Clinical development of a failure detection-based online repositioning strategy for prostate IMRT—Experiments, simulation, and dosimetry study

Wu Liu^{a)}

Department of Radiation Oncology, Stanford University School of Medicine, Stanford, California 94305-5847 and Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, Connecticut 06510

Jianguo Qian, Steven L. Hancock, Lei Xing, and Gary Luxton^{b)}

Department of Radiation Oncology, Stanford University School of Medicine, Stanford, California 94305-5847

(Received 27 April 2010; revised 27 July 2010; accepted for publication 23 August 2010; published 17 September 2010)

Purpose: To implement and evaluate clinic-ready adaptive imaging protocols for online patient repositioning (motion tracking) during prostate IMRT using treatment beam imaging supplemented by minimal, as-needed use of on-board kV.

Methods: The authors examine the two-step decision-making strategy: (1) Use cine-MV imaging and online-updated characterization of prostate motion to detect target motion that is potentially beyond a predefined threshold and (2) use paired MV-kV 3D localization to determine overthreshold displacement and, if needed, reposition the patient. Two levels of clinical implementation were evaluated: (1) Field-by-field based motion correction for present-day linacs and (2) instantaneous repositioning for new-generation linacs with capabilities of simultaneous MV-kV imaging and remote automatic couch control during treatment delivery. Experiments were performed on a Varian Trilogy linac in clinical mode using a 4D motion phantom programed with prostate motion trajectories taken from patient data. Dosimetric impact was examined using a 2D ion chamber array. Simulations were done for 536 trajectories from 17 patients.

Results: Despite the loss of marker detection efficiency caused by the MLC leaves sometimes obscuring the field at the marker's projected position on the MV imager, the field-by-field correction halved (from 23% to 10%) the mean percentage of time that target displacement exceeded a 3 mm threshold, as compared to no intervention. This was achieved at minimal cost in additional imaging (average of one MV-kV pair per two to three treatment fractions) and with a very small number of repositionings (once every four to five fractions). Also with low kV usage (~ 2 /fraction), the instantaneous repositioning approach reduced overthreshold time by more than 75% (23% to 5%) even with severe MLC blockage as often encountered in current IMRT and could reduce the overthreshold time tenfold (to $<2\%$) if the MLC blockage problem were relieved. The information acquired for repositioning using combined MV-kV images was found to have submillimeter accuracy.

Conclusions: This work demonstrated with a current clinical setup that substantial reduction of adverse targeting effects of intrafraction prostate motion can be realized. The proposed adaptive imaging strategy incurs minimal imaging dose to the patient as compared to other stereoscopic imaging techniques. © 2010 American Association of Physicists in Medicine.

[DOI: [10.1118/1.3488887](https://doi.org/10.1118/1.3488887)]

Key words: intrafraction prostate motion, motion tracking, image-guided radiation therapy, portal imaging, on-board imaging, IMRT, imaging dose reduction

I. INTRODUCTION

A prostate motion management technique is critical for modern high-conformality dose-escalated prostate IMRT. Numerous clinical studies^{1–5} show that in comparison to skin tattoo or bony anatomy alignment, the use of gold markers in conjunction with pretreatment portal MV or on-board kV imaging can significantly reduce the setup margins and therefore potentially lead to decreased normal tissue toxicity. Intrafraction prostate motion is considered to be a limiting factor on

margin reduction,^{1,3} at least for patients with relatively large intrafraction motion.⁶ Because intrafraction prostate motion is generally more unpredictable than respiration motion, techniques developed for respiratory motion correction, such as gating based on external surrogates, are often not directly applicable.

Although recently developed electromagnetic transponders provide real-time 3D localization without radiation dose, they are physically much larger than the gold markers conventionally used in radiographic tracking and produce se-

vere MRI artifacts, hindering MR-based post-treatment assessment.^{7,8} Real-time simultaneous acquisition of two x-ray images from different viewing angles for 3D target localization has also been implemented with submillimeter accuracy, e.g., fluoroscopic imaging using two kV systems^{9–11} and MV-kV imaging using cine-MV and fluoroscopic kV systems.^{12–14} Stereoscopic x-ray imaging with one or two kV sources, however, poses the problem of accumulating excessive patient imaging dose. A reliable reduction of kV beam use would be highly desirable.¹⁵

The prostate is mostly stationary and drifts slowly with abrupt motion occurring only occasionally.^{16–23} In contrast with current motion monitoring techniques, which seek to accurately and continuously localize a moving target, we proposed and simulated a “failure” detection strategy²⁴ to detect in a first step only motion that is potentially beyond a predefined threshold using treatment beam MV imaging, available at no tracking dose cost. The correlative relationship between directional components of prostate motion^{17–19} was used for the first step estimation.²⁴ In a second step, combined MV-kV imaging is performed by turning on the kV imager to assess the overthreshold event. This step also obtains more accurate position information which is later used for interventional motion correction. The kV usage is significantly reduced because cine-MV monitoring alone is sufficient during most of the treatment session. This scheme of using the kV imager adaptively (on an “as-needed” basis) has the potential to significantly improve the current “one-protocol-for-all-treatment” approach in prostate IGRT.

In this work, we implemented the two-step decision-making strategy in the linac’s clinical mode using in-house developed online tracking software and show experimental results for field-by-field based intrafraction motion correction and for hypothetical instantaneous couch repositioning. In a second step, computer simulation is done to compare population-based performance of the different correction strategies. During IMRT treatments, MLC leaf positions can obscure the detection of markers during cine-MV imaging. Therefore, the experiments and simulations were done for IMRT delivery that included the possibility of MLC blockage to demonstrate the performance of the algorithm under conditions similar to what would be encountered in clinical treatment. Methods to mitigate this problem are also discussed.

II. MATERIALS AND METHODS

II.A. Experimental setup

A Varian Trilogy linac (Varian Medical Systems, Palo Alto, CA) equipped with an aSi EPID (PortalVision aS-1000, Varian Medical Systems, Palo Alto, CA) and on-board kV imaging [a 125 kV x-ray tube together with an aSi flat panel imager (PaxScan 4030CB, Varian Medical Systems, Salt Lake City, UT)] devices was used in the study. Physical pixel sizes of the MV and kV detectors are 0.39 mm. Both detectors have a resolution of 1024×768 , corresponding to an effective area of detection of approximately 40×30 cm². The MV and kV source to imager distances were set to 150

and 180 cm, respectively, in all experiments. The MV and kV pixel sizes as scaled to treatment isocenter (100 cm) were therefore 0.26 and 0.22 mm, respectively. Calibration of the on-board imaging system¹³ was done to account for gantry angle-dependent geometric errors caused by gantry sag and imager shift/tilt. The residual geometric error of MV-kV stereoscopic 3D localization was found to be less than 0.5 mm based on measurements of static markers.

The performance of the technique was evaluated experimentally using a 5 cm cubic Styrofoam phantom placed on a 4D motion platform (Washington University, St Louis, MO)²⁵ with either one or three embedded gold markers (1 mm in diameter, 3 mm in length). The motion platform is capable of moving in accordance with a preprogrammed trajectory with a mean positional error of less than 0.2 mm from the inputted trajectory. There are three kinds of intrafraction prostate trajectories in general. The majority of the trajectories are stationary with little movement. Less frequently, the prostate drifts continuously. A small fraction of the trajectories exhibit high-frequency excursions superimposed on a stationary or continuous drift trajectory. Representatives of each of the two types of prostate motion tracks (continuous target drifting and high-frequency excursion) selected from a total of 536 real-time Calypso-measured 3D position tracks of 17 patients¹⁸ were used to program the motion platform for experimental studies. We omitted the stationary tracks because they are not instructive.

A seven-field (30°, 80°, 130°, 180°, 230°, 280°, and 330° gantry angle Varian convention) prostate IMRT treatment plan was delivered to the 4D phantom. All experiments were performed twice to confirm reproducibility. An in-house developed software package installed on a research computer was used to process remotely the clinical images cached on the treatment console computer during treatment delivery in clinical mode.

II.B. Correction, experiment, and simulation strategies

Although prostate motion is generally unpredictable, Calypso real-time monitoring data demonstrated that it is not completely random. The AP and SI motions are highly correlated and the LR motion is small compared to the other two, consistent with the pelvis and prostate anatomy.^{17–19} We detect initial 3D marker position by MV-kV triangulation at the beginning of the treatment. Real-time 2D marker displacement from its original position in the MV image plane is obtained by analyzing cine-MV images. The marker’s in-line movement (perpendicular to the imager plane), and thus its time-varying 3D position, is estimated by combining the 2D projection data with the previously established correlative relationship between the directional components of prostate motion.²⁴ A confirmation request for more accurate localization using MV-kV triangulation is triggered when the estimated prostate displacement based on the cine-MV data is greater than a preset threshold (e.g., 3 mm in this study). The patient is repositioned upon positive MV-kV confirmation (that displacement is greater than an action threshold,

e.g., 2.5 mm in this study) and an accurately measured 3D marker position.²⁴ Using an action level of <3 mm enhanced our confidence level in catching overthreshold motion, although at the cost of a slightly increased number of checkpoint repositioning events. The 3D position is needed because 2D motion information is not sufficient for 3D couch adjustment. The correlative relationship between AP and SI motion is also updated every time a MV-kV pair is acquired. This is a rough-to-accurate approach or an adaptive imaging strategy based on real-time estimation signal and other information. The estimation may not be and does not have to be very accurate due to its 2D nature, but is capable of capturing greater than threshold displacement and thus alerts us to abnormal events; accurate position for motion correction is acquired in the second step, i.e., MV-kV triangulation.

II.B.1. Field-by-field repositioning—Both motion tracking and dosimetric analysis

Most current commercial linacs, including the one used in this study, do not have the option to turn on the kV imager and do not provide automatic remote couch motion function during treatment beam-on. Therefore, in order to implement it in clinical mode, the strategy was first applied on a field-by-field basis, i.e., if a potential overthreshold event is detected by cine-MV imaging, then MV-kV verification is done right before the beginning of the next field instead of instantaneously.

The dosimetric impact was evaluated by attaching a PTW Seven29 2D (27×27) ion chamber array (PTW, Freiburg, Germany) to the motion platform. The 2D array was placed in a horizontal plane perpendicular to the beam central axis for the gantry, oriented so that the beam was pointed vertically down. The array position was the same for all the gantry angles. The marker was placed 3 cm anteriorly to the central ion chamber, which was positioned at isocenter.

II.B.2. Hypothetical instantaneous repositioning—Motion tracking analysis

In a second study, we delivered the IMRT plan in service mode with both cine-MV and fluoroscopic kV imaging on. The kV images were acquired continuously during the second set of experiments because we are currently not able to control the kV-on time, but they were used in the analysis as if they were acquired on an as-needed basis. Hypothetical instantaneous automatic couch repositioning was assumed when necessary.

II.B.3. Simulations—both field-by-field and instantaneous correction—motion tracking analysis

To demonstrate the feasibility and accuracy of the proposed method for the general population, simulation studies were done using all 536 Calypso-measured prostate trajectories.¹⁸ The simulation geometrically projected a fiducial onto the MV and kV imagers and provided the projected

positions as a function of time, which were then used as input for the marker tracking algorithms to estimate the status of prostate motion. The original prostate tracks were used without smoothing. The inaccuracy of the data acquisition system was assumed to be either negligible or correctable through careful system calibration.¹³ A Gaussian detection noise with zero mean and 0.5 pixel standard deviation was, however, added to the projected marker positions based on our experimental results of measuring a static fiducial marker. We simulated seven-field (30° , 80° , 130° , 180° , 230° , 280° , and 330° gantry angle, Varian convention) IMRT with 15 s beam-on time for each field and 50 s between fields. The angles and time intervals were chosen based on typical treatments at Stanford Hospital. To simulate the MLC blockage, we assumed that no fiducial marker was detected for the first and last 3.5 s of each field and at least one marker was detected for the remaining 8 s (i.e., 53% of the time) in good agreement with the experimental findings in Sec. III A. For simulation of the field-by-field correction, we used the 3D marker position 20 s before the field as the MV-kV position if a MV-kV pair was theoretically triggered. In other words, the delay from the imaging to the start of treatment dose delivery was taken as 20 s.

III. RESULTS

III.A. Experimental results

Figure 1 shows two examples of marker tracking and repositioning during a seven-field IMRT delivery using the field-by-field motion correction strategy (Sec. II B 1). There was only one marker used for this set of experiments. Because of MLC blockage during IMRT delivery, the marker was only detected for 41% and 43% of overall beam-on time for the two cases, respectively [see red traces in Figs. 1(c) and 1(d)]. The percentage varied from field to field because of modulation differences and prostate motion differences among the fields. The first case (left panels) represents a continuous target drift. Because the motion magnitude was small and therefore no intervention was done from fields 1 to 4, the black and green traces are the same. One can imagine that stationary prostate motion trajectories are all similar to the situation of fields 1–4. Based on the detection of a potential overthreshold marker displacement during field 5 through cine-MV imaging, orthogonal MV-kV imaging was taken right before field 6. Since the MV-kV measured displacement was greater than our preset 2.5 mm action threshold, the couch was shifted to compensate for the motion. Because of the marker motion from the time when the MV-kV pair was taken to the time when field 6 started and errors of imaging and couch motion, residual displacement existed at the beginning of field 6, i.e., the repositioned marker was not exactly at its original position at the beginning of treatment. The second case (right panels) is selected to represent a high-frequency excursion situation and to show that field-by-field correction is at a disadvantage in fast motion cases compared to instantaneous correction strategy (Sec. II B 2). Cine-MV imaging detected potential overthreshold displacements during fields 2, 3, 4, and 6. The

FIG. 1. Examples of field-by-field correction during a seven-field IMRT delivery. Panels (a) and (b) display two typical Calypso-measured patient prostate motion curves in LR, SI, and AP directions. The gray vertical bars represent the times (compressed scale, actually representing more than 30 s) of gantry rotation between IMRT fields. Panels (c) and (d) show the tracking results using the field-by-field correction method for the two cases corresponding to panels (a) and (b), respectively. The light gray traces represent the magnitude of the marker's vector distance from its position at the beginning of the treatment if no motion correction is done; the black traces represent the true distance with repositioning; and the dark gray traces represent the 3D displacement (with repositioning) estimated by the cine-MV 3D motion estimation method. The dark gray circle symbols in the gray vertical bars indicate the time before the field for which a MV-kV imaging pair occurred and the light gray square symbols denote couch repositioning events determined from MV-kV triangulation.

MV-kV pairs were taken right before fields 3, 4, 5, and 7. Repositioning was done for fields 3 and 4, but not for fields 5 and 7 because the MV-kV pairs showed the 3D marker displacements before fields 5 and 7 were below the 2.5 mm action threshold. The repositionings at fields 3 and 4 were not ideal due to the fast target motion. By the time the fields started, the target had already moved significantly from its position when the MV-kV pairs were taken. The residual displacements were therefore large. The displacements from the repositioned marker to its original position during fields 3 and 4 [black traces in Fig. 1(d)] were even greater than these displacements without intervention (green traces). However, one should note that this is a rare case selected for its unusual characteristics for demonstration purposes.

Dosimetric impact of the field-by-field correction was studied using a 2D ion chamber array. The total delivered dose accumulated from seven fields was measured in three scenarios: Static target, moving target without motion correction, and moving target with motion correction. The static target result was considered as ground truth. Figure 2 shows the gamma analysis results²⁶ for the two test cases with 3% dose difference and 3 mm distance-to-agreement criteria. For the continuous target drift case, the dosimetric benefit with repositioning is clearly shown. This is expected because of the much reduced marker displacement in fields 6 and 7 [Fig. 1(c)]. There were still failed points [Fig. 2(c)] after motion correction. This is because the relatively large marker displacement during field 5 was not corrected instantaneously

FIG. 2. Dosimetric impact of the field-by-field motion correction method: Gamma test results corresponding to the cases of continuous target drift (left panels) and high-frequency excursion (right panels) shown in Fig. 1 without repositioning (top panels) and with field-by-field correction (bottom panels). The measured dose is shown in grayscale. The points with gamma index > 1 are shown in dark gray for cold spots and in light gray for hot spots.

for the field-by-field correction. For the high-frequency excursion case, no matter whether field-by-field correction was performed or not, the target spent a large portion of time at a distance more than 3 mm from its original position [Fig. 1(d)]. Dosimetric benefit with repositioning is not evident in this case, indicating that, as expected, the field-by-field correction may not be robust for fast prostate motions.

The field-by-field correction may be easily implemented clinically with the current equipment as we have demonstrated, with the drawback as mentioned, however. New-generation linacs have the ability to remotely control couch motion and to perform MV-kV imaging during treatment beam-on. Figure 3 shows the real-time marker tracking results with hypothetical instantaneous couch repositioning. The left panels are the results for a continuous drift case and the right panels are for a high-frequency excursion case. The high-frequency case is the same one used for field-by-field experiments to demonstrate the advantage of instantaneous repositioning. The middle panels display the experiments done with open-field monitoring; the bottom panels show the results with IMRT delivery. Three fiducial markers were used for this set of experiments rather than the single marker used in the experiments for field-by-field correction. For 55%–60% of the beam-on time, at least one marker was detected. Marker position information from a planning CT was used to reduce the confusion of detected markers. The percentage of time that the marker displacement exceeded the preset threshold of 3 mm was reduced to 1% and 17% for the two IMRT delivery cases, respectively, compared to 10% and

49% without adaptively moving the couch. For the continuous drift case without correction, the target moved out of range in the last field for most of the field time. The overthreshold motion was picked up and corrected using the instantaneous correction method. In this case, the field-by-field correction method, however, would not have been able to correct it even though it could have been detected. MLC blockage sometimes delayed detection of potential overthreshold motion, therefore reducing the efficiency of repositioning, as indicated in the high-frequency excursion case. Another important source of this overthreshold percentage is the 3D position estimation error of our algorithm. This is demonstrated in field 4 of the high-frequency excursion case. In combination of the facts that the AP and SI motions were not correlated well in this field and the gantry angle was at 180° , which therefore failed to resolve AP motion, for a period of time in field 4, the target was moved more than 3 mm from its original position undetected even when one or more markers could be seen in cine-MV images. Continuous MV-kV imaging could solve the problem at the time when the markers are not completely blocked. This is an example of a tradeoff between undetected large displacement and the excessive usage of kV imaging. Again one should note that this case is rare and was selected to illustrate some of the possible problems. Simulation studies on all the available tracks in Sec. III B will shed some light on whether or not we should give large patient kV imaging dose to catch the rare cases. Although not used for our motion correction algorithm, the continuous MV-kV measured marker displacements are displayed in Figs. 3(e) and 3(f) as blue traces. It shows that the MV-kV triangulation had submillimeter fiducial detection accuracy.

III.B. Simulation results

Three useful evaluation quantities were studied for the 536 patient trajectories as listed in results shown in Tables I and II: (i) The percentage of time that the marker displacement exceeded the preset threshold of 3 mm, which quantified the undetected overthreshold displacement; (ii) the number of kV-on events; and (iii) the number of target repositionings confirmed by simultaneous MV-kV imaging. Table I lists the results for fraction-specific (track-specific) analysis. Table II provides patient-specific results. Two kV-triggering strategies were simulated for the field-by-field correction method, i.e., acquiring a MV-kV pair right before the beginning of the next field after gantry rotation if *any* of the MV-estimated displacements in this field is greater than 3 mm (field-by-field option 0 in Tables I and II) or if the MV-estimated displacement based on the position of the *last* (in time) detected marker is greater than 3 mm (field-by-field option 1 in Tables I and II). If the MV-kV measured displacement is greater than a 2.5 mm action threshold, the patient is repositioned. As shown in Tables I and II, as expected, option 0 provides more opportunity for MV-kV check than option 1 does. Therefore option 0 has slightly better targeting performance with slightly more, but still very negligible, kV usage. In the simulation, we included the MLC problem, but we

FIG. 3. Examples of real-time marker tracking during a seven-field IMRT delivery. The top panels display the programmed prostate motion curves in LR, SI, and AP directions. The middle and bottom panels show the tracking results using the proposed method with open-field delivery (no MLC blockage) and IMRT delivery (with MLC blockage). The dark gray traces in (e) and (f) represent the MV-kV measured displacement only for comparison purpose. They are not used in the correction strategy. For the meanings of other curves, refer to the caption of Fig. 1 for more details.

TABLE I. Track-specific statistical comparison of different repositioning strategies comprising all 536 prostate patient tracks.

	Original motion tracks (no intervention)	Field-by-field (option 0)	Field-by-field (option 1)	Instantaneous repositioning (IMRT)	Instantaneous repositioning (open field)
Mean of percentage of overthreshold time ^a	22.9%	10.1%	12.0%	5.2%	1.5%
Mean number of kV-on per track (treatment fraction) ^b	0	0.48	0.29	1.9	2.5
Mean number of repositioning per track (treatment fraction) ^b	0	0.25	0.21	0.72	1.02

^aThese numbers are obtained based on the 211 3D tracks that contained overthreshold motion.^bThese numbers are obtained by averaging over all 536 3D tracks.

assumed perfect couch repositioning accuracy. The results simulated under open-field situation, i.e., no MLC blockage, are also reported in the last column of Tables I and II. They represent the best possible performance of the different methods. Since there would be about 1500 kV images if regular 15 Hz fluoroscopic imaging were used, the kV usage shown in Table I represents a reduction to much less than 0.5% of that of fluoroscopic kV imaging. For prostate IMRT treatment of 39 fractions, the additional imaging dose is less than 10 cGy for the developed motion correction methods.

The results in Table I show that even though at least one fiducial marker could be detected for only 53% of the MV beam-on time and the repositioning was done field-by-field, the mean percentage of overthreshold time would be reduced to about half compared to the case in which no intervention is taken. This is achieved at a very low cost of additional imaging of an MV-kV pair every two or three treatment fractions (row 3) and a very small number of repositionings of once every four or five treatment fractions (row 4). This protocol can be readily implemented on any linacs equipped with EPID and onboard kV imaging devices. With the new-generation linacs equipped with automatic couch and with kV imaging capability during treatment, the instantaneous repositioning approach has the potential to reduce the overthreshold time by more than 75% (column 5) even with severe MLC blockage. The percentage could be potentially reduced by more than 90% (column 6) if MLC blockage problem can be minimized through inverse planning (see Sec. IV). For instantaneous repositioning, the usage of kV imaging is still minimal at ~ 2 –3 shots per fraction and no additional MV before field is required because a simultaneously acquired MV can be used for pairing with the kV image.

For each patient, the percentage of time that the marker displacement exceeded the preset 3 mm image guidance objective was averaged over all of that patient's fractions. Fig-

ure 4 plots for each patient the averaged percentage of time using the different motion correction methods. Two patients (numbers 6 and 15) had very small prostate motion and for these patients, the total overthreshold time was negligible, even without motion tracking. For all the other patients with noticeable amounts of overthreshold motion, all motion tracking methods significantly reduced the fractional overthreshold time. Instantaneous motion correction is an improvement over field-by-field correction. Tracking performance without MLC blockage is, of course, better than in the presence of MLC blockage. However, even with MLC blockage, the targeting improvement is obvious. Table II lists the mean and maximum percentages over the 17 patients of overthreshold time. It is noteworthy that the maximum patient-specific percentage is about 11% and 6% for field-by-field correction and instantaneous correction, respectively, for IMRT delivery, whereas the corresponding value is as large as 25% if no motion tracking were performed. Clearly, the proposed motion correction methods lead to an improvement from a dosimetric point of view, especially for those patients who have overall large intrafraction prostate motion.

IV. DISCUSSION

Intrafraction prostate motion can compromise highly conformal IMRT delivery. Real-time monitoring of prostate/tumor position is a critical step in dealing with the problem. The solution using prostate position tracking with electromagnetic transponders²⁷ has the drawback that MR-based post-treatment assessment is impeded because the large metallic transponders produce severe MRI artifacts.^{7,8} Stereoscopic fluoro-kV imaging^{9–11} induces undesirably large imaging dose,¹⁵ whereas paired MV-kV imaging^{12–14} uses a single kV source, which reduces the imaging dose. Using single-source continuous MV or kV imaging to estimate 3D marker position has also been studied.^{28–30} Because the latter

TABLE II. Patient-specific statistical comparison of different repositioning strategies comprising all 536 prostate patient tracks.

	Original motion tracks (no intervention)	Field-by-field (option 0)	Field-by-field (option 1)	Instantaneous repositioning (IMRT)	Instantaneous repositioning (open field)
Mean of percentage of overthreshold time	9.0%	4.0%	4.8%	2.0%	0.6%
Maximum percentage of overthreshold time	24.8%	10.8%	12.4%	6.1%	1.4%

FIG. 4. Total percentage of time that the marker displacement exceeded the preset 3 mm image guidance objective for each patient using the different motion correction methods.

methods try to infer 3D information from a single 2D image, any target motion is assumed either to take the shortest possible path^{28,29} or to follow a pre-established probability density distribution.³⁰ Motion correction would therefore be based on estimated 3D coordinates that may not represent the true position and could cause uncontrollable correction error. We have proposed rough-to-accurate failure detection motion correction strategies using cine-MV with as-needed kV imaging for IMRT (Ref. 24) and volumetric modulated arc therapy³¹ treatments by taking advantage of the correlative relationship between directional components of prostate motion and/or continuous gantry rotation. The failure detection method incorporates the advantages of both single-source and dual-source imaging. It uses the kV beam adaptively (only when MV information is not enough for decision making), thus significantly reduces the kV imaging dose while maintaining high clinically relevant targeting accuracy. Motion correction is accomplished based on MV-kV measured “true” target position. Our previous publications^{24,31} presented the failure detection-based adaptive imaging concept and simulation results without taking into account MLC blockage problem. In this study, we evaluated the concept experimentally, taking into account the MLC blockage, and introduced a new field-by-field correction method which is ready for clinical use. We developed a software package that implements the field-by-field correction in a linac’s clinical mode. The present experiments were done using patient IMRT plans and dosimetric effects were investigated.

Once real-time prostate position information is obtained, the next step is to utilize it to guide motion compensation. One straightforward way is to adjust the couch position once an overthreshold motion is detected. Although shifting the patient position can alter source to skin distance and effective depth of a target volume, these changes have a negligible dosimetric effect.³² No adjustment to the number of monitor units is necessary. In this work we experimentally

implemented, within a linear accelerator’s clinical treatment mode, a method of detecting potential large motion of the target and correcting for it by shifting the couch before the next field, if, by prescribed additional imaging, the target movement was confirmed to be above a defined threshold. The results showed significant improvement on tumor targeting efficiency with little additional kV imaging dose or effort. This technique can readily be used on present-day linacs equipped with EPID and OBI. No additional hardware or complex software is required. Treatment flow is generally unaltered. No complex statistical model is required; thus training data are not needed. No complicated optimization is used, so real-time decision making is unimpeded. Intrafraction motion can also be compensated for by automatically moving a robotic couch in real time in response to detected organ motion.^{33–35} Although the linac used in this study does not currently have this function, we experimentally studied the performance of the failure detection strategy with instantaneous correction by retrospectively adding hypothetical automatic couch control. Targeting efficiency was further improved compared to using the field-by-field method. Dynamic MLC tracking is an alternative method to compensate for intrafraction motion in real time. Although not yet available for clinical use, tracking under the guidance of our proposed continuous MV-kV method^{12,13} has been demonstrated.³⁶ The proposed failure detection strategy has also been implemented using dynamic MLC. Those results will be reported elsewhere.

With respect to MV imaging during IMRT, an obvious concern is the effect of the MLC blockage problem, i.e., when multisegmented intensity-modulated MV beams are used for imaging during treatment, fiducial markers may be partially or completely blocked by MLC leaves at certain times, reducing tracking efficiency. Traditional step-and-shoot IMRT, like the ones we used in our experiments, first optimizes the intensity map and then does leaf sequencing to obtain deliverable aperture shapes. There are about 20–30 beam segments in each field. Many segments, especially at the beginning and end of each field, have relatively small aperture. Complete blockage of all markers happens mostly at these small-aperture segments, which tend to be inefficient and less dosimetrically important than segments of larger aperture. This is the reason we assumed for our simulation studies that no marker was detected during the first and last part of each field.

The continuously growing popularity of the use of direct aperture optimization³⁷ and most recent compressed sensing-based optimization^{38,39} suggests that the marker blockage problem will be greatly diminished. Those optimizations lead to a plan with a significant reduction in the number of segments (typically around five) while maintaining the dosimetric benefits of IMRT. Segment apertures are generally large and the chance of blocking all the markers is much smaller than with conventional segments. In addition, McNiven *et al.*⁴⁰ showed that the IMRT deliverability favors less complex plans.

A fiducial blockage avoidance strategy has been investigated in the context of a 4D inverse planning study.⁴¹ It was

shown that it is possible to ensure “seeing” at least one of the implanted metallic markers in any of the IMRT segments during step-and-shoot dose delivery by adding to the objective function a hard or soft constraint that characterizes a level of preference for the fiducial to be included in segmented fields. It was found that the final dose distributions of three plans (constraint-free, soft, and hard constraints) were very similar, which is understandable because the fiducial markers are generally placed inside the target volume, which in this case is the prostate. Therefore, we do not expect dosimetric disadvantage to the patients when using a plan that avoids fiducial blockage. Several other sources of information that could help estimate the coordinates of a MLC-blocked marker were discussed in a previous report.¹³ Even though highly segmented plans were used in our experiments and severe marker blockage was assumed in our simulation, our results demonstrated significant improvement of targeting efficiency from applying our motion correction strategy.

Combined marker and MLC motion with use of multiple markers leads to possible detection confusion among markers, especially when not all markers can be seen in the aperture. Taking into account the prior position knowledge from planning CT and the efficient use of information from neighboring image frames and application of speed constraints alleviate the problem in our experiments. Based on the discussion above, the MLC blockage problem is not critical. Therefore, the present work has been focused on the more important issues of reducing of imaging dose to the patient and correcting motion using measured true target 3D position.

Intrafraction prostate motion is generally considered to be a limiting factor on margin reduction^{1,3} because the setup margin may be much reduced with IGRT.¹⁻⁵ By incorporating geometrical uncertainties of target delineation, localization device, and delivery system, Li *et al.*,⁶ however, reported that intrafraction prostate translation plays a minor role in the CTV-to-PTV treatment margin for the general population. This is because the general population intrafraction motion uncertainty is small. But for a small fraction of patients with large intrafraction motion, motion correction could improve treatment outcome.⁶ That study supports the advantage of failure detection-based correction because the algorithm is more sensitive for detecting and correcting large prostate motion and therefore ensuring that the margin set for the general population can be safely used for the patients with large intrafraction motion. In principle, it is possible to develop a patient-specific adaptive therapy strategy which modifies the failure detection parameters for different fractions based on observed intrafraction motion in the delivered treatment fractions. This is because, although large intrafraction prostate motion is generally unpredictable, patients with large intrafraction prostate motion in early fractions may be more likely to have large intrafraction motion in later fractions. Studies show that the percentage of time that the prostate moves out of a certain range increases with treatment time. Thus, with increased interest in hypofractional treatment, which protracts the delivery, the need for intrafraction motion correction will be further increased.

In comparison to dose in the absence of intrafraction prostate motion, Hossain *et al.*⁴² found that dose volume histograms exhibited very small changes for the case of small intrafraction movements, but showed significant change when the prostate moved sporadically more than 5 mm. Dosimetric effects caused by small motions are more likely to wash out due to fractionated treatment than those caused by large motions. Gold marker segmentation can be achieved in real time with relatively high accuracy from simultaneously acquired MV and kV pelvis phantom images⁴³ and from EPID thorax phantom images.⁴⁴ Due to the limitations of the segmentation algorithm, marker detection error cannot be ignored. Although not critically for marker detection, scattering from the other modality can reduce the quality of images in paired MV-kV imaging for clinical cases,^{43,45} causing deteriorated accuracy in marker localization. Due to geometry calibration and couch positioning error, correcting small displacements (e.g., 1 mm) would not be necessary because the whole tracking system can achieve at best 0.5–1 mm accuracy. All the above reasons led us to ignore those below-threshold displacements for the sake of reducing resource-intensive and imaging dose-costly operations. One can reasonably conclude that continuous accurate localization is not necessary. The choice of 3 mm threshold balances the dosimetric benefits against kV imaging dose, complexity of motion management, and the CTV-to-PTV margin. For patients with implanted fiducials, our department typically uses a ~5 mm CTV-to-PTV margin with reduction to ~3 mm posteriorly with manual adjustment to avoid the rectum based on individual anatomy. Our proposed technique is toward further margin reduction to reduce the dose to OARs so as to enable benefits from dose escalation.

Although not as significant as for respiratory motion correction due to the much lower prostate motion speed, system latency may slightly degrade performance. On the other hand, because of the randomness of prostate motion, prediction is unsuitable to compensate for latency. For the proposed technique, because MV images do not incur additional dose, they can be acquired at the fastest possible frame rate to reduce system latency caused by the waiting time between successive images. The displacement estimation error, such as the one shown at field 4 of the high-frequency excursion case (Sec. III A), can be reduced by using more sophisticated estimation algorithms such as giving preference to performing lateral kV imaging, because AP motion is usually larger than LR motion. The undetected overthreshold motions were mainly in the inline direction because displacements in this direction were estimated, whereas those parallel to the MV imager were measured. Dosimetric consequences of uncorrected inline motions, however, are generally less important than those of overthreshold motions perpendicular to the treatment beam direction.

V. CONCLUSION

This failure detection-based intrafraction motion management strategy is suitable for the correction of “unpredictable” motion, which is the nature of prostate intrafraction motion,

but not only prostate motion. This is the first time implementation of online 3D patient motion correction strategy in clinical mode during IMRT delivery utilizing existing treatment equipment. This strategy is characterized by minimal kV imaging because of informed exploration of “dose-free” cine-MV imaging. The problem that fiducial markers may be blocked by MLC leaves in cine-MV images during IMRT is not impossible or difficult to solve. Even with severe blockage, targeting efficiency was significantly improved by using either a clinic-ready field-by-field method or a more accurate instantaneous correction approach. This rough-to-accurate two-step decision-making strategy significantly reduces the kV usage because marker displacement is estimated using only cine-MV information in a first step, and furthermore, the estimation does not have to be very accurate because accurate 3D target position is acquired in a second stereoscopic imaging step and only as needed. This also ensures motion correction is always based on true target position. It represents a critical, but straightforward, translation of advanced physics research into clinical application. This imaging and repositioning protocol can potentially rival other real-time target monitoring devices.

ACKNOWLEDGMENTS

The authors thank Dr. P. Kupelian and Dr. K. Langen for providing the Calypso data, and Dr. P. Keall, Dr. B. Choi, and Dr. P. Poulsen for their useful discussion in this study. This project was supported in part by grants from the Department of Defense Prostate Cancer Research Program (Grant Nos. W81XWH-09-1-0180 and W81XWH-09-1-0281) and NIH (Grant No. 1R01 CA104205).

^{a)} Author to whom correspondence should be addressed. Electronic addresses: wu.liu@yale.edu

^{b)} Telephone: (650) 498-5866; Fax: (650)498-4015; Electronic mail: gluxton@stanford.edu

¹ J. F. Aubry *et al.*, “Measurements of intrafraction motion and interfraction and intrafraction rotation of prostate by three-dimensional analysis of daily portal imaging with radiopaque markers,” *Int. J. Radiat. Oncol., Biol., Phys.* **60**(1), 30–39 (2004).

² J. M. Pawlowski *et al.*, “Reduction of dose delivered to organs at risk in prostate cancer patients via image-guided radiation therapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **76**(3), 924–934 (2010).

³ C. Beltran, M. G. Herman, and B. J. Davis, “Planning target margin calculations for prostate radiotherapy based on intrafraction and interfraction motion using four localization methods,” *Int. J. Radiat. Oncol., Biol., Phys.* **70**(1), 289–295 (2008).

⁴ I. Gauthier *et al.*, “Dosimetric impact and theoretical clinical benefits of fiducial markers for dose escalated prostate cancer radiation treatment,” *Int. J. Radiat. Oncol., Biol., Phys.* **74**(4), 1128–1133 (2009).

⁵ D. W. Litzberg *et al.*, “Influence of intrafraction motion on margins for prostate radiotherapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **65**(2), 548–553 (2006).

⁶ J. S. Li *et al.*, “Gains from real-time tracking of prostate motion during external beam radiation therapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **75**(5), 1613–1620 (2009).

⁷ X. Zhu *et al.*, “Tradeoffs of integrating real-time tracking into IGRT for prostate cancer treatment,” *Phys. Med. Biol.* **54**(17), N393–N401 (2009).

⁸ L. Xing, L. Lee, and R. Timmerman, in *Image Guided and Adaptive Radiation Therapy*, edited by R. Timmerman and L. Xing (Lippincott Williams and Wilkins, Philadelphia, 2009).

⁹ R. I. Berbeco *et al.*, “Integrated radiotherapy imaging system (IRIS): Design considerations of tumour tracking with linac gantry-mounted diagnostic x-ray systems with flat-panel detectors,” *Phys. Med. Biol.* **49**(2),

243–255 (2004).

¹⁰ K. R. Britton *et al.*, “Evaluation of inter- and intrafraction organ motion during intensity modulated radiation therapy (IMRT) for localized prostate cancer measured by a newly developed on-board image-guided system,” *Radiat. Med.* **23**(1), 14–24 (2005).

¹¹ H. Shirato *et al.*, “Real-time tumour-tracking radiotherapy,” *Lancet* **353**(9161), 1331–1332 (1999).

¹² R. D. Wiersma, W. H. Mao, and L. Xing, “Combined kV and MV imaging for real-time tracking of implanted fiducial markers,” *Med. Phys.* **35**(4), 1191–1198 (2008).

¹³ W. Liu *et al.*, “Real-time 3D internal marker tracking during arc radiotherapy by the use of combined MV-kV imaging,” *Phys. Med. Biol.* **53**(24), 7197–7213 (2008).

¹⁴ W. Mao, R. D. Wiersma, and L. Xing, “Fast internal marker tracking algorithm for onboard MV and kV imaging systems,” *Med. Phys.* **35**(5), 1942–1949 (2008).

¹⁵ M. J. Murphy *et al.*, “The management of imaging dose during image-guided radiotherapy: Report of the AAPM Task Group 75,” *Med. Phys.* **34**(10), 4041–4063 (2007).

¹⁶ A. N. T. J. Kotte *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.* **69**(2), 419–425 (2007).

¹⁷ P. Kupelian *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.* **67**(4), 1088–1098 (2007).

¹⁸ K. M. Langen *et al.*, “Observations on real-time prostate gland motion using electromagnetic tracking,” *Int. J. Radiat. Oncol., Biol., Phys.* **71**(4), 1084–1090 (2008).

¹⁹ H. S. Li *et al.*, “Dosimetric consequences of intrafraction prostate motion,” *Int. J. Radiat. Oncol., Biol., Phys.* **71**(3), 801–812 (2008).

²⁰ K. T. Malinowski *et al.*, “Efficient use of continuous, real-time prostate localization,” *Phys. Med. Biol.* **53**(18), 4959–4970 (2008).

²¹ T. R. Willoughby *et al.*, “Target localization and real-time tracking using the Calypso 4D localization system in patients with localized prostate cancer,” *Int. J. Radiat. Oncol., Biol., Phys.* **65**(2), 528–534 (2006).

²² Y. Q. Xie *et al.*, “Intrafractional motion of the prostate during hypofractionated radiotherapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **72**(1), 236–246 (2008).

²³ C. Noel *et al.*, “Prediction of intrafraction prostate motion: Accuracy of pre- and post-treatment imaging and intermittent imaging,” *Int. J. Radiat. Oncol., Biol., Phys.* **73**(3), 692–698 (2009).

²⁴ W. Liu, G. Luxton, and L. Xing, “A failure detection strategy for intrafraction prostate motion monitoring with on-board imagers for fixed-gantry IMRT,” *Int. J. Radiat. Oncol., Biol., Phys.* (to be published).

²⁵ K. Malinowski *et al.*, “Development of the 4D phantom for patient-specific, end-to-end radiation therapy QA,” in Proceedings of the SPIE Medical Imaging Conference, Physics of Medical Imaging, 2007, San Diego, CA, Vol. 65100E.

²⁶ D. A. Low and J. F. Dempsey, “Evaluation of the gamma dose distribution comparison method,” *Med. Phys.* **30**(9), 2455–2464 (2003).

²⁷ J. M. Balter *et al.*, “Accuracy of a wireless localization system for radiotherapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **61**(3), 933–937 (2005).

²⁸ J. Adamson and Q. Wu, “Prostate intrafraction motion evaluation using kV fluoroscopy during treatment delivery: A feasibility and accuracy study,” *Med. Phys.* **35**(5), 1793–1806 (2008).

²⁹ J. Adamson and Q. Wu, “Optimizing monoscopic kV fluoro acquisition for prostate intrafraction motion evaluation,” *Phys. Med. Biol.* **54**(1), 117–133 (2009).

³⁰ P. R. Poulsen *et al.*, “Three-dimensional prostate position estimation with a single x-ray imager utilizing the spatial probability density,” *Phys. Med. Biol.* **53**(16), 4331–4353 (2008).

³¹ W. Liu, R. D. Wiersma, and L. Xing, “Optimized hybrid MV-kV imaging protocol for volumetric prostate arc therapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **78**(2), 595–604 (2010).

³² A. B. Hwang, E. Kinsey, and P. Xia, “Investigation of the dosimetric accuracy of the isocenter shifting method in prostate cancer patients with and without hip prostheses,” *Med. Phys.* **36**(11), 5221–5227 (2009).

³³ W. D. D’Souza, S. A. Naqvi, and C. X. Yu, “Real-time intra-fraction-motion tracking using the treatment couch: A feasibility study,” *Phys. Med. Biol.* **50**(17), 4021–4033 (2005).

- ³⁴P. Qiu *et al.*, "Inferential modeling and predictive feedback control in real-time motion compensation using the treatment couch during radiotherapy," *Phys. Med. Biol.* **52**(19), 5831–5854 (2007).
- ³⁵J. Wilbert *et al.*, "Tumor tracking and motion compensation with an adaptive tumor tracking system (ATTS): System description and prototype testing," *Med. Phys.* **35**(9), 3911–3921 (2008).
- ³⁶B. Cho *et al.*, "First demonstration of combined kV/MV image-guided real-time dynamic multileaf-collimator target tracking," *Int. J. Radiat. Oncol., Biol., Phys.* **74**(3), 859–867 (2009).
- ³⁷D. M. Shepard *et al.*, "Direct aperture optimization: A turnkey solution for step-and-shoot IMRT," *Med. Phys.* **29**(6), 1007–1018 (2002).
- ³⁸L. Zhu *et al.*, "Using total-variation regularization for intensity modulated radiation therapy inverse planning with field-specific numbers of segments," *Phys. Med. Biol.* **53**(23), 6653–6672 (2008).
- ³⁹L. Zhu and L. Xing, "Search for IMRT inverse plans with piecewise constant fluence maps using compressed sensing techniques," *Med. Phys.* **36**(5), 1895–1905 (2009).
- ⁴⁰A. L. McNiven, M. B. Sharpe, and T. G. Purdie, "A new metric for assessing IMRT modulation complexity and plan deliverability," *Med. Phys.* **37**(2), 505–515 (2010).
- ⁴¹Y. Ma *et al.*, "Four-dimensional inverse treatment planning with inclusion of implanted fiducials in IMRT segmented fields," *Med. Phys.* **36**(6), 2215–2221 (2009).
- ⁴²S. Hossain *et al.*, "Simulated real time image guided intrafraction tracking-delivery for hypofractionated prostate IMRT," *Med. Phys.* **35**(9), 4041–4048 (2008).
- ⁴³W. H. Mao *et al.*, "A fiducial detection algorithm for real-time image guided IMRT based on simultaneous MV and kV imaging," *Med. Phys.* **35**(8), 3554–3564 (2008).
- ⁴⁴S. J. Park *et al.*, "Automatic marker detection and 3D position reconstruction using cine EPID images for SBRT verification," *Med. Phys.* **36**(10), 4536–4546 (2009).
- ⁴⁵W. Luo *et al.*, "Analysis of image quality for real-time target tracking using simultaneous kV-MV imaging," *Med. Phys.* **35**(12), 5501–5509 (2008).