCT₂ localization to predict the maximum displacement (3D position & scalar excursion) of the prostate at MV delivery from the treatment plan. The difference in 3D position between CBCT₂ and the max displacement at MV delivery is:

$$v = \sqrt{(x_{CBCT} - x_{fluoro})^2 + (y_{CBCT} - y_{fluoro})^2 + (z_{CBCT} - z_{fluoro})^2} \quad 4$$

and the absolute difference in scalar excursion is:

$$s = \left| \sqrt{x_{fluoro}^2 + y_{fluoro}^2 + z_{fluoro}^2} - \sqrt{x_{CBCT}^2 + y_{CBCT}^2 + z_{CBCT}^2} \right| \quad 5$$

where x , y , and z refer to the displacements from the plan in the RL, PA, and SI axes for CBCT₂ and kV fluoroscopy. We also calculated the sensitivity and specificity of detecting a

maximum displacement from the treatment plan greater than 3, 5, and 7 mm (equations 2 and 3). In this situation, a true positive is a fraction in which the displacement measured by kV fluoroscopy and predicted by CBCT₂ was above the threshold. A false positive is a fraction in which the maximum displacement measured by kV fluoroscopy did not exceed the threshold, but was predicted to be above the threshold by CBCT₂. A true negative is a fraction in which neither the maximum displacement measured by kV fluoroscopy or predicted by CBCT₂ exceeded the threshold. And a false negative is a fraction in which the maximum displacement measured by kV fluoroscopy exceeded the threshold, but was not predicted to be above the threshold by CBCT₂.

Results

Rectal Filling

Subjective and objective measures of rectal filling were well correlated, with CBCT images subjectively classified as empty rectum having a gas volume of $0.6 \pm 1.1 \text{ cm}^3$ (mean $\pm$ standard deviation), and CBCT images classified as a full rectum having a gas volume of $15.9 \pm 31.0 \text{ cm}^3$. Pre and post-treatment rectal filling was a significant predictor of prostate intrafraction motion. The difference in prostate motion was found to be significant for pre- and post-treatment rectal filling status classified by visual inspection, with $p < 0.001$ using a Wilcoxon Rank Sum test. Volume of gas in CBCT₁ was correlated with the maximum vector displacement at MV delivery with a CC of 0.37 ($p < 0.001$). Figure 4 shows the ROC analysis using various indicators to predict the maximum displacement at MV delivery. The indicators shown are if the rectum was subjectively classified as full for CBCT₁, and if the gas volume in CBCT₁ was greater than 0.5 and 20 cm^3 . The area under the ROC curve was 0.65 using subjective classification, 0.68 using a gas volume threshold of 0.5 cm^3 , and 0.72 using a threshold of 20 cm^3 , with an area of 1.0 signifying perfect prediction and 0.5 signifying random ranking. Results were similar for post-treatment rectal filling status. 71% of CBCTs were classified as full rectum using the subjective classification. 56% of fractions had an initial gas volume $> 0.5 \text{ cm}^3$ and 12% of fractions had an initial gas volume $> 20 \text{ cm}^3$.

Figure 5 shows the probability of the mean (A) and maximum (B) displacement during MV delivery exceeding a threshold for fractions with initial gas volume $\leq 0.5 \text{ cm}^3$, $> 0.5 \text{ cm}^3$, and $> 20 \text{ cm}^3$. The probability of prostate displacement during MV delivery was greater for larger volumes. Table 1 shows the increased distribution of motion in each axis for fractions with initial gas volume $> 0.5 \text{ cm}^3$. Intrafraction motion increased in all axes for higher gas volume, with the most pronounced increase in PA. Figure 6 is a plot of percentage of fractions per patient with initial gas volume $> 0.5 \text{ cm}^3$ versus the mean vector displacement at MV delivery, and shows the patient-specific effect of rectal filling status. The mean vector displacement at MV delivery increased with the percentage of fractions with gas volume $> 0.5 \text{ cm}^3$ roughly at a rate of 0.02 mm per percent, with $cc = 0.52$ and $p = 0.028$.

Bladder Filling

The ellipsoidal estimates of bladder volume correlated well with the volumes measured by contouring ($cc = 0.93$), with a difference of $4.6 \pm 20.2 \text{ cm}^3$ (mean $\pm$ standard deviation). This is a fairly small considering the bladder volume was $116 \pm 56 \text{ cm}^3$. Bladder volume increased between CBCT₁ and CBCT₂ (median increase = 14%). Figure 7 shows the PA-axis drift of the prostate throughout each fraction versus the percent change in bladder volume, including only fractions with measured initial rectal gas volumes $\leq 0.5 \text{ cm}^3$. Here drift is defined as the difference between the CBCT₂ localization and the mean of all kV fluoroscopy localizations. A weak but statistically significant correlation was measured for this plot ($cc = -0.17$, $p_{PA} = 0.046$). Similar analyses found no significant results in RL and SI axes ($p_{RL} = 0.76$, $p_{SI} = 0.74$), and no correlation was found with initial bladder volume.

Prostate Localization

Plotted in Figure 8A is the error in evaluating intrafraction motion using CBCT₁ only (this is also the distribution of the combined residual setup error and intra-fraction motion measured by kV fluoroscopy), CBCT₂ only (assume CBCT₂ position throughout treatment), and both CBCT₁ and CBCT₂ (linear trajectory model). Both CBCT₂ only and linear trajectory model performed similarly, with the median error decreasing from 2.1 mm (95% within 6.1 mm) for CBCT₁ only to 1.0 mm (95% within 3.8 mm) for CBCT₂ only, and to 1.1 mm (95% within 3.1 mm) for linear trajectory model.

Plotted in Figure 8B is the probability of the maximum vector displacement at MV delivery exceeding a threshold, as well as the vector difference from CBCT₂ (equation 4) and the difference in scalar excursion from CBCT₂ (equation 5). The median error of using post-treatment localization as the maximum displacement at MV delivery was 1.0 mm (95% within 3.6 mm), and the median error of the difference in scalar excursion was, as expected, smaller at 0.6 mm (95% within 2.9 mm). Figure 9 is a plot of max vector displacement from the plan during MV delivery versus the vector displacement from the plan at the post-treatment CBCT acquisition, and shows the high degree of correlation between predicted and actual maximum displacement. Also shown in Figure 9 is the classification of points into TP, TN, FP, & FN for a threshold of 5 mm. The sensitivity and specificity of using CBCT₂ prostate localization to detect maximum displacement during MV delivery greater than 3, 5, and 7 mm is shown in Table 2. The specificity was high for all cases ($\geq 94\%$), while the sensitivity ranged between 75% and 81%.

Discussion

Rectal Filling

There have been multiple studies of the effect of rectal filling on prostate motion. Padhani *et al.* classified rectum status in cine-MRI images based on a subjective grading scale and observed a correlation between moderate rectal distension and prostate motion (5). Mah *et al.* used cine-MRI and observed a statistically significant difference in PA-axis prostate motion between different rectal filling status (6). Ghilezan *et al.* found full rectum to be a predictor of large prostate intrafraction motion (7). Our results are in agreement with these studies, and demonstrate that rectal filling status from pre and post-treatment volumetric imaging is indicative of prostate motion throughout treatment delivery. This was true when rectal filling information was obtained by subjective examination or by using morphological operators to objectively measure the gas volume within the imaged volume. Such information can be easily extracted and used for motion assessment. Furthermore, the effect was shown to be patient specific: patients with gas volume $>0.5 \text{ cm}^3$ on a consistent basis also had larger motion. Our results emphasize the suggestion by Padhani *et al.*, that patients with little or no rectal air are less likely to have significant prostate movement and thus smaller planning margins may be considered (5). Potentially, initial gas volume measured from pre-treatment imaging could be used to make decisions of margin size on a daily basis, or gas volume could be measured in early fractions and used for margin calculation of subsequent fractions in adaptive strategies.

Bladder Filling

Most studies of prostate motion have failed to show any relation to bladder filling for supine (4,14,15) or prone patients (16). Correlation between daily bladder filling status and relative prostate position has been observed in some studies (17,18), however these studies did not investigate intrafraction motion. We found that intrafraction bladder filling was weakly correlated with posterior drift of the prostate when little or no rectal gas ($\leq 0.5 \text{ cm}^3$) was present. Although a slight posterior drift of the prostate due to bladder filling may have significant dosimetric consequences when it occurs over multiple fractions, it can be monitored directly

using post-treatment localization of the prostate. The extraction of bladder volume from volumetric imaging requires either human measurement or sophisticated contouring software, which may be difficult to perform on CBCT due to imaging artifacts. Furthermore, prostate drift correlated with the percent change in bladder volume rather than initial volume, so that the effect cannot be measured prospectively. In summary, analysis of bladder filling from pre and post-treatment volumetric imaging is of little practical benefit to evaluate prostate intrafraction motion.

Prostate Localization

We reported the sensitivity and specificity of using post-treatment prostate localization to predict if a vector displacement greater than 3, 5, and 7mm occurred during MV delivery. This is somewhat similar to the sensitivity reported by Noel *et al.* of using pre- and post-treatment localization to predict if a displacement had occurred lasting for various time periods (3). The sensitivity for Noel *et al.* was never greater than 60%, whereas we report a sensitivity of 75-81%. There are two reasons for this difference. First, there is an underlying difference in what is being measured. For our study we detect whether a displacement above a threshold occurs at each beam, whereas the sensitivity measured by Noel is for all motion throughout the treatment fraction exceeding a particular time duration, regardless of beam delivery schedule. The sensitivity and specificity given by Noel characterize intrafraction motion at a high imaging frequency throughout the treatment fraction and is more useful in prospective prediction of the intra-fraction motion, while our definition is more protocol specific as it is dependant upon the treatment delivery schedule and is more focused on prostate position at beam delivery and more relevant for retrospective dose reconstructions. Furthermore, we use the post-treatment vector displacement as the predicted maximum at MV delivery, which does not require that the linear trajectory between pre- and post-treatment localization exceed a specified threshold for a given time duration. Also our technique differs in that it includes residual setup error in both the CBCT₂ and kV fluoroscopy measurements. Large residual errors will tend to increase the correlation between measurements from kV fluoroscopy and CBCT₂, therefore increasing the underlying sensitivity.

Second, limitations to the kV fluoroscopy measurement technique may tend to underestimate the intrafraction motion and overestimate the sensitivity. We averaged multiple fluoroscopy frames to obtain 1 localization per gantry angle; hence high frequency motion at each gantry angle was not detected with kV fluoroscopy. Also we assume the shortest 3D trajectory that satisfies all fluoroscopy localizations (9). A previous study of the limitations of this technique showed that it will slightly underestimate the prostate motion (12) although SI-axis motion will not be affected by this assumption which is highly correlated with motion in the PA-axis (8,19). These limitations to the kV fluoroscopy intrafraction motion measurement should be taken into consideration in the interpretation of results presented here.

The measured motion by our technique was similar in magnitude to previous studies. Kupelian *et al.* measured 41% of fractions exceeding 3mm, and 15% exceeding 5mm for at least 30s (1). The percentage of fractions with a maximum vector displacement measured by kV fluoroscopy exceeding 3 and 5mm in Figure 8B were similar: 45% were greater than 3mm and 19% greater than 5mm.

Determination of whether pre and post-treatment imaging is adequate will depend upon the localization accuracy required for each specific treatment protocol. Our results indicate that for accuracy of 95% within 6.1 mm, pre-treatment localization is sufficient, i.e., no monitoring or measuring during and after treatment is necessary. To improve the accuracy to 95% within 3.1 mm, pre and post-treatment localization are required. To achieve accuracy higher than 95% within 3.1 mm will require intrafractional localization. It is surprising to learn that the CBCT₂ alone is almost as accurate as the linear trajectory interpolation using both CBCT₁ and

CBCT₂. This shows that the intra-fraction motion measured during MV delivery occurred mostly before the first beam-on. One reason might be that the residual setup errors caused by automatic table correction can be pronounced. Another reason is that the patient may need several minutes to settle down on the treatment table after which the prostate position becomes relatively stable.

In conclusion, in the absence of intrafractional prostate localization information from pre and post-treatment volumetric imaging is useful for assessment of prostate intrafraction motion. Rectal filling status is a significant predictor of prostate motion and is patient specific. Bladder filling does occur throughout treatment duration, and leads to a slight posterior drift of the prostate when little or no gas was present in the digestive system. Prostate motion can be estimated using pre and post treatment imaging with an error of 95% within 3.1 mm, and the sensitivity of detecting a scalar excursion at MV delivery >3 mm using the post-treatment localization was 76%.

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References

1. Kupelian P, Willoughby T, Mahadevan A, et al. Multi-institutional clinical experience with the Calypso System in localization and continuous, real-time monitoring of the prostate gland during external radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;67:1088–1098. [PubMed: 17187940]
2. Kitamura K, Shirato H, Seppenwoolde Y, et al. Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions. *Int J Radiat Oncol Biol Phys* 2002;53:1117–1123. [PubMed: 12128110]
3. Noel C, Parikh PJ, Roy M, et al. Prediction of Intrafraction Prostate Motion: Accuracy of Pre- and Post-Treatment Imaging and Intermittent Imaging. *Int J Radiat Oncol Biol Phys*. 2008In Press, Corrected Proof
4. Beard CJ, Kijewski P, Bussiere M, et al. Analysis of prostate and seminal vesicle motion: implications for treatment planning. *Int J Radiat Oncol Biol Phys* 1996;34:451–458. [PubMed: 8567348]
5. Padhani AR, Khoo VS, Suckling J, et al. Evaluating the effect of rectal distension and rectal movement on prostate gland position using cine MRI. *Int J Radiat Oncol Biol Phys* 1999;44:525–533. [PubMed: 10348281]
6. Mah D, Freedman G, Milestone B, et al. Measurement of intrafractional prostate motion using magnetic resonance imaging. *Int J Radiat Oncol Biol Phys* 2002;54:568–575. [PubMed: 12243837]
7. Ghilezan MJ, Jaffray DA, Siewerdsen JH, et al. Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). *Int J Radiat Oncol Biol Phys* 2005;62:406–417. [PubMed: 15890582]
8. Adamson J, Wu Q. Prostate intrafraction motion evaluation using kV fluoroscopy during treatment delivery: a feasibility and accuracy study. *Med Phys* 2008;35:1793–1806. [PubMed: 18561654]
9. Kotte AN, Hofman P, Lagendijk JJ, et al. Intrafraction motion of the prostate during external-beam radiation therapy: analysis of 427 patients with implanted fiducial markers. *Int J Radiat Oncol Biol Phys* 2007;69:419–425. [PubMed: 17513059]
10. Letourneau D, Wong JW, Oldham M, et al. Cone-beam-CT guided radiation therapy: technical implementation. *Radiother Oncol* 2005;75:279–286. [PubMed: 15890424]
11. Hristov DH, Fallone BG. A grey-level image alignment algorithm for registration of portal images and digitally reconstructed radiographs. *Med Phys* 1996;23:75–84. [PubMed: 8700035]
12. Adamson J, Wu Q. Optimizing monoscopic kV fluoro acquisition for prostate intrafraction motion evaluation. *Physics in Medicine and Biology* 2009;54:117–133. [PubMed: 19075358]
13. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;143:29–36. [PubMed: 7063747]

14. Artignan X, Smitsmans MH, Lebesque JV, et al. Online ultrasound image guidance for radiotherapy of prostate cancer: impact of image acquisition on prostate displacement. *Int J Radiat Oncol Biol Phys* 2004;59:595–601. [PubMed: 15145181]
15. Hoogeman MS, van Herk M, de Bois J, et al. Strategies to reduce the systematic error due to tumor and rectum motion in radiotherapy of prostate cancer. *Radiother Oncol* 2005;74:177–185. [PubMed: 15734206]
16. Zelefsky MJ, Crean D, Mageras GS, et al. Quantification and predictors of prostate position variability in 50 patients evaluated with multiple CT scans during conformal radiotherapy. *Radiother Oncol* 1999;50:225–234. [PubMed: 10368047]
17. Zellars RC, Roberson PL, Strawderman M, et al. Prostate position late in the course of external beam therapy: patterns and predictors. *Int J Radiat Oncol Biol Phys* 2000;47:655–660. [PubMed: 10837948]
18. Roeske JC, Forman JD, Mesina CF, et al. Evaluation of changes in the size and location of the prostate, seminal vesicles, bladder, and rectum during a course of external beam radiation therapy. *Int J Radiat Oncol Biol Phys* 1995;33:1321–1329. [PubMed: 7493857]
19. Poulsen PR, Cho B, Langen K, et al. Three-dimensional prostate position estimation with a single x-ray imager utilizing the spatial probability density. *Phys Med Biol* 2008;53:4331–4353. [PubMed: 18660559]

Figure 1.

CBCT images classified as having empty or full rectums. The rectum was considered full when feces and/or gas were visible in the CBCT images. In each image the area of the rectum used in the subjective classification is highlighted by the box.

Figure 2. Method for bladder volume estimation. The bladder volume was estimated to be ellipsoidal, with the length in each axis being the maximum from the CBCT.

Figure 3. Prostate motion modeled as a linear trajectory between CBCT₁ and CBCT₂ (dashed lines) and the measured positions using kV fluoroscopy at MV delivery.

Figure 4. Receiver Operator Characteristic (ROC) curve showing the ability of rectal filling status from the pre-treatment CBCT to predict the maximum vector displacement of the prostate at MV delivery.

Figure 5. Probability of the mean (A) and maximum (B) displacement of the prostate at MV delivery exceeding a threshold, for fractions with initial gas volume $\leq 0.5 \text{ cm}^3$, $> 0.5 \text{ cm}^3$, and $> 20 \text{ cm}^3$.

Figure 6.
Mean vector displacement of the prostate at MV delivery vs. percentage of fractions with initial gas volume > 0.5 cm³.

Figure 7. Posterior-Anterior (PA) axis drift of the prostate vs. percentage increase in bladder filling between CBCTs for fractions with initial gas volume $\leq 0.5 \text{ cm}^3$.

Figure 8.

Plot A is the error of predicting prostate motion using $CBCT_1$ only, $CBCT_2$ only, and $CBCT_1$ with $CBCT_2$ (assume linear trajectory). Plot B is the probability of maximum vector displacement of prostate at MV delivery exceeding a threshold and the error of measuring max vector displacement (equation 4) & excursion (equation 5) using $CBCT_2$.

Figure 9.

Plot of max vector displacement of the prostate at MV delivery as measured by kV fluoroscopy, versus the vector displacement measured at the post-treatment CBCT.

Table 1

Mean prostate displacement during MV delivery for fractions classified by gas volume measured in the pre-treatment CBCT

axis	mean of absolute prostate displacement (mm)		Wilcoxon Rank Sum test significance (p)
	gas volume $\leq 0.5 \text{ cm}^3$	gas volume $> 0.5 \text{ cm}^3$	
right-left	0.6	0.7	0.066
posterior-anterior	1.2	2.0	<0.001
superior-inferior	1.3	1.6	0.027

Table 2

Ability of post-treatment imaging to predict maximum prostate displacement during MV delivery

displacement (mm)	sensitivity	specificity
3	76%	94%
5	75%	97%
7	81%	97%