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Comparison of Localization Performance with Implanted Fiducial Markers and Cone-Beam Computed Tomography for On-line Image-Guided Radiotherapy of the Prostate

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Abstract

Purpose—To assess the accuracy of kV cone-beam CT (CBCT) based setup corrections as compared to orthogonal MV portal image-based corrections for patients undergoing external-beam radiotherapy of the prostate.

Method and Materials—Daily cone-beam CT volumetric images were acquired after setup for patients with three intra-prostatic fiducial markers. The estimated couch shifts were compared retrospectively to patient adjustments based on two orthogonal MV portal images (the current clinical standard of care in our institution). The CBCT soft-tissue based shifts were also estimated by digitally removing the gold markers in each projection to suppress the artifacts in the reconstructed volumes. A total of 256 volumetric images for 15 patients were analyzed.

Results—The Pearson coefficient of correlation for the patient position shifts using fiducial markers in MV vs kV was ($R^2 = 0.95, 0.84, 0.81$) in the L/R, A/P and S/I directions respectively. The correlation using soft-tissue matching was ($R^2 = 0.90, 0.49, 0.51$) in the L/R, A/P and S/I directions. A Bland-Altman analysis showed no significant trends in the data. The percentage of shifts within a ± 3 mm tolerance (the clinical action level) was (99.7, 95.5, 91.3) for fiducial marker matching and (99.5, 70.3, 78.4) for soft-tissue matching.

Conclusions—Cone-beam CT is an accurate and precise tool for image-guidance. It provides an equivalent means of patient setup correction for prostate patients with implanted gold fiducial markers. Use of the additional information provided by the visualization of soft-tissue structures is an active area of research.

Keywords

cone-beam CT; image-guided; prostate radiotherapy; fiducial markers; surrogates

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Conflict of Interest:

This work was performed in conjunction with the Elekta Synergy Research Group.

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I. Introduction

Highly conformal radiation therapy fields for the treatment of prostate cancer have been shown to reduce the risk of rectal toxicity compared to conventional radiation therapy^{1, 2}. This has permitted dose escalation, with phase II & III trials showing improved biochemical relapse-free survival compared to standard dose radiation therapy^{3, 4}.

Conformal radiotherapy techniques require greater precision in treatment set-up and delivery than conventional techniques if target coverage is to be assured. A geometric margin around the clinical target volume (CTV) is added to account for uncertainties in prostate position as a result of prostate motion and patient set-up errors. However, additional steps in the planning and treatment process are required to minimize these potential sources of error to ensure the target is localized within this planning target volume (PTV). Daily localization of the gland or its surrogate prior to treatment allows this volume to be reduced and provides verification of target coverage. It has been recognized that the prostate is a moveable structure and the nature of its motion is well-documented⁵⁻⁷. Bony anatomy is not a strong surrogate for daily prostate position, therefore portal imaging alone is not sufficient for substantial PTV reductions.

Various methods have been employed to localize the gland. Three-dimensional localisation of the prostate gland using ultrasound has been shown to be an efficient and accurate method^{8, 9}. However, some of the literature reports user difficulty due to poor image quality and there are concerns that the ultrasound probe itself may displace the prostate^{10, 11}. Acquiring CT images using the treatment beam, or Megavoltage CT (MVCT), has been offered as another solution to the online imaging problem^{12, 13}. This permits soft-tissue visualisation but at the cost of high imaging doses (5–15cGy in MV CBCT¹⁴ and 1.5–12cGy in the case of helical MVCT¹⁵) and reduced image quality compared to conventional CT.

A common method is to implant fiducial markers, which can be visualised on megavoltage (MV) electronic portal images (EPIs), as a surrogate for prostate position¹⁶⁻¹⁸. This technique has been used in an online fashion at our institution for more than 7 years and a reduction of post-treatment error to ≤ 3 mm in 99% of treatment set-ups has been demonstrated^{5, 19}. Disadvantages of marker implantation include; an invasive procedure with a potential for discomfort that requires an additional appointment, possible bleeding and infection, and the services of an interventional radiologist. Furthermore, markers provide little information on deformation of the target, localization of the seminal vesicles, or changes in the surrounding normal anatomy. There is data to suggest that the prostate may deform by up to 10 mm irrespective of seed location²⁰.

Cone beam computed tomography (CBCT) is a new technology that permits the acquisition of 3-dimensional (3D) volumetric images while the patient is in treatment position²¹. These images are acquired using a flat panel detector by rotation of a kilovoltage (kV) X-ray source mounted on the accelerator gantry orthogonal to the primary treatment axis (Fig. 1a). Unlike conventional CT scanners, CBCT reconstructs an entire image volume from a single gantry rotation. The resulting image is of high spatial resolution (~ 0.6 mm²²) and has a field of view (FOV) in excess of 40 cm in diameter and 26 cm in the superior-inferior extent. Daily visualization and localization of soft-tissue immediately prior to treatment delivery is now feasible and initial studies have highlighted the potential for this technology to improve the accuracy of treatment delivery²³.

The aim of this study was to compare CBCT guidance using soft-tissue (Fig. 1b) and MV EPI guidance using fiducial markers (Fig. 1c) and assess if they are equivalent methods of determining isocentre corrections. This was achieved by acquiring CBCT and MV EPI datasets

within the same fraction, prior to isocentre correction. MV imaging was used to correct patient position, as per institutional protocol, and the CBCT data was stored for retrospective analysis. The design of this study provided the unique opportunity of acquiring information of daily prostate position over an entire treatment course using three different measurement tools: MV EPIs localizing fiducial markers (MV-FM), CBCT localizing fiducial markers (CBCT-FM), and CBCT localizing soft-tissue (CBCT-ST). A summary of each imaging modality is detailed in Table 2. The required couch shift to correct the isocentre position was compared between these three methods and the level of correlation reported. Ambiguity in interpretation of the images generated by both MV EPIs and kV CBCT was quantified through inter-observer variability studies.

II. Methods and Materials

Sixteen patients with low to intermediate risk prostate cancer provided their informed consent under an ethics approved protocol. This investigation was considered to be a descriptive feasibility study. A sample size of 16 was therefore deemed adequate to evaluate the study objectives and a statistical evaluation was not required. The treatment prescription was 79.8Gy in 42 fractions using 3DCRT⁵. Patients were treated on an Elekta Precise® linear accelerator equipped with cone-beam CT imaging. To target the prostate, three gold fiducial markers (24k, 3mm × 0.8mm) were implanted in the prostate under trans-rectal ultrasound (TRUS) guidance prior to radiation therapy planning².

Positioning and EPI

Patients were immobilized in a VacLok™ bag (MedTec, Orange City, IA) and aligned to the treatment room isocentre using skin marks and a couch height specification. Prior to treatment delivery, orthogonal EPIs (10 cm × 10 cm field @ 6 MV, 3MU's per beam) were acquired and referenced to DRR's generated from the planning CT (voxels: 1 mm × 1 mm × 2 mm slice thickness). Template matching tools available in commercial electronic portal imaging software (iViewGT™, Elekta Limited, Crawley U.K.) were employed to manually calculate the mismatch. Manual adjustments to the couch were performed if the recommended correction was greater than 3mm in any of the cardinal directions. If a shift was executed, a second set of images was acquired for verification. Changes to the initial set-up isocentre position were made if a systematic trend was observed as described in Alasti et al². The EPIs were analyzed offline for a second time by a single observer and all mismatches were recorded in a database for the purposes of this study.

Cone-Beam CT Imaging Process

Acquisition—One CBCT dataset was acquired at every fraction for each patient, immediately after set-up to skin marks and immediately prior to localization of the markers with MV EPIs. The kV source and detector rotate in a circular trajectory capturing approximately 320 2-D radiographs through 360°. This is achieved by slowing the gantry to 2 minutes to complete a full rotation. Each 2-D projection was captured on an amorphous silicon flat-panel detector (RID1640 Perkin-Elmer, Wiesbaden, Germany) with a 133 mg/cm²Gd₂O₂S:Tb scintillator. The detector has an active area of approximately 41 cm × 41 cm with a 1024 × 1024 image matrix and a pixel pitch of 0.4 mm. The x-ray generated image is digitized to a 16-bit depth. In order to generate a field of view (FOV) of sufficient size to image the entire pelvis, the detector is offset 10 cm laterally and a complete 360° of projection data need to be acquired. The FOV in the z-direction was symmetrically collimated to 10 cm, which reduces scatter and the dose applied to the patient. The imaging geometry consists of a 100 cm source-to-axis distance (SAD), and a 153 cm source-to-detector distance (SDD), which yields a magnification factor of 1.53. A technique of 120 kVp, 100 mA, 20ms per exposure for a charge of 2 mAs per projection, was used. The imaging dose delivered was estimated to be 2.1 cGy to the center of

the patient and 3.3 cGy at the periphery (depth 2 cm) per scan²⁴. The reliability and geometric accuracy of the CBCT system has been reported upon previously²⁵. The geometric calibration of the kV cone-beam CT system was performed intermittently based on service to the kV imaging panel and x-ray tube changes. This totaled 12 calibrations over the course of this study.

The projection images are corrected for variations in pixel dark signal and gain. A filtered back-projection technique is employed in the reconstruction²⁶. Flex in the mechanical structure of the gantry system is also corrected for. The reconstruction resolution was set at 1 mm³ for these investigations over a 40 cm × 40 cm × 25.6 cm FOV. All data was processed using a PowerEDGE 4 CPU server (Dell, Austin, TX) with 4 GB memory and 3 TB of RAID5 storage.

A. MV-FM Vs CBCT-FM

The targeting and geometric accuracy were evaluated offline by comparing the MV marker locations to the marker locations imaged via kV cone-beam CT (Fig. 2a). The kV markers were auto-segmented (Fig. 2b) and a center-of-mass (CoM) method was employed to determine the translational shift. A high-resolution reconstruction on a small FOV centered about the isocentre was performed. The 250µm voxel grid allowed for detailed positioning of the kV markers. A histogram-based threshold was applied to recover the marker voxels. These voxels were further segmented into the individual markers based on their slice location. The couch shift is computed as the displacement of the CoM of all three markers.

B. MV-FM Vs CBCT-ST

The markers in the prostate produce artifacts in the reconstructed CBCT image sets and can confound the localization of the prostate boundary. For this reason, the seeds were digitally removed from the images post-acquisition using a novel approach²⁷. A 5 cm × 5 cm × 5 cm cube that encompasses all three of the gold markers was identified and each seed was located in the reconstruction space. These locations were then projected on to each of the 320 projections and were digitally masked from the projection by replacing it with a regional average pixel value and noise. The corrected projections were then reconstructed again to provide the same CBCT dataset with the seeds suppressed (Fig. 2c).

The resulting 'marker-less' cone-beam CT datasets were imported into a commercial treatment planning system (Pinnacle3®, Philips, Madison, WI) to perform a fusion using soft-tissue anatomy. The central voxel of the cone-beam CT datasets were loaded and placed onto the isocentre of the treatment plan according to the geometric calibration process²⁵. The CTV contour from the plan was overlaid upon the cone-beam CT data set. Observers (1 Radiation Therapists + 1 Radiation Oncologist) then performed a manual 3D registration, using translational shifts only, to align the prostate gland (as visualized on the cone-beam CT dataset) with the CTV contour. These shifts were recorded in a database for comparison to the results of the MV and kV marker approaches described in the previous sections.

D. Inter-Observer Study

An observer study was performed to evaluate the influence of inter-observer variation for CTV matching on the CBCT image sets. An image set was randomly chosen from 5 patients. These patients were selected from the 16 study patients and represented a cross-section of patient size. In the intended image-guidance model for cone-beam CT, fraction-by-fraction repositioning will be achieved by therapist-driven registration of the CBCT image to the CT defined CTV (prostate volume). Five radiation therapists with experience using the planning system alignment tools and who are involved in the image-guidance program participated. The observers were given technical instructions with regards to the process but were free to window and level and manipulate the display of the cone-beam CT images as desired. Access to the planning CT images was not permitted in the alignment process. Observers performed a 3D

registration, using translational shifts only, to align the prostate gland as visualized on the CBCT dataset with the CTV contour. The resulting isocentre shift was computed and recorded for each observer and for each dataset.

Statistical Analysis—The Pearson Product Moment Correlation Coefficient was used to measure the correlation in couch shifts between CBCT (FM or ST) and MV EPI results. The difference between the measured couch shifts was then plotted against the average couch shift as recommended by Bland-Altman²⁸ when a new method of measurement is to be compared against a gold standard. If the two measures are equivalent, the difference should show a zero mean and no significant trends. The 95% confidence interval of the error distribution is also reported.

The random (σ), systematic (Σ) and group systematic (M) errors for each guidance method were also calculated²⁹. The distribution of the systematic error was estimated by taking the standard deviation of the mean values for each patient. Inter-observer variation was measured using the same technique for 5 observers over 5 different CBCT images. The difficulty with inter-observer studies using patient data is that there is no ground truth. To overcome this pitfall, the 60% concordance of the shift value for MV marker observations was defined as the truth.

III. Results

The study was well tolerated by all participants with no adverse events. The total elapsed time for participant accrual was 6 months. Treatment appointment times were extended from the normal 15 minutes to 30 minutes to allow for the additional imaging. The clinical workflow was evaluated to measure efficiency and the total time necessary for each fraction was approximately 25 minutes. When compared to the current clinical workflow using EPI, the time for image acquisition was 1.5 min longer for CBCT and the reconstruction of the CBCT images took an additional 1 min. The matching of the images, however, took on average the same amount of time for both the MV-FM and CBCT-ST methods (2 mins).

One patient was excluded from the analysis due to migration of the posterior gold marker during the treatment course. The data from fifteen patients were therefore analyzed, rendering a possible 630 image datasets (15 patients $\times$ 42 fractions). Of these, 83 datasets (~13%) were lost due to either down time of the linear accelerator or the kV imaging system, or rendered unusable due to poor image quality caused by incorrect imaging technique or patient movement during acquisition. The remaining 547 CBCT datasets were deemed useful for the purposes of this study. Overall, a total of 1098 GB of data was collected and stored online.

The elapsed time for data analysis was approximately 9 months. Due to the prohibitive number of man-hours involved in the digital removal of the markers from each dataset, only every second one was analyzed resulting in a total of 256 datasets being employed in the analysis reported here. Fig. 3 contains a trace of the couch shifts for all fractions for one patient as measured by MV-FM, CBCT-FM and CBCT-ST in each of the cardinal directions. This patient was selected, as it is typical of that seen in the study.

MV-FM vs. CBCT-FM

The two-dimensional correlation plots are shown in Fig. 4. Here, the couch shifts measured by the markers from the MV EPIs and by the markers from the volumetric cone-beam CT images for all 15 patients (256 data points) are plotted (x's). A linear regression analysis finds a Pearson's correlation coefficient (R^2) of 0.95, 0.84, and 0.81 in the left-right (LR) (Fig. 4a), anterior-posterior (AP) (Fig. 4b) and superior-inferior (SI) (Fig. 4c) directions, respectively. To discern trends, a Bland-Altman analysis is shown in Fig. 5. The 95% CI is (−0.22, +2.5) LR, (−3.57, +2.43) AP, and (−3.85, +1.86) SI. In our current clinical practice, shifts of greater

than 3 mm are considered to be significant and the computed shift is implemented. The percentage of couch shift agreements within ± 3 mm was 99.7, 95.5 and 91.3 in the LR, AP and SI directions respectively.

Fig. 6(a) plots the computed shift differences between these two modalities in 3D. The ellipsoid represents the 95% CI. Ideally, this ellipsoid should be small (random error), centered on the origin (group systematic error), and its principal components should be aligned with the coordinate axis (data independence). The frequency histograms, Figures 6 (b, c, d), indicate the ensemble mean and SD for the distribution of couch shift differences between MV-FM and CBCT-FM. These are: -1.1 mm (SD 0.7), 0.6 mm (SD 1.5), and 1.0 mm (SD 1.5) in the LR, AP, and SI directions respectively.

MV-FM vs. CBCT-ST

The methods are repeated for comparison of the MV fiducial markers to the CBCT soft-tissue. Here the Pearson's correlations are: $R^2 = 0.90, 0.49, 0.51$ (Fig. 4d-f). The Bland-Altman analysis reveals that the 95% CI of shift-differences is $(-1.14, +2.79)$, $(-5.57, +6.07)$, $(-3.95, +5.57)$ in LR, AP, SI respectively (Fig 5d-f). The percentage of agreement within ± 3 mm was 99.6, 70.3, 78.4% for LR, AP and SI. The mean shift differences between MV markers and soft-tissue matching are -0.8 mm (SD 1.0), -0.2 mm (SD 3.0), -0.8 mm (SD 2.5) in the LR, AP, and SI directions, respectively (Fig7 b-d).

CBCT-FM vs. CBCT-ST

The same results are presented for CBCT fiducial markers vs. CBCT soft-tissue. Here, the shift proposed by the kV fiducial marker is considered to be ground truth. This comparison removes possible uncertainties between the two imaging modalities and the temporal uncertainties since the CBCT and EPI's were taken approximately 2 minutes apart. The Pearson's correlations are: $R^2 = 0.90, 0.55, 0.41$ (Fig. 4g-i), while the Bland-Altman analysis reveals that the 95% CI of shift-differences is $(-2.15, +1.63)$, $(-4.56, +6.31)$, $(-3.74, +7.30)$ in LR, AP, SI respectively (Fig 5g-i). The percentage of agreement within ± 3 mm was 90.8, 63.7, 64.1% for LR, AP and SI. Mean couch shift discrepancies of 0.3 mm (SD 1.0), -0.9 mm (SD 2.8), and -1.8 mm (SD 2.8) in the LR, AP and SI directions (Fig. 8b-d).

Inter-observer Results

The group systematic error, systematic error and random error for the 5 observers over 5 different datasets for MV marker and soft-tissue matching are reported in Table 1. The systematic error was higher for soft-tissue matching using the CTV $\Sigma = (0.61, 1.61, 2.21)$ [mm], than for MV marker matching which was $\Sigma = (0.09, 0.36, 0.28)$ [mm] in the LR, AP and SI directions, respectively. The random error was also higher for the kV soft-tissue matching $\sigma = (1.50, 2.86, 2.85)$ [mm] as compared to the random error in the MV matching $\sigma = (0.26, 0.95, 0.47)$ [mm] in the LR, AP and SI directions, respectively.

Random and Systematic Error

Table 3 represents a summary of the mean (M), random (σ) and systematic errors (Σ) based on the residual differences for MV-FM:CBCT-FM, MV-FM:CBCT(ST), and CBCT-FM:CBCT-ST. The largest value in systematic error is seen in the A/P direction for fiducial markers vs. soft-tissue. Overall, the systematic error for fiducial markers is less than that for soft-tissue. Also, the random errors for soft-tissue matching are greater than corresponding systematic errors.

IV. Discussion

This study has shown that CBCT can successfully acquire daily volumetric images for the purposes of online assessment for image-guidance. The high correlation for the measured isocentre shifts between MV markers and kV markers demonstrates that the CBCT system is capable of sub-mm precision and accuracy when localizing unambiguous objects such as fiducial markers. It is also indicative of the geometric accuracy and robustness of the complete guidance system. The rotated ellipsoidal shape of the 95% CI cloud indicates that the shift differences in AP and SI directions are not independent and this could be attributed to the known rotational motion of the gland about the left-right axis.

There is also a correlation between MV markers and kV soft-tissue although it is less strong. One possible explanation for this is the fact that 2D projection data is being compared with 3D volumetric data, which could render differing results. Another is that, while both the MV and kV data were acquired within the same treatment fraction, there was a time lapse of approximately 2 minutes between the two acquisitions. During this time period it is possible that the prostate could have undergone a displacement, rotation or deformation resulting in a difference in position or shape.

Both of these arguments can be dismissed when examining the correlations between kV markers and kV soft-tissue. These results are derived from exactly the same dataset, therefore, both are volumetric and acquired at precisely the same time. Yet, the correlations are similar to those for MV markers to kV soft-tissue and certainly not as strong as those for MV markers to kV markers. It was therefore concluded that the predominant reason for weaker correlations for soft-tissue registration is due to the uncertainty in locating soft-tissue organs from CT data, which is well documented in the literature for conventional CT³⁰. The inter-observer results from this study show that there is more uncertainty when locating the prostate on CBCT images than when manually registering the markers on the MV EPIs. Contouring of the prostate from the CBCT images was not a component of this study, therefore, the inter-observer variability was not fully evaluated. It can be assumed however, that it would be at the very best comparable to results reported for conventional CT images of the prostate. It may be possible to reduce this uncertainty by using automatic grey-value registration for the prostate which is currently being investigated^{31, 32}.

It was also observed that the correlation data for all modalities were best in the left-right direction compared to the anterior-posterior and superior-inferior directions. This is in concordance with the literature with regards to observers having difficulty in locating the prostate-bladder interface and the prostate apex on conventional CT. The L/R positioning is also supported by the clear symmetry in the pelvic anatomy in this region.

The small population-wide systematic errors within the data could be explained by errors in the geometric coordination of the various software tools and calibrations that are embedded within the system. At the level of precision achieved in this investigation (sub-mm) it is possible to detect systematic errors on the order of 1 mm (as demonstrated in the comparison of MV and kV markers). For example, a 1 mm discrepancy could be due to deviations in the interpretation of a coordinate to be the edge or center of a voxel, errors in the location of line drawing in graphic overlay, or mechanical calibrations at the edge of acceptability. Patient specific systematic errors can be attributed to the comparisons involving CTV contours and markers, which are also subject to inter-observer uncertainties. An error occurring at this stage would therefore influence all subsequent treatment fractions if a contour-based alignment were to be implemented³³. Court et al³⁴ conclude that the inter-observer uncertainties for a contour-based method of alignment are sufficiently small to permit its use. However, Langen et al³⁵ suggest that this may not be the best method of registration for volumetric data and that

anatomy-based registrations are more accurate. Their study, however, also assumes that the CoM for the fiducial markers represents the true prostate position. Recent investigations in our facility have highlighted the imperfect correlation between implanted marker and MR-defined gland position.³⁶

The use of online image-guidance is intended to reduce random and systematic errors. According to certain margin 'recipes', systematic errors have the largest impact on the size of PTV margins²⁹. Craig et al³⁷ relate the effects of errors to tumor control probability (TCP) and state that systematic errors can strongly influence TCP. Our results have shown that systematic errors are very small for the CBCT online localization of the prostate without markers (0.35, 0.99, 0.98) [mm] (L/R, A/P, S/I), assuming MV markers can be taken as the ground truth. Currently, the PTV margins used for patients on this protocol are 10 mm from the CTV isotropically, with the exception of 7 mm on the posterior border. These are considered to be generous for the daily online guidance model in operation here. It is therefore feasible to move to online cone-beam CT guidance for soft-tissue localization without the use of fiducial markers, provided that current PTV margins are maintained.

V. Conclusion

This investigation has shown that cone-beam CT is feasible for daily online image-guidance of the prostate. The methodology of this study was designed to compare a new technology (cone-beam CT) to an existing standard of care (EPI localization of markers). However, markers may not be the best method to test cone-beam CT against since they are a surrogate for daily prostate position. The wealth of additional information provided by cone-beam CT images such as target visualization, critical organ avoidance and assessment of treatment response, offers many potential benefits to radiation therapy delivery that require investigation.

The hardware and software components of cone-beam CT technology are constantly evolving to improve image quality, efficiency and data analysis tools. Further studies have been initiated at our institution to investigate the inter-observer error for prostate delineation on cone-beam CT images and to evaluate the workflow in terms of efficiency in order to further explore the merits of this online guidance system.

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Figure 1.
(a) Photograph of the medical linear accelerator imaging platform with portal imaging system marked in yellow and volumetric imaging system in cyan. Currently, implanted gold fiducial

markers (b) are used to guide daily set-up correction. The same markers appear distinctly using the kV volumetric imaging system (c) as well as bone and soft-tissue structures.

Figure 2.

(a) Volumetric cone-beam CT data set captured after patient set-up. The volumetric data set here is $40 \times 40 \times 25.6 \text{ cm}^3$ with 1 mm^3 voxels and a total imaging dose of 1.4–2.8 cGy. A single coronal slice of the acquisition volume with fiducial markers in FOV is shown in (b). To support

soft-tissue matching of the target volume the markers are digitally suppressed in the projections and reconstructed to yield (c).

Figure 3.

Daily set-up corrections for a typical patient applied in the (a) left/right, (b) anterior/posterior and (c) superior/inferior directions. The (x)'s represents the couch shifts estimated using two orthogonal portal images. The (o)'s represent the shifts based on 3D localization of the center-of-mass of the markers using on-line cone-beam CT while the (diamonds) represent the couch shift estimated by matching the CTV contours to the planning CT.

Figure 4.

Two-dimensional correlations of the applied MV shifts vs. the predicted kV cone-beam CT shifts (a-c), the soft-tissue based shifts (d-e) for all 15 patients. The cone-beam only shifts (fiducial markers vs. soft-tissue) are shown in (g-i). The shift directions were in the (a, d, g) left/right, (b, e, h) anterior/posterior and (c, f, i) superior/inferior directions.

Figure 5.

Bland-Altman error analysis for MV portal image based shifts vs. CBCT fiducial marker based shifts (a-c) and soft-tissue matching (d-f) as well as shifts based on cone-beam soft-tissue vs. cone-beam fiducial markers (g-i) for all 15 patients and all fractions in the (a, d, g) left/right, (b, e, h) anterior/posterior and (c, f, i) superior/inferior directions. The current clinical action levels of ± 3 mm are drawn for reference (dot-dash line).

The (x)'s represent the difference between the predicted shifts based on the CofM of the three fiducial markers measured in kV and MV plotted as a function of the average couch shift. The analysis is repeated for the CTV soft-tissue matching (d, e, f) as denoted by the (o)'s. The final analysis (diamonds) compares the CTV shift to the kV shift (g, h, i).

Figure 6.

Plot of differences between applied MV shift and predicted shift based on kV fiducial markers. The 3D differences are shown in (a). The shaded ellipsoid represents the 95% confidence interval. A histogram of the differences for each cardinal direction is shown for (b) left/right (c) anterior/posterior and (d) superior/inferior.

Figure 7.

Plot of differences between applied MV shift and predicted shift based on CTV. The 3D differences are shown in (a). The shaded ellipsoid represents the 95% confidence interval. The ellipsoid appears rotated about the x-axis. This indicates the shift differences in y, and z are not independent. A histogram of the differences for each cardinal direction is shown for (b) left/right (c) anterior/posterior and (d) superior/inferior.

Figure 8.

Plot of differences between the predicted shift based on kV markers and that based on CTV contours. The 3D differences are shown in (a). The shaded ellipsoid represents the 95% confidence interval. The ellipsoid appears rotated about the x-axis. Again this indicates the shift differences in y, and z are **not** independent. A histogram of the differences for each cardinal direction is shown for (b) left/right (c) anterior/posterior and (d) superior/inferior.

Table 1

Inter-observer variability (group systematic error M , systematic error Σ and random error σ) in MV marker targetting [MV(FM)] and soft-tissue targeting based on CTV contours [CBCT(ST)] for 5 observers over 5 patients in each of the three orthogonal planes. The reference value ("the truth") is chosen to be the 60% concordance between observers.

		x (L/R) [mm]	y (A/P) [mm]	z (S/I) [mm]
MV(FM)	M	0.03	0.15	0.01
	Σ	0.09	0.36	0.28
	σ	0.26	0.95	0.47
CBCT(ST)	M	-1.37	-0.40	1.28
	Σ	0.61	1.61	2.21
	σ	1.50	2.86	2.85

Table 2

Comparison of the three setup correction schemes: fiducial makers in orthogonal MV radiographs MV(FM), fiducial markers localized in cone-beam CT reconstruction CBCT(FM) and soft-tissue matching of the CTV planning contours to the on-line cone-beam CT images CBCT(ST).

Criteria	Comparison of Image-Guided Modality		
	Orthogonal MV Radiographs	Cone-Beam CT	
		Fiducially Markers	Soft-Tissue
Dose	8cGy	2.1–3.3cGy	2.1–3.3cGy
Correction Scheme	use DRR's to match marker locations	CofM shift based on auto-segmented 3D marker locations	Manual match of CTV contours and on-line image
Targeting Accuracy	0.36 [mm]	0.12 [mm]	2.2 [mm]
Acquisition Time	20 sec	2 mins	2 mins
Largest Source of Uncertainty	Marker localization	Intra-fraction motion	Inter-observer variability

Table 3

Estimates of group systematic error (M), systematic error (Σ) and random error (σ) when comparing the 3 different methods of couch shift estimates. The results are based on 15 study patients.

		x (L/R) [mm]	y (A/P) [mm]	z (S/I) [mm]
MV(FM) vs. CBCT(FM)	M	-1.05	0.69	1.00
	Σ	0.35	0.99	0.98
	σ	0.58	1.29	1.27
MV(FM) vs. CBCT(ST)	M	-0.79	-0.35	-0.78
	Σ	0.51	2.22	1.17
	σ	0.89	2.24	2.27
CBCT(FM) vs. CBCT(ST)	M	0.27	-1.01	-1.83
	Σ	0.57	1.97	2.07
	σ	0.85	2.15	2.29