An optimization algorithm for 3D real-time lung tumor tracking during arc therapy using kV projection images

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Purpose: To develop a real-time markerless 3D tumor tracking using kilovoltage (kV) cone-beam CT (CBCT) projection images during volumetric modulated arc therapy (VMAT) treatment of lung tumors.

Methods: The authors have developed a method to identify the position of lung tumors during VMAT treatment, where the current mean 3D position is detected and subsequently the real time 3D position is obtained. The mean position is evaluated by iteratively minimizing an observation error function between the tumor coordinate detected in the imaging plane and the coordinate of the corresponding projection of the estimated mean position. The 3D trajectory is reconstructed using the same optimization formalism, where an observation error function is minimized for tumor positions confined within a predefined amplitude bin as determined from the superior-inferior tumor motion. Dynamic phantom experiments were performed and image data acquired during patient treatment were analyzed to characterize the reconstruction ability of the proposed method.

Results: The proposed algorithm needs to acquire kV projection data until a certain gantry angle is passed through, termed the black-out angle, before accurate estimation mean 3D tumor position is possible. The black-out angle for the mean position method is approximately 20°, while for the 3D trajectory reconstruction an additional ∼15° is required. The mean 3D position and 3D trajectory reconstruction are accurate within ±0.5 mm.

Conclusions: The authors present a real-time tracking framework to locate lung tumors during VMAT treatment using an optimization algorithm applied to CBCT kV projection images taken concomitantly with the treatment delivery. The authors’ technique does not introduce significant additional dose and can be used for real-time treatment monitoring.

Key words: CBCT, VMAT, lung tumor tracking, kV projection images

1. INTRODUCTION

The intrafraction variability of lung tumor position during radiotherapy treatment may cause large dose discrepancy between planned and delivered dose.1–4 This effect is increased when the duration of treatment delivery is longer, such as in hypofractionated lung treatment or highly modulated techniques such as volumetric intensity modulated arc therapy (VMAT).5 Motion compensation technology has been proposed and used to reduce the intrafraction variability, including respiratory gating and active breathing control.6–8 However, gating and breathing control techniques lead to greatly increased treatment times and are not feasible for complex treatment plans, where the treatment beam is gated and turned on and off multiple times.9 Therefore, free breathing planning and treatment delivery is most commonly used clinically, using the temporally averaged position in the respiratory cycle.7,10,11 To improve on such treatment, methods to monitor in real time the target position and to quantify the intrafraction shift from the planned position are needed.

Several research groups11–15 have studied lung tumor motion characteristics during free breathing and have proposed various strategies for its motion management. These management strategies can be grouped in four categories. The first strategy uses anatomic landmarks as a surrogate of the respiratory cycle.16,17 The most commonly used anatomic surrogate for lung tumor motion is the anterior–posterior (AP) motion of the abdominal surface.18–21 However, several studies22–24 have shown that the relationship between the external surrogate motion and the internal tumor motion can change and decorrelate during the treatment. Therefore, the internal-external correlation is patient specific and may not be generalized.25,26

The second strategy uses real-time portal images of the tumor itself, termed markerless tracking.13,26–29 However, the low contrast of the tumor with respect to surrounding tissue, and the partial occlusion that occurs at different treatment angles, make the MV portal imaging difficult to implement and use clinically.30

The third strategy uses fluoroscopic tracking of radiopaque fiducial markers implanted in, or close to, the lung tumor.31–33 Although the tracking accuracy of this method can be better than 1.5 mm,34 robust implantation of fiducial markers in the lung has proven to be difficult with regards to
marker stability during respiratory motion and the risk of pneumothorax.\textsuperscript{11,35,36}

The fourth strategy uses fluoroscopic tracking of the lung tumor without radiopaque markers. Since this method is not invasive and offers the best tumor contrast, there has been a growing interest recently in the scientific literature.\textsuperscript{12,15,37-43} For example, Zeng et al.\textsuperscript{37} estimated 3D respiratory motion based on kV projection images using a generic B-spline motion model, where a minimum of 180° gantry rotation is required to solve the parameters in the model. Li et al.\textsuperscript{38} developed a 3D lung tumor localization method based on principal component analysis (PCA), where the accuracy of the tracking algorithm is limited by the accuracy of training deformable vector field derived using the demons algorithm.\textsuperscript{44} Lewis et al.\textsuperscript{42,43} developed a phase-binned tumor trajectory reconstruction method. The method can only provide one representative phase-binned tumor trajectory from a CBCT scan, however, with the aid of a breathing signal provided by an additional device.

Several methods have been developed where the most prevalent technique involved was using fluoroscopic images\textsuperscript{39,40,45} but with drawbacks as being relatively cumbersome and with long time to clinical implementation as well as difficulty in applying the techniques to rotational therapy. A comprehensive review of tracking lung tumors using markerless techniques is presented in the papers by Lewis et al.\textsuperscript{42,43}

This work presents a markerless 3D tumor tracking technique that provides real-time tumor trajectory reconstruction using the most common kilovoltage imaging technology (kV) by employing the cone-beam CT (CBCT) projection images acquired during treatment.

The proposed method has the ability to construct a representative trajectory based on amplitude binning of the detected SI motion. A representative trajectory may be nearly as useful as a complete motion trace.\textsuperscript{42,43} The SI motion is extracted via kV projection images in real-time, thus, no extra breathing information is needed. Our study is focused on the VMAT treatment modality, which is capable of delivering high dose rates while the gantry is continuously rotating. Due to the dynamic nature of VMAT, monitoring the position of moving lung tumors during the radiation treatment is highly desirable.\textsuperscript{5} When intrafraction tumor motion variation occurs, there is a possibility of delivering high dose outside of the planned target volume, making tumor monitoring to validate dose delivery imperative. The technique developed allows us to characterize the target trajectory using its mean position, standard deviation, and excursion, based on which decisions can be made to reposition the patient during the treatment or to reconsider the treatment plan.

2. METHODS AND MATERIALS

We have developed a method to identify the target mean 3D position until sufficient information is acquired to further obtain a representative trajectory in real-time. The clinical data acquisition steps are described below along with specifics of the algorithms developed.

2.A. Simulation and planning procedure

A respiratory correlated CT (4DCT) was acquired on a multislice helical CT simulator (Brilliance Big Bore; Philips Medical Systems, Andover, MA). The 4DCT was sorted into 10 phases using equally distributed temporal bins. An average intensity CT is constructed from the 4DCT and used for the treatment planning process. The gross tumor volume (GTV) is delineated in one of the exhale phase CT (phase 4 or 5) and propagated to all remaining phases using an in-house developed deformable registration algorithm.\textsuperscript{46} An Internal Target Volume (ITV) is constructed by the union of the phase dependent GTVs. The ITV is transferred to the average CT scan where the treatment plan is generated. The process described above is applied to all lung cancer patients treated in our clinic.

2.B. Reference image set

The average CT cannot always be identified with a particular phase CT set, especially if the tumor motion shows a large hysteretic trajectory,\textsuperscript{9} as the average tumor position may not be part of the tumor trajectory. A mid-ventilation phase CT, corresponding to the middle of the respiratory process (phase 4 or 5), was chosen to create an angle dependent reference image set based on Digital Radiography Reconstruction (DRR) images. The DRRs were generated with 1° resolution, resulting in 360 reference DRR images. The mid-ventilation CT phase of the DRR set is chosen so that the target is at the closest position to its corresponding position within the average 4DCT set. This way, for a given angle, the reference DRR represents a temporal target position as similar as possible to the target position in the planning CT. The DRRs were scaled to match the size of the CBCT projection images. The GTV corresponding to the mid-ventilation CT set was also projected onto the reference DRR images.

2.C. Target identification on CBCT projection images

The GTV contour projection is transferred from the angle dependent DRR (mid-ventilation) to the corresponding CBCT projection via 2D mutual information registration. The registration is based on pixel gray value,\textsuperscript{47} where the targeted region consists of a rectangular area enclosing the ITV projection expanded by 1.5 cm in both orthogonal directions, the superior-inferior (SI) direction and an orthogonal direction consisting of a linear combination of the lateral (LAT) and AP directions. The values of the translations obtained from the registration process are applied to the center of mass of the GTV projection and the contour subsequently gets transferred onto the CBCT projection (Fig. 1).

For a given gantry angle, the CBCT projection image can be optimally registered with the closest corresponding phase DRR image; however, we found this procedure to be computationally intensive. We also noted that the projected target contour stayed relatively invariant between the planning image set and the CBCT images at the time of treatment. Therefore, in this investigation, we have not considered any
FIG. 1. The GTV contour transfers procedure onto the CBCT projection. A soft tissue registration box is delineated to enclose the ITV structure plus a margin. After the registration, the translation matrix was applied to the GTV contour and transferred on the CBCT projection image.

deformation of the target between the planning time and the treatment delivery time.

2.D. Target mean position reconstruction

The relationship between the target position within room coordinates system \((X_j, Y_j, Z_j)\) and its projection position \((x_j, y_j)\) on an imaging plane orthogonal to the kV source-isocenter direction (Fig. 2) for a given gantry angle \(\alpha_j\) can be defined using the following equations:

\[
x_j = \frac{[X_j \cos(\alpha_j) - Y_j \sin(\alpha_j)] \cdot \text{SAD}}{\text{SAD} - [X_j \sin(\alpha_j) + Y_j \cos(\alpha_j)]},
\]

(1)

\[
y_j = \frac{Z_j \cdot \text{SAD}}{\text{SAD} - [X_j \sin(\alpha_j) + Y_j \cos(\alpha_j)]},
\]

(2)

where the source-to-axis distance (SAD) of 100 cm is the distance between the kV source and the imaging plane.

Due to lung physiology, lateral motion \(X_j\) and AP motion \(Y_j\) are very small when compared to SAD [Fig. 2(b)], provided that the distance between the isocenter and the target mean

FIG. 2. (a) The 3D room and 2D imaging panel coordinate systems are depicted (adapted from the Elekta user manual). (b) The target trajectory in the room \((X,Y)\) plane is shown. The instantaneous position of the target and its mean position along with the corresponding projection coordinates are shown for two different gantry angles. For clarity we have assumed the mean position in the same \((X,Y)\) plane.
position is very small when compared with SAD. Therefore, the following assumption can be made:

\[ X_j \sin(\alpha_j) + Y_j \cos(\alpha_j) \ll \text{SAD}. \] (3)

Based on this assumption, Eqs. (1) and (2) can be re-written as follows:

\[ x_j = X_j \cos(\alpha_j) - Y_j \sin(\alpha_j), \] (4)

\[ y_j = Z_j. \] (5)

The target average position is evaluated by minimizing the observation error function, \( J \):

\[ J = \sum_{j \in \mathcal{A}_i} (x_j - \bar{x}_j)^2 + (y_j - \bar{y}_j)^2, \] (6)

where \((x_j, y_j)\) is the target coordinate detected in the imaging plane and \((\bar{x}_j, \bar{y}_j)\) is the gantry angle dependent projection of the target mean position \((\bar{X}, \bar{Y}, \bar{Z})_0\) onto the imaging plane [Fig. 2(b)]. Once Eqs. (4) and (5) are used to substitute \(x_j\) and \(y_j\) in Eq. (6), the optimization was obtained via a least square algorithm with respect to the target position in room coordinates \((X, Y, Z)\). The optimization function was sequentially generated using the projection images at gantry angles (indexed by \(\alpha\)) spanning from zero to gantry current location \((\mathcal{A}_i)\). Initially, our method needs to acquire images until a certain angle span is achieved. This initial arc, \(\mathcal{A}_0\), corresponds to a black-out angle span (Fig. 3) needed to obtain a robust and convergent minimization result with less than 1 mm detection error for the target mean position \((\bar{X}, \bar{Y}, \bar{Z})_0\). Within the initial arc, only the target position along the SI or Z direction can be determined, as it is invariant with gantry angle [Eq. (5)]. Depending on the treatment starting angle, the \(\mathcal{A}_0\) arc spanning angle will vary having an approximate value of 20°, as detailed in Secs. 3 and 4. Once the gantry completes the initial arc and using the images detected, our method is capable to detect the target 3D mean position in real-time as the gantry rotates. For a typical VMAT treatment the gantry speed is less than 3°/s, the kV panel acquisition frequency is 5.5 Hz, making the angle dependent image acquisition frequency to be at least 1.8 frames per degree.

2.E. Amplitude-binned representative trajectory

The representative trajectory is an approximation of the real 3D trajectory.\(^{42, 43}\) Recovering a representative trajectory is nearly as useful as a complete 3D trajectory allowing extraction of mean position, standard deviation, and excursion.\(^{42, 43}\) The representative trajectory is generated based on amplitude binning. The amplitude binning employed in this work is dynamic, where new bins are generated if needed (for example, in the case of baseline shifts) during the image acquisition.

The reconstruction of the real-time representative trajectory is obtained by minimizing the error function \( J \) [Eq. (6)] within an amplitude bin. More specifically, to resolve the 3D trajectory—the AP and LAT positions—multiple projection images are needed to be acquired. Once enough images are acquired, all the available SI trajectory (to the start of detection) is initially binned in 10 equal amplitude bins and then are dynamically changed if tumor position is detected outside of the initial excursion range.

In essence, to detect the 3D representative trajectory, four breathing periods are needed (approximately 35°). While these images are acquired, our method is “blind” only for the initial 20° (black-out angle) but can provide valuable information in the form of real-time mean 3D trajectory for the last 15° part of the 35°/4 breathing period region. More specifically, there are three detection regions (Fig. 3): first region, where only the SI trajectory is available—the initial black-out angle; a second region where the 3D mean trajectory gets resolved; and a third region where the 3D representative trajectory gets reconstructed practically in real-time. After the black-out angle is passed, only the mean 3D position of the target is available. The mean position is calculated through feeding Eq. (6) with all images available. Once the black-out angle and time duration equivalent with \(\sim 4\) breathing periods are cleared, the real-time trajectory detection starts and all the images available are used in the optimization process. Four breathing periods from the beginning of detection are needed to ensure the robustness of the method. Each image bin will collect images from four well defined time points where the chosen amplitude level intersects the SI trajectory, going from inhale to exhale to avoid possible image degeneracy due to tumor motion hysteresis. Each of the initial 10 bins will contain at least 6 images, with typically more than 2 images per

![Fig. 3. Depiction of the method’s three detection regions. During the black-out arc region, \(\mathcal{A}_0\) (approx 20°) images are acquired while only the SI trajectory is available. Once the gantry clears the \(\mathcal{A}_0\) region, enough images are collected to generate the mean 3D target position. After the gantry clears the second region—defined based on at least 4 breathing periods from the beginning of detection (an additional 15° over the black-out angle)—the real time 3D representative trajectory is reconstructed. At this time, AP and LAT trajectories are retrospectively reconstructed to time zero (beginning of black-out angle). For simplicity, the respiratory traces are only partially depicted.](image-url)
time point and 4 time points per bin. Images corresponding to a particular bin and in the same breathing direction are selected and the target positions are entered in the optimization function $J$ [Eq. (6)]. This result is then attributed to four time points corresponding to the particular amplitude bin considered. Even more, once the second region is cleared, the AP and LAT trajectories can be retrospectively reconstructed to time zero.

2.F. Technique validation

We have set up the experiments in increasing complexity as follows:

1. Simulation study. A simulation of target position was performed to validate the optimization algorithm and establish the parameters needed for robust detection, in particular, the dependency of the black-out angle on the treatment starting angle.

2. Phantom study. The study involved a dynamic phantom using a thorax phantom with a programmable moving insert (CIRS Inc, Norfolk, VA). The device has the ability to move in three dimensions under predefined motion curves. The phantom body simulates an average human thorax in shape, proportion, and composition. A high density sphere with diameter of 2 cm was inserted into a lung equivalent rod, which moved inside the lung equivalent lobe of the phantom along predefined motion curves using 3D tumor trajectories obtained from daily treatment imaging of lung cancer patients. The tumor AP and LAT motion was achieved through rod rotation. Figure 4 shows the experimental setup of the phantom on the treatment couch and the phantom cut-away view.

3. Patient study. The image data from two patients was tested using our methodology. Each patient received a simulation 4DCT scan from which an average CT was generated, as described in Sec. 2.A. A precorrection CBCT was acquired before treatment, which was registered based on soft tissue with the average CT region of interest prior to applying the couch correction. Then, a verification CBCT was acquired right before treatment which was also registered to the planning CT. Typically, there is no need for a second correction, as the target position overlaps with the average CT within 1–2 mm. The precorrection CBCT was used to test our technique.

3. RESULTS

3.A. Simulation study

A simulation was performed to validate the optimization algorithm and establish the algorithm parameters that yield a robust detection of a stationary target. As described in Sec. 2, the estimation of the mean position and 3D trajectory reconstruction converges after images are collected through a certain angle. The initial estimated tumor position was displaced to $-2.0 \text{ mm AP}, -2.0 \text{ mm LAT}, \text{ and } 0.0 \text{ mm SI}$, with the actual position of the target at $0.0 \text{ mm AP}, 0.0 \text{ mm LAT}, \text{ and } 0.0 \text{ mm SI}$. This target displacement served as the starting position error, and represents the positioning error made after a typical CBCT-guided patient registration. Projection positions of the 2 cm diameter sphere target were obtained for a complete gantry rotation with images taken at every 1°, resulting in 360 projections. To better simulate a biological target whose exact position is less well defined, noise with a mean of $0.0 \text{ mm}$ and standard deviation of $1.0 \text{ mm}$ was added to the calculated projection positions. As shown in Fig. 5, the 3D static position reconstruction of the target converges and is recovered within $\pm 0.5 \text{ mm}$ of the real target position within the first 20°. The reconstruction along AP shows a larger error than along LAT due to the geometry of the scan, with scanning starting at 0° where there is no information along the AP direction. The initial nonzero values for the initial LAT

![Fig. 4. (a) Phantom cut-away view (b) Phantom experimental setup.](Image)

![Fig. 5. Position error as a function of gantry angle when an $[-2.0, -2.0, 0.0] \text{ mm}$ error is initialized into the detection algorithm. The 3D static position error is reduced to $\pm 0.5 \text{ mm}$ after a black-out angle of 20° is passed.](Image)
reconstruction is attributed to the added noise. This simulation performed determined the black-out angle, in the range of approximate \(20^\circ\), within which the reconstruction algorithm converges to the actual target position from the estimated position during setup.

3.B. Phantom study – patient based tumor trajectories

To further evaluate the 3D and average reconstruction methods, a phantom study was designed using real patient breathing traces. In Fig. 6 we illustrate the result of 3D reconstruction where a relatively irregular breathing trace was used. The ability to accurately reconstruct the 3D trajectory gradually increases as more images are acquired and after the black-out angle and minimum breathing cycles are passed with a mean difference of \(0.2 \pm 0.2\) mm in all directions. Typically, the reconstruction optimization was considered to converge robustly if the difference between the reconstructed and input trajectories was smaller than the detection or registration error of 1.0–2.0 mm. 3D reconstruction along AP is more robust than along LAT due to the LAT motion pattern being significantly noisier and irregular (Fig. 6). Also, when the amplitude becomes comparable to the registration errors the 3D reconstruction becomes more inaccurate.

Using our mean position detection algorithm, the mean position of the tumor can be reconstructed robustly in less time than a full 3D trajectory reconstruction (less than 7 s since the treatment start) and requires approximate \(20^\circ\) span of the black-out angle (Fig. 7). The mean reconstruction modality is extracting the target mean position within less than 0.5 mm from the input mean position. However, the method loses the

![Fig. 6. The 3D reconstruction method is applied using predetermined trajectories used for induced motion in the dynamic phantom. Phantom results are presented for AP and LAT directions. The reconstructed trajectory (continuous line) is shown against the input trajectory (dotted) as a function of recorded images available within an arc. The grey region represents the angle span (that includes the black-out angle \(\sim20^\circ\)) needed for the reconstruction to become robust. Traces (a) to (e) show reconstruction progress as more images become available. Please note the different scale for AP and LAT reconstruction.](image)

![Fig. 7. Reconstruction of the target mean position is compared with the target mean position obtained from the phantom input data for the LAT, AP and SI direction. The black-out angle is shown in grey.](image)
ability to follow the main feature of the input mean position curve (Fig. 7, upper panel) but remains within 0.5 mm of the true mean.

### 3.C. Patient study – clinical application

Twelve kV scans were collected from two patients over a period of 5 treatment days, employing stereotactic body radiotherapy (SBRT) treatment regimen with 12 Gy per fraction. Each kV scan was reconstructed into a 4DCBCT through commercial software XVI Symmetry release 4.0 (Elekta Oncology Systems Ltd) and one representative trajectory is reconstructed after 4D registration. For comparison, we also used our representative trajectory reconstruction method to provide one trajectory based on all images collected from each scan. The comparison between the representative trajectory obtained from the 4D CBCT registration and the 3D reconstruction method (3DkV) is shown in Table I. For clarity, we have chosen to report only the dataset containing the mean position and standard deviation. In general, the differences between the mean tumor position and standard deviation obtained from the 4D CBCT registration and from the 3DkV method are quite small, below 2.0 and 1.0 mm, respectively.

### 4. DISCUSSION

We propose a detection technique developed for determining the position of a target from kV imaging during radiotherapy delivery with an arc, estimating either real-time position or mean target position.

The phantom experiments demonstrate that the proposed methods can accurately reconstruct the 3D representative trajectory as well as the average position of the target using the projection images collected either during the CBCT or during the treatment. Many trajectories have been tested, with findings of 3D trajectory reconstruction accuracy below 0.5 mm (average difference between reconstruction and ground truth). However, when small, noisy amplitudes and irregular patterns are considered, our 3D reconstruction method is losing accuracy as the mean position is computed within each amplitude bin (Fig. 6). This is expected as the reconstruction algorithm performs better when the amplitude bins are large enough so that the kV sequential projections can be positively associated to a certain amplitude bin (where the binning time interval is of 4–5 breathing periods). This effect becomes worse as the amplitude becomes comparable with the system detection and registration error of 1.0–2.0 mm introducing more noise, or when the motion pattern is irregular (as seen in Fig. 6, along LAT direction). For trajectories with larger than 2 mm amplitude; the 3D reconstruction localizes the target mean position within less than 0.5 mm from the actual position. Such small differences are inconsequential for patient treatment as they are smaller than the image guidance positioning error, as well as changes in the trajectory baseline [Fig. 6(e)]. Nevertheless, leaving aside the detection errors, irregular motion patterns are more likely to lead to worse 3D reconstruction accuracy than regular motion patterns. Theoretically, the average

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### Table I. Tumor mean position obtained from the CBCT scans and detected mean position and standard deviation obtained using the 3D reconstruction method are shown for two patients during five treatment days.

| Patient | CB scan on day 1 | CB scan on day 2 | CB scan on day 3 | CB scan on day 4 | CB scan on day 5 |
|---------|------------------|------------------|------------------|------------------|------------------|
| Pat 1   | 3DkV ± 0.5       | 4DCB ± 1.5       | 3DkV ± 2.1       | 4DCB ± 0.3       | 3DkV ± 1.2       |
| Pat 2   | 3DkV ± 0.8       | 4DCB ± 1.0       | 3DkV ± 1.6       | 4DCB ± 0.1       | 3DkV ± 1.5       |

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difference between the reconstructed trajectory and the ground truth will be on the order of half of the bin size. Adaptive binning can be used to limit the bin to a smaller size and get better reconstruction accuracy as long as there are enough images in each bin but taking longer time. For regular motion patterns, it is not difficult to limit the bin size and have enough images in each bin. However, the bin size has to be enlarged to include more images to get a robust average position for irregular motion patterns, especially when a large baseline shift is present.

Once the blackout angle and minimum breathing cycles are passed through, the 3D reconstruction method delivers the trajectories along SI, Lat, and AP directions, from which the mean positions and corresponding standard deviations are obtained.

The average position of the tumor can be reconstructed robustly in less than a full 3D trajectory reconstruction, requiring less than approximately 20° span of the black-out angle (Fig. 7). The mean reconstruction modality is extracting the target mean position within less than 0.5 mm from the input mean position, however not being capable to follow the main feature of the input mean position curve (Fig. 7 upper panel). The reconstruction along the lateral direction is the least accurate due to the target’s small lateral amplitude. This effect is expectedly similar with the 3DkV trajectory reconstruction method where the small lateral amplitude generates a larger input-reconstruction discrepancy, albeit small in absolute value (Fig. 6). On the other hand, along the anterior–posterior direction where the motion amplitude is larger than 2 mm, the mean position reconstruction is quite accurate; the difference between input mean position and reconstruction was below 0.5 mm at all time while the features of the input AP mean position curve are preserved in the reconstructed curve.

While the phantom based experiments reveal the accuracy of the proposed methods under dynamic conditions, the algorithms need to be evaluated under treatment conditions where uncertainty is introduced due to the less well defined nature of tumors when compared with spherical targets. The first variable consists of the residual error after the CBCT, typically in the range of 1–2 mm. A second variable is the registration accuracy between the pretreatment angle dependent DRR and the projection images where the mutual information registration error used in our technique is also in the range of 1–2 mm. Therefore, well-defined DRR tumor projections and projection images are required to get reliable result for clinical use. Retrospective analysis of kV projection images for several patients has shown that the cutoff for reconstruction reliability is approximately tumors with diameter larger than 2 cm. The mutual information registration takes an average of 200 ms per image due to the need to access a network based database. Nevertheless, the reconstruction process can be significantly sped up by using a local hard drive based database, thus enabling us to perform on-treatment monitoring without any clinically significant time lag.

Currently, for patient observation during treatment, the mean position reconstruction method is used first due to its fast onset in reconstructing the tumor 3D mean position (the target mean position is the main factor affecting the ability to deliver the dose as planned). When a threshold value in the mean position of the target is exceeded, such as 3 mm, the treatment can be interrupted to allow repositioning of the patient. Once more images are acquired (an additional ~15° over the black-out angle), the representative trajectory provides more useful information as standard deviation and excursion. The standard deviation and excursion can be further used to calculate delivered dose or make margin assessments. Aside from baseline shifts affecting the dose deposition and normal structure sparing, the excursion is also important where the target may extend its motion outside of the planned aperture while keeping its mean position. Therefore, once available, the representative trajectory methodology offers more information regarding the target behavior during the treatment.

In this work, amplitude binning is employed rather than phase binning. Abdelnour et al. shows that amplitude binning can be more accurate than phase binning when using 4DCT imaging. Moreover, for irregular target trajectories, phase binning can lead to large reconstruction errors that need to be addressed using complex iterative techniques. Not only the amplitude binning makes the proposed method more robust and fast but it also provides a real-time updated representative trajectory. The tumor motion along SI direction is available in real-time during the entire scan functioning as the base for the amplitude binning algorithm. This method overcomes the need for surrogate-tumor correlation as methods based on surrogate motion guidance. Tumor mean position and motion standard deviation derived from our methods can be used as critical for decision making. Compared to most markerless tracking techniques that only provide 2D tracking, the real-time directly detected SI trajectory and real-time AP/LAT representative trajectory can offer more information to be used in advanced clinical applications (e.g., aperture tracking).

The proposed method can be further used in conjunction with the pretreatment CBCT where the projection images are used to reconstruct the representative trajectory before the black-out angle is spanned. Nevertheless, if such strategy is employed, one has to be aware of possible baseline shifts (detected along SI directions) occurring during the black-out angle because of the weight attributed to the images taken before the treatment starts. This history effect is strongly manifested at beginning of the treatment and gradually decreases in intensity as treatment images are acquired and replace the pretreatment images. In turn, the effect may mask a baseline shift hence, the need to carefully monitor in real-time the behavior of SI trajectory.

In order to estimate the additional dose from kV imaging we will consider VMAT as the treatment modality. In our clinic, a hypofractionated lung treatment is delivered in 4 or 5 fractions for a total of 48 or 60 Gy. A typical VMAT plan delivers this dose in 2000–3000 MUs per fraction. A typical Elekta Linac delivers an average of 400 MU/min, such that the treatment time per fraction is approximately 7 min. The Elekta CBCT system delivers approximately 2.2 cGy to the surface of a 32 cm diameter CTDI body phantom over a
360° rotation, which takes 2 min to complete (using a large field size, 120 kV energy, 80 mA/frame, and 20 ms/frame). Although using VMAT for hypofractionated lung treatments will never span a complete rotation due to sparing of the contralateral lung and other factors, for the sake of the argument we will use 2.2 cGy/2 min to estimate the total dose $D = 7 \text{ min}/\text{fx} \times 2.2 \text{ cGy/min} \times 5 \text{ fx} = 38.5 \text{ cGy}$, considerably less than 1% of the total treatment dose. Therefore, the additional dose induced by our technique is quite small.

On the other hand, the ability of our method to capture major real-time tumor position variations, hence avoiding delivering dose to adjacent structures or underdosing the tumor, outweighs the small additional dose delivered.

5. CONCLUSION

We have developed a real-time tracking framework to locate lung tumors during arc therapy using an optimization algorithm applied to kV projection images taken concomitantly with the treatment delivery. Tumor tracking achieves the real time status once an initial blackout angle is passed. The methods described here are accurate and do not introduce significant additional dose. Moreover, the 3D trajectory reconstruction method can be employed prior to the treatment to obtain the tumor trajectory in three dimensions from a simple volumetric Cone Beam CT with no additional dose to the patient, allowing parameters like tumor excursion to be assessed prior to the treatment.

The proposed technique can be further used in a decision making process whether the treatment should continue or be stopped based on mean tumor position and excursion variation.

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1T. Bortfeld, K. Jokivarsi, M. Goitein, J. Kung, and S. B. Jiang, “Effects of intra-fraction motion on IMRT dose delivery: Statistical analysis and simulation,” Phys. Med. Biol. 47(13), 2203–2220 (2002).

2T. Bortfeld, S. B. Jiang, and E. Rietzel, “Effects of motion on the total dose distribution,” Semin. Radiat. Oncol. 14(1), 41–51 (2004).

3W. A. Beckham, P. J. Keall, and J. V. Siebers, “A fluence-convolution method to calculate radiation therapy dose distributions that incorporate random set-up error,” Phys. Med. Biol. 47(19), 3465–3473 (2002).

4C. X. Yu, D. A. Jaffray, and J. W. Wong, “The effects of intra-fraction organ motion on the delivery of dynamic intensity modulation,” Phys. Med. Biol. 43(1), 91–104 (1998).

5J. B. Shen, B. R. Fireah, R. A. Popple, and I. A. Brezovich, “Dosismetric and radiobiological impact of dose fractionation on respiratory motion induced IMRT delivery errors: A volumetric dose measurement study,” Med. Phys. 33(5), 1380–1387 (2006).

6S. Shimizu, H. Shirato, B. Xo, K. Kagei, T. Nishioka, S. Hashimoto, K. Tsushita, H. Aoyama, and K. Miyasaka, “Three-dimensional movement of a liver tumor detected by high-speed magnetic resonance imaging,” Radiat. Oncol. 50(3), 367–370 (1999).

7M. Goitein, “Organ and tumor motion: An overview,” Semin. Radiat. Oncol. 14(1), 2–9 (2004).

8H. Shirato, Y. Seppenwoolde, K. Kitamura, R. Onimura, and S. Shimizu, “Intrafractual motion: Lung and liver,” Semin. Radiat. Oncol. 14(1), 10–18 (2004).

9J. J. Sonke, J. Lebesque, and M. van Herk, “Variability of four-dimensional computed tomography patient models,” Int. J. Radiat. Oncol., Biol., Phys. 70(2), 590–598 (2008).

10P. J. Keall, V. R. Kini, S. S. Vedam, and R. Mohan, “Motion adaptive x-ray therapy: A feasibility study,” Phys. Med. Biol. 46(1), 1–10 (2001).

11E. B. Jiang, “Radiotherapy of mobile tumors,” Semin. Radiat. Oncol. 16(4), 239–248 (2006).

12R. Li, J. H. Lewis, R. I. Berbeco, and L. Xing, “Real-time tumor motion estimation using respiratory surrogate via memory-based learning,” Phys. Med. Biol. 57(15), 4771–4786 (2012).

13R. I. Berbeco, F. Hacker, D. Ionascu, and H. J. Mamon, “Clinical feasibility of using an EPID in CINE mode for image-guided verification of stereotactic body radiotherapy,” Int. J. Radiat. Oncol., Biol., Phys. 69(1), 258–266 (2007).

14W. Luo, S. Yoo, Q. J. Wu, Z. Wang, and F. F. Yin, “Analysis of image quality for real-time target tracking using simultaneous kV-MV imaging,” Med. Phys. 35(12), 5501–5509 (2008).

15G. R. Hoffman, J. Liang, and D. Yan, “Marker-free lung tumor trajectory estimation from a cone beam CT sinogram,” Phys. Med. Biol. 55(9), 2637–2650 (2010).

16C. Bert, K. G. Methaney, K. Doppke, and G. T. Chen, “A phantom evaluation of a stereo-vision surface imaging system for radiotherapy patient setup,” Med. Phys. 32(9), 2753–2762 (2005).

17S. B. Jiang, “Technical aspects of image-guided respiration-gated radiation therapy,” Med. Dosim. 31(2), 141–151 (2006).

18E. Kanoulas, J. A. Aslam, G. C. Sharp, R. I. Berbeco, S. Nishioka, H. Shirato, and S. B. Jiang, “Derivation of the tumor position from external respiratory surrogates with periodical updating of the internal/external correlation,” Phys. Med. Biol. 52(17), 5443–5456 (2007).

19H. Wu, Q. Zhao, R. I. Berbeco, S. Nishioka, H. Shirato, and S. B. Jiang, “Gating based on internal/external signals with dynamic correlation updates,” Phys. Med. Biol. 53(24), 7137–7150 (2008).

20D. Ruan, J. A. Fessler, J. M. Balter, R. I. Berbeco, S. Nishioka, and H. Shirato, “Inference of hysteresis respiratory tumor motion from external surrogates: A state augmentation approach,” Phys. Med. Biol. 53(11), 2923–2936 (2008).

21S. S. Vedam, V. R. Kini, P. J. Keall, V. Ramakrishnan, H. Mostafavi, and R. Mohan, “Quantifying the predictability of diaphragm motion during respiration with a noninvasive external marker,” Med. Phys. 30(4), 505–513 (2003).

22Z. D. Hoisak, K. E. Sixel, R. Tirona, P. C. Cheung, and J. P. Pignol, “Correlation of lung tumor motion with external surrogate indicators of respiration,” Int. J. Radiat. Oncol., Biol., Phys. 60(4), 1298–1306 (2004).

23D. Ionascu, S. B. Jiang, S. Nishioka, H. Shirato, and R. I. Berbeco, “Internal-external correlation investigations of respiratory induced motion of lung tumors,” Med. Phys. 34(10), 3893–3907 (2003).

24E. N. Bruce, “Temporal variations in the pattern of breathing,” J. Appl. Physiol. 80(4), 1079–1087 (1996).

25Y. Tsunashima, T. Sakae, Y. Shioyama, K. Kagei, T. Terunuma, A. Nohtomi, and Y. Akine, “Correlation between the respiratory waveform measured using a respiratory sensor and 3D tumor motion in gated radiotherapy,” Int. J. Radiat. Oncol., Biol., Phys. 60(3), 951–958 (2004).

26J. Rotmann, M. Apostolopoulos, A. Chen, L. Court, and R. Berbeco, “A multi-region algorithm for markerless beam’s-eye view lung tumor tracking,” Phys. Med. Biol. 55(18), 5585–5598 (2010).

27J. S. Park, D. Ionascu, F. Hacker, H. Mamon, and R. Berbeco, “Automatic marker detection and 3D position reconstruction using cine EPID images for SBRT verification,” Med. Phys. 36(10), 4536–4546 (2009).

28W. Mao, A. Hsu, N. Riaz, L. Lee, R. Wiersma, G. Lutxon, C. King, L. Xing, and T. Solberg, “Image-guided radiotherapy in near real time with intensity-modulated radiotherapy megavoltage treatment beam imaging,” Int. J. Radiat. Oncol., Biol., Phys. 75(2), 603–610 (2009).

29W. Liu, R. D. Wiersma, and L. Xing, “Optimized hybrid megavoltagekilovoltage imaging protocol for volumetric prostate arc therapy,” Int. J. Radiat. Oncol., Biol., Phys. 78(2), 595–604 (2010).

30P. J. Keall, A. D. Todor, S. S. Vedam, C. L. Bartee, J. V. Siebers, R. V. Kini, and R. Mohan, “On the use of EPID-based implanted marker tracking for 4D radiotherapy,” Med. Phys. 31(12), 3492–3499 (2004).

31X. Tang, G. C. Sharp, and S. B. Jiang, “Fluoroscopic tracking of multiple implanted fiducial markers using multiple object tracking,” Phys. Med. Biol. 52(14), 4081–4098 (2007).

32H. Shirato, S. Shimizu, T. Kunieda, K. Kitamura, M. van Herk, K. Kagei, T. Nishioka, S. Hashimoto, K. Fujita, H. Aoyama, K. Tsushita, K. Kudo, and K. Miyasaka, “Physical aspects of a real-time tumor-tracking system for gated radiotherapy,” Int. J. Radiat. Oncol., Biol., Phys. 48(4), 1187–1195 (2000).
33Y. Yue, M. Aristophanous, J. Rottmann, and R. I. Berbeco, “3D fiducial motion tracking using limited MV projections in arc therapy,” Med. Phys. 38(6), 3222–3231 (2011).
34P. R. Geraghty, S. T. Kee, G. McFarlane, M. K. Razavi, D. Y. Sze, and M. D. Bake, “CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: Needle size and pneumothorax rate,” Radiology 229(2), 475–481 (2003).
35S. Arslan, A. Yilmaz, B. Bayrampur, O. Uzman, E. Nver, and E. Akkaya, “CT-guided transthoracic fine needle aspiration of pulmonary lesions: Accuracy and complications in 294 patients,” Med. Sci. Monit. 18(7), CR493–CR497 (2002).
36N. Kothary, J. J. Heit, J. D. Louie, W. T. Kuo, B. W. Loo, A. Koong, D. T. Chang, D. Hovsepian, D. Y. Sze, and L. V. Hofmann, “Safety and efficacy of percutaneous fiducial marker implantation for image-guided radiation therapy,” J. Vasc. Interv. Radiol. 20(2), 235–239 (2009).
37R. Zeng, J. A. Fessler, and J. M. Balter, “Estimating 3D respiratory motion from orbiting views by tomographic image registration,” IEEE. Trans. Med. Imaging 26(2), 153–163 (2007).
38R. Li, X. Jia, J. H. Lewis, X. Gu, M. Folkerts, C. Men, and S. B. Jiang, “Real-time volumetric image reconstruction and 3D tumor localization based on a single x-ray projection image for lung cancer radiotherapy,” Med. Phys. 37(6), 2822–2826 (2010).
39T. Lin, L. I. Cerviño, X. Tang, N. Vasconcelos, and S. B. Jiang, “Fluoroscopic tumor tracking for image-guided lung cancer radiotherapy,” Phys. Med. Biol. 54(4), 981–992 (2009).
40Y. Cui, J. G. Dy, G. C. Sharp, B. Alexander, and S. B. Jiang, “Multiple template-based fluoroscopic tracking of lung tumor mass without implanted fiducial markers,” Phys. Med. Biol. 52(20), 6229–6242 (2007).
41Q. Xu, R. J. Hamilton, R. A. Schowengerdt, and S. B. Jiang, “A deformable lung tumor tracking method in fluoroscopic video using active shape models: A feasibility study,” Phys. Med. Biol. 52(17), 5277–5293 (2007).
42J. H. Lewis, R. Li, W. T. Watkins, J. D. Lawson, W. P. Segars, L. I. Cerviño, W. Y. Song, and S. B. Jiang, “Markerless lung tumor tracking and trajectory reconstruction using rotational cone-beam projections: A feasibility study,” Phys. Med. Biol. 55(9), 2505–2522 (2010).
43J. H. Lewis, R. Li, X. Jia, W. T. Watkins, Y. Lou, W. Y. Song, and S. B. Jiang, “Mitigation of motion artifacts in CBCT of lung tumors based on tracked tumor motion during CBCT acquisition,” Phys. Med. Biol. 56(17), 5485–5502 (2011).
44X. Gu, H. Pan, Y. Liang, R. Castillo, D. Yang, D. Choi, E. Castleo, A. Majumdar, T. Guerrero, and S. B. Jiang, “Implementation and evaluation of various demons deformable image registration algorithms on a GPU,” Phys. Med. Biol. 55(1), 207–219 (2010).
45Q. Xu, R. J. Hamilton, R. A. Schowengerdt, B. Alexander, and S. B. Jiang, “Lung tumor tracking in fluoroscopic video based on optical flow,” Med. Phys. 35(12), 5351–5359 (2008).
46T. Zhang, Y. Chi, E. Meldolesi, and D. Yan, “Automatic delineation of online head-and-neck computed tomography images: Toward on-line adaptive radiotherapy,” Int. J. Radiat. Oncol., Biol., Phys. 68(2), 522–530 (2007).
47D. Mattes, D. R. Haynor, H. Vesselle, T. K. Lewellen, and W. Eubank, “PET-CT image registration in the chest using free-form deformations,” IEEE Trans. Med. Imaging 22(1), 120–128 (2003).
48P. R. Poulsen, B. Cho, and P. J. Keall, “A method to estimate mean position, motion magnitude, motion correlation, and trajectory of a tumor from cone-beam CT projections for image-guided radiotherapy,” Int. J. Radiat. Oncol., Biol., Phys. 72(5), 1587–1596 (2008).
49A. F Abdelnour, S. A. Nehmeh, T. Pan, J. L. Humm, P. Vernon, H. Schöder, K. E. Rosenzweig, G. S. Mageras, E. Yorke, S. M. Larson, and Y. E. Erdi, “Phase and amplitude binning for 4D-CT imaging,” Phys. Med. Biol. 52(12), 3515–3529 (2007).