Extraction of tumor motion trajectories using PICCS-4DCBCT: A validation study

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Purpose: As a counterpart of 4DCT in the treatment planning stage of radiotherapy treatment, 4D cone beam computed tomography (4DCBCT) method has been proposed to verify tumor motion trajectories before radiation therapy treatment delivery. Besides 4DCBCT acquisition using slower gantry rotation speed or multiple rotations, a new method using the prior image constrained compressed sensing (PICCS) image reconstruction method and the standard 1-min data acquisition were proposed. In this paper, the PICCS-4DCBCT method was combined with deformable registration to validate its capability in motion trajectory extraction using physical phantom data, simulated human subject data from 4DCT and *in vivo* human subject data.

Methods: Two methods were used to validate PICCS-4DCBCT for the purpose of respiratory motion delineation. The standard 1-min gantry rotation Cone Beam CT acquisition was used for both methods. In the first method, 4DCBCT projection data of a physical motion phantom were acquired using an on-board CBCT acquisition system (Varian Medical Systems, Palo Alto, CA). Using a deformable registration method, the object motion trajectories were extracted from both FBP and PICCS reconstructed 4DCBCT images, and compared against the programmed motion trajectories. In the second method, using a clinical 4DCT dataset, Cone Beam CT projections were simulated by forward projection. Using a deformable registration method, the tumor motion trajectories were extracted from the reconstructed 4DCT and PICCS-4DCBCT images. The performance of PICCS-4DCBCT is assessed against the 4DCT ground truth. The breathing period was varied in the simulation to study its effect on motion extraction. For both validation methods, the root mean square error (RMSE) and the maximum of the errors (MaxE) were used to quantify the accuracy of the extracted motion trajectories. After the validation, a clinical dataset was used to demonstrate the motion delineation capability of PICCS-4DCBCT for human subjects.

Results: In both validation studies, the RMSEs of the extracted motion trajectories from PICCS-4DCBCT images are less than 0.7 mm, and their MaxEs are less than 1 mm, for all three directions. In comparison, FBP-4DCBCT shows considerably larger RMSEs in the physical phantom based validation. PICCS-4DCBCT also shows insensitivity to the breathing period in the 4DCT based validation. For the *in vivo* human subject study, high quality 3D motion trajectory of the tumor was obtained from PICCS-4DCBCT images and showed consistency with visual observation.

Conclusions: These results demonstrate accurate delineation of tumor motion trajectory can be achieved using PICCS-4DCBCT and the standard 1-min data acquisition. © 2011 American Association of Physicists in Medicine. [DOI: 10.1118/1.3637501]

Key words: four-dimensional cone beam CT, tumor motion trajectory, image guided radiation therapy

I. INTRODUCTION

Due to respiratory motion, the efficacy of radiotherapy is compromised for tumors located in the thorax and the upper abdomen. To improve the outcome of radiotherapy, in particular, intensity modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT), image guidance using 4D imaging becomes crucial in both the treatment planning stage and the treatment delivery stage.

In the absence of 4D imaging capability, an increased internal margin is often required to define the planning target volume (PTV) to achieve adequate irradiation of the target.

However, the increased margin leads to more irradiation of normal tissues and limits the success of dose escalation, which is needed for better tumor control probability. With motion information available from 4D imaging, the treatment margin can be reduced when advanced treatment techniques are used, such as gated treatment and tumor tracking delivery. Specifically, motion information can be used to improve target volume definition, map dose distribution, and guide beam delivery in the presence of respiratory motion.

Among the many 4D imaging proposals, 4D computed tomography (4DCT) using diagnostic CT scanners¹⁻⁶ has been successfully developed and integrated into radiation oncology

practice over the past few years. Due to sub-second gantry rotation time of diagnostic CT scanners, multiple images can be formed within a breathing cycle, and then sorted into about 4–10 phase bins according to a respiratory surrogate, usually provided by a real-time position management (RPM) system (Varian Medical Systems, Palo Alto, CA). However, the limitation of 4DCT is that it is acquired at the treatment planning stage and must assume the same respiratory motion for the treatment delivery stage when the similar 4D imaging capability is not integrated into the treatment delivery system.

In recent years, 4D cone beam computed tomography (4DCBCT) using an on board imager (OBI) has been proposed.^{7–13} It can be used to address the limitation of 4DCT: CBCT is taken right before the treatment delivery and therefore can be used to verify the patient's tumor motion trajectory which has been used in the treatment plan. Currently, a standard CBCT scan acquires about 600 cone-beam projections over a full scan of 360° within 1 min. Based on such a static CBCT acquisition, 4DCBCT can be implemented by retrospectively sorting the acquired cone beam projections into several phase bins before image reconstruction takes place for each phase bin. If a standard one minute scan is used and data are sorted into 8–10 phase bins, fewer than 100 projections will be assigned to each phase bin. As a result of the conventional filtered back-projection (FBP) reconstruction, under-sampling streaking artifacts will be rampant in 4DCBCT images and impede accurate and reliable extraction of the tumor motion trajectory.

To mitigate streaking artifacts and improve image quality in 4DCBCT images, a slow gantry rotation data acquisition scheme were proposed.^{8,14–23} By slowing down the gantry rotation speed by a factor of 2 to 4 (or more), streak artifacts can be effectively reduced using an increased number of cone beam projections within each phase bin. Although promising, a potential drawback of this slow rotation acquisition scheme is the concomitantly increased inadvertent patient motion during the scan, which may generate additional image artifacts. Moreover, the slower gantry rotation acquisition also requires hardware modifications and reduces patient throughput of the treatment in clinical practice.

With the attempt to maintain the same data acquisition scheme as the static CBCT scan, both streaking artifacts correction methods^{24–27} and a novel image reconstruction algorithm, prior image constrained compressed sensing (PICCS), were recently proposed to solve reconstruction problems with vastly under-sampled projection data.^{28–32} The challenge of data under-sampling in 4DCBCT can be addressed with the PICCS reconstruction method. It was demonstrated that 4DCBCT using PICCS (PICCS-4DCBCT) is able to reconstruct high temporal resolution (~100 ms) and streak-free images without slowing down the standard gantry rotation.³³ The method was initially evaluated using numerical phantoms and a relatively simple physical phantom with rigid motion.³³ However, in order to demonstrate the power and the robustness of the PICCS-4DCBCT method in clinical practice, it is important to demonstrate that: (1) the PICCS-4DCBCT method works for realistic clinical anatomical background and (2) the PICCS-4DCBCT method can

reconstruct high quality images to enable extraction of tumor motion trajectories using a deformable registration method. These requests motivated the work presented in this current paper. To be more specific, in this paper, the PICCS-4DCBCT method was combined with a deformable registration method to validate its capability in motion trajectory extraction using physical phantom data, simulated human subject data from 4DCT, and *in vivo* human subject data.

II. METHODS AND MATERIALS

II.A. 4D Cone Beam CT reconstruction using the PICCS algorithm

In the PICCS algorithm, an image is reconstructed by solving the following constrained optimization problem:

$$\min_I \left(\alpha \|\Psi_1(I - I_p)\|_1 + (1 - \alpha) \|\Psi_2(I)\|_1 \right), \quad \text{s.t. } AI = p. \quad (1)$$

In the application of PICCS-4DCBCT, I is the target image to be reconstructed for a respiratory phase bin and p is the projection measurements sorted into the phase bin. Ψ_1 and Ψ_2 are both sparsifying transforms, and $\|\bullet\|_1$ is the l_1 -norm of a vectorized image. The prior image, I_p , in the current implementation, is an image reconstructed from all the acquired projection data using the standard FDK algorithm.³⁴ The FDK algorithm is a widely used FBP-type reconstruction method in practical cone-beam CT applications. This algorithm will still be denoted as FBP for consistency in the rest of the paper.

The minimization of $\|\Psi_1(I - I_p)\|_1$ enforces the similarity between I and I_p , and more importantly, serves to transfer the high SNR of I_p to I . Since I_p usually contains motion induced artifacts, the term $\|\Psi_2(I)\|_1$ was introduced to suppress those artifacts by minimizing the variations in I . The weighting parameter, α , balances the contributions of the two minimization terms. It was selected as 0.6 in all PICCS reconstructions in this paper.

The constraint term, $AI = p$, is to ensure data consistency between the target image and the measured projection data within a respiratory phase bin (A is the system matrix). Applying this constraint will encode the temporal information of the phase bin into the reconstructed image.

By incorporating the minimization terms and the constraint term in the optimization problem, PICCS is capable of accurate reconstruction from highly under-sampled projection data. In this paper, the constrained minimization problem was solved in two steps. The first is to apply the simultaneous algebraic reconstruction technique (SART)³⁵ to approximately satisfy the constraint $AI = p$. The second is to minimize the objective function $\alpha \|\Psi_1(I - I_p)\|_1 + (1 - \alpha) \|\Psi_2(I)\|_1$ using the gradient descent method.³⁶ The two steps are alternated until the mean squared difference between two successive iterations becomes smaller than a predetermined threshold (0.5% used in this paper).

II.B. Motion trajectory extraction using deformable registration

From the reconstructed 4DCBCT images, the motion trajectory for an object of interest can be extracted using

deformable registration methods. Instead of rigid registration method, a deformable registration is desirable in motion trajectory extraction due to the fact that respiratory motion usually leads to deformation of internal anatomy in the thorax and upper abdomen. A two-step procedure will be used in this paper to obtain tumor motion trajectory: (1) deformable registration is applied to register the PICCS-4DCBCT image at a given respiratory phase bin to the preselected reference phase, e.g., the end-expiration phase which is generally considered the most stable phase; (2) an average of motion vectors within a given small volume ($3 \times 3 \times 3$ pixel³ in this paper) is taken to generate a representative tumor motion trajectory.

Many deformable registration methods have been proposed and investigated for clinical applications in recent years.^{37–42} In this work, a fast free-form deformable registration algorithm via calculus of variations was used.^{43,44} In this algorithm, the registration between a moving image R and a fixed template image T is accomplished by minimizing the objective function defined as:

$$F(\vec{u}) = \int_{\Omega} (R(\vec{x} + \vec{u}) - T(\vec{x}))^2 d\vec{u} + \lambda \int_{\Omega} \|\nabla \vec{u}\|^2 d\vec{u}, \quad (2)$$

where $\vec{x}$ is a vector representing the location of a pixel and $\vec{u}$ is the displacement vector of the pixel. The first component of this objective function measures the dissimilarity between the two images after the displacement field is applied and the second component regularizes the smoothness of the displacement field. λ is a weighting parameter to control the relative contributions of these two components. A multiresolution approach was also taken to accelerate the convergence of the registration,^{43–45} and four resolution levels were used in all the studies.

III. VALIDATION OF MOTION EXTRACTION FROM PICCS RECONSTRUCTED 4DCBCT IMAGES

Two methods were used in this study to validate the extracted motion trajectories from the PICCS reconstructed 4DCBCT images. These methods aim to perform the validation under conditions similar to a variety of clinical situations. The first validation method is based on a physical motion phantom, for which the programmed motion is the ground truth and used as reference for evaluation. Since the physical phantom involves rigid motion only, a second validation is performed based on a 4DCT dataset of a human subject where nonrigid motion is present. Using the 4DCT data set, a forward projection procedure was used to generate 4D cone beam CT data sets²⁷ under different assumptions of respiratory periods (different breathing periods from 2 to 6 s were simulated in this paper). The simulated 4DCBCT data were then reconstructed using the aforementioned PICCS-4DCBCT strategy. Using the described deformable registration method, motion profiles were extracted from both the 4DCT images and the PICCS-4DCBCT images. Using this strategy, the motion trajectories extracted from 4DCT images can be used as reference to evaluate the accuracy of PICCS-4DCBCT motion trajectories.

III.A. Quantitative evaluation of the extracted motion trajectory

Two figures of merit are used in this paper to quantify the accuracy of the extracted motion trajectories. The root mean square errors (RMSEs) of the extracted motion trajectories were calculated relative to the reference trajectories. The definition of RMSE in these evaluations is given below,

$$\text{RMSE} = \sqrt{\frac{1}{N} \sum_{i=1}^N [f(p_i) - f_0(p_i)]^2}, \quad (3)$$

where $f(p_i)$ is the calculated displacement from the reconstructed images at the i -th phase, $f_0(p_i)$ is the corresponding reference value, and N is the number of phase bins. Equation (3) can be used to evaluate motion trajectories in left–right (LR), anterior–posterior (AP), and superior–inferior (SI) directions, and the corresponding notations are RMSE_{LR} , RMSE_{AP} , and RMSE_{SI} , respectively. To combine RMSEs in all three directions, $\text{RMSE}_{3\text{D}}$ is defined as,

$$\text{RMSE}_{3\text{D}} = \sqrt{\text{RMSE}_{\text{LR}}^2 + \text{RMSE}_{\text{AP}}^2 + \text{RMSE}_{\text{SI}}^2}. \quad (4)$$

Another figure of merit, the maximum of the errors (MaxE), was also used to evaluate the accuracy. The absolute difference between the extracted motion trajectory and the reference profile at each phase was calculated, and the maximum value of these differences was defined as the MaxE. It describes the largest discrepancy at a respiratory phase between two motion trajectories.

III.B. Registration error quantification

The accuracy of the extracted motion trajectories is influenced by both the accuracy of the registration method itself and the image quality. To better understand how much error is intrinsically caused by the registration method, a numerical phantom study was performed for this purpose. In this phantom, a sphere with a diameter of 2 cm moves and deforms inside a thoraxlike structure (Fig. 1). The sphere undergoes a linear motion with a maximum displacement of 1.5 cm in each of the three directions. Deformation is also incorporated by changing its semiaxis lengths. Figure 1 shows images of this motion phantom at 0 and 50% phases. Over 900 views of projection data were simulated for each of 20 phases and images were reconstructed by FBP with a pixel size of 0.8 mm. The fast free-form deformable registration was applied to a $64 \times 64 \times 64$ pixel³ sub-volume around the moving sphere to extract the object motion trajectories and their errors are quantified. Since these images are reconstructed with fully sampled data and contain no artifacts or noise, the errors can be considered to be solely from the image registration method.

III.C. Physical phantom based validation

This validation method is based on a CBCT scan of a physical motion phantom, presented in a previous publication on PICCS-4DCBCT.³³ The details of phantom and the CBCT scan can be found in Ref. 33, in which a rigid

FIG. 1. The numerical phantom used to study the accuracy of the registration algorithm for the task of motion extraction. From left to right are 0 and 50% phases, respectively. From top to bottom are axial, coronal, and sagittal slices, respectively.

registration method was used to validate the motion trajectories from PICCS reconstructed images. Although the phantom motion is rigid only, it is highly desirable to also validate the motion trajectories using deformable registration method, which is required when applied to analyze breathing motion for human subjects. The fast free-form deformable registration algorithm introduced before was used to extract the tumor motion trajectory.

For image reconstruction, the projection views were sorted into 20 phase bins, and both FBP and PICCS algorithms were used to reconstruct 4D images. The pixel size of the reconstructed images is 0.8 mm. Then, for each phase bin, the free-form registration is performed over a $64 \times 64 \times 64$ pixel³ sub-volume around the moving sphere. The sub-volume is selected to be large enough to include the moving sphere at each phase bin. The phase bin corresponding to the home position of the sphere was chosen as the reference phase for calculating motion fields via deformable registration. Then, the center of the moving sphere was tracked to calculate its motion trajectories in all three directions.

The weighting parameter λ in Eq. (2) may affect the quantitative accuracy of the extracted motion fields. Hence, it is of importance to optimize the choice of λ . Also, the optimal value may vary when images are reconstructed by different algorithms. Therefore, the fast free-form deformable registration was performed on both FBP and PICCS reconstructed images with a series of λ values for the optimization purpose. The extracted motion trajectories from FBP- and PICCS-4DCBCT will be compared when each of them uses its λ value that gives the lowest RMSE_{3D}. The optimal λ will be used in the remainder of this paper for registration.

III.D. 4DCT based validation

A second validation is based on a numerically simulated CBCT scan using the data acquisition geometry of the Var-

ian on-board CBCT (Varian Medical Systems, Palo Alto, California). A clinical 4DCT dataset acquired from a diagnostic CT scanner (Lightspeed VCT, GE Healthcare, Waukesha, WI) was used as the image object for this simulated CBCT scan. The motion trajectory extracted from the 4DCT images was used as ground truth to validate the PICCS-4DCBCT reconstruction.

The 4DCT data set contains 10 CT image volumes to depict how patient anatomy changes over a breathing cycle. The breathing period, however, can be freely adjusted in the simulation. This freedom provides us an opportunity to study how the breathing period affects the performance of motion extraction using PICCS-4DCBCT images, as the breathing period may vary from patient to patient. The breathing period may also affect the angular distribution of projection views within a phase bin.²⁴ longer breathing period would cause the projection views to be grouped into fewer clusters (the number of clusters equal to the breathing cycles). To study whether PICCS-4DCBCT is sensitive to the breathing period, five simulations were conducted assuming breathing periods of 2, 3, 4, 5, and 6 s.

For all breathing periods, projection data were simulated for a 1-min CBCT scan through 360° with a total of 600 views of projection. At each view angle, the respiratory phase was calculated, and the 4DCT image volume with the closest phase was then selected for calculating the forward projected cone beam projection data at that view angle. The Siddon ray tracing algorithm was used to calculate projection data.⁴⁶ The original 4DCT images were resampled to have the pixel size of $(0.88 \text{ mm})^3$ and the same was used for CBCT reconstruction. The geometric parameters of the simulated CBCT scan include a 100 cm source-to-isocenter distance (SID), a 150 cm source-to-detector distance (SDD), and a detector of 40×30 cm in size with a matrix of 512×384 pixels. The detector was shifted by 14.8 cm toward one side to cover the image without in-plane truncation. The simulated CBCT projections were sorted into the same number of phase bins, 10, as the original 4DCT data set, and the PICCS algorithm was applied for 4DCBCT reconstruction. Then the motion field was calculated for each phase bin using the fast free-form deformable registration algorithm, with the end-expiration phase as the reference phase. The registration was performed over a $128 \times 128 \times 128$ pixel³ sub-volume. The motion trajectory of the tumor was calculated by tracking its centroid.

IV. HUMAN SUBJECT STUDY

To demonstrate that PICCS-4DCBCT enables the extraction of motion trajectories in human subjects, a lung cancer patient dataset was used for image reconstruction and motion trajectory extraction. The patient was scanned using a Varian Trilogy system and an RPM respiratory gating system (Varian Medical System, Palo Alto, CA). To achieve a sufficiently large field of view (FOV), the half-fan mode was used in which the flat panel detector was shifted 14.8 cm to one side. The CT acquisition parameters were 125 kVp, 80 mA, and 25 ms. 636 projections were acquired over a 60 s

TABLE I. Motion extraction errors for the numerical motion phantom to quantify the accuracy of the registration algorithm (the image pixel size is 0.8 mm.)

Anterior–Posterior		Left–Right		Superior–Inferior	
RMSE (mm)	MaxE (mm)	RMSE (mm)	MaxE (mm)	RMSE (mm)	MaxE (mm)
0.14	0.21	0.14	0.21	0.15	0.26

gantry rotation through 360° , and then sorted into 20 phase bins. The reconstructed image pixel size was $(0.88 \text{ mm})^3$, and the registration was performed over a $256 \times 256 \times 128$ pixel³ sub-volume.

V. RESULTS

V.A. Registration error quantification

The errors of the extracted motion trajectories in all three directions for the numerical motion phantom are listed in Table I. The λ value used for the registration is 0.03. Overall, the error caused by the registration method is about 0.2–0.3 times a pixel size (0.8 mm). This registration error quantification could be used as a baseline error in the assessment of the PICCS-4DCBCT method.

V.B. The physical phantom based validation

Figure 2 plots the RMSE_{3D} values when different λ values are used for the registration of both PICCS and FBP reconstructed 4DCBCT images of the physical phantom. The list of λ values includes 0.005, 0.007, 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.1, 0.2, and 0.3. For PICCS, the RMSE_{3D} value reaches its minimum when $\lambda = 0.03$; for FBP, the minimum occurs when $\lambda = 0.1$. The minimal RMSE_{3D} achieved by PICCS is considerably lower than that achieved by FBP, indicating higher accuracy of the motion trajectories from PICCS reconstructed images and than those from FBP reconstructed ones. The optimal λ value for FBP is larger than that for PICCS because the quantification of the dissimilarity term in Eq. (2) would be severely biased by streaking artifacts, and thus the smoothness regularization weight needs to be increased to compensate for the influence of the streaking artifacts. Table II lists the RMSEs and MaxEs for FBP and PICCS reconstructed images when their optimal values are used. For PICCS images, the RMSEs are less than 0.6 mm and the MaxEs are less than 1 mm (the pixel size is 0.8 mm), for all three direc-

FIG. 2. The RMSE_{3D} values when different λ values are used for the registration of the PICCS-4DCBCT images of the physical phantom.

tions. In comparison, the RMSEs and MaxEs for FBP reconstructed images are on average more than five times larger.

Figure 3 plots the motion trajectories of the physical phantom extracted from both PICCS and FBP reconstructed images. The programmed trajectories are also plotted as a reference. The measured trajectories from PICCS-4DCBCT images agree well with the programmed trajectories. In comparison, those extracted from FBP images give unrealistic tumor motion trajectories with significantly exaggerated lateral (AP and LR) motion.

Figure 4 demonstrates the root causes of the difference between FBP and PICCS observed in Fig. 3. Figure 4 illustrates the calculated motion fields for a respiratory phase (the 30% phase is chosen here) from both PICCS images and FBP images. According to the programmed motion, the sphere moved twice as fast in the SI-direction as in the AP-direction (2 cm SI motion amplitude versus 1 cm AP motion amplitude), i.e., the angle between the motion vectors and the SI axis is $\tan^{-1} 0.5 \approx 26.6^\circ$. The measurement of this angle at the center of the sphere on both PICCS and FBP generated motion fields shows that motion vectors in PICCS images point to the correct motion direction (the angle is 25.8°), whereas FBP images overestimates the horizontal motion such that the motion vector deviate from the true motion direction (the angle is 47°). The large deviation in FBP images is caused by the nonstationary characteristic of the streaking artifacts. In other words, the changes in the streaking artifacts from phase to phase generate an artifactual motion in deformable registration, and therefore lead to incorrect motion delineation. Figure 4 demonstrates that streaking artifact reduction in 4DCBCT images is crucial for

TABLE II. Motion quantification errors for the physical phantom based validation using different reconstruction methods (The image pixel size is 0.8 mm. FBP- and PICCS-4DCBCT use λ values of 0.1 and 0.03, respectively.)

	Anterior–posterior		Left–right		Superior–inferior	
	RMSE (mm)	MaxE (mm)	RMSE (mm)	MaxE (mm)	RMSE (mm)	MaxE (mm)
PICCS-4DCBCT	0.60	0.95	0.25	0.61	0.51	0.80
FBP-4DCBCT	2.26	3.81	2.61	6.63	1.34	2.86

FIG. 3. The plots of the programmed motion trajectories and those by deformable registration from FBP and PICCS images for the physical motion phantom. (a)–(c) are the trajectories projected onto AP, LR, and SI directions, respectively. (d) shows the 3D motion trajectories.

accurate extraction of motion trajectory. As a result, PICCS-4DCBCT enables faithful motion delineation.

V.C. The 4DCT based validation

Figure 5 shows both 4DCT images and PICCS-4DCBCT images at the end-expiration phase and the end-inspiration phase. The tumor is located at the right upper lung and

shows shape deformation between phases. With 4DCT images as reference, 4DCBCT images capture the nonrigid tumor motion correctly. In addition, the differences among 4DCBCT images of different breathing periods are unnoticeable.

Figure 6 shows the extracted motion trajectories of the tumor centroid from both 4DCT images and 4DCBCT images.

FIG. 4. Comparisons of the calculated motion fields for PICCS-4DCBCT (top row) and FBP-4DCBCT (bottom row) images. These images are all sagittal slices. From left to right are: the image at the 0% phase (reference phase), the image at the 30% phase, and the difference image with the calculated motion field overlaid. Each vector in the motion field indicates how the corresponding pixel in the reference image moves (the amplitude and the direction) in order to find the best match in the other image. The directions of the motion vectors from PICCS images agree with the programmed motion trajectory, i.e., the AP-motion is half of the SI-motion. In comparison, FBP images show erroneous directions of motion; the AP-motion approximately equals the SI-motion.

FIG. 5. The original 4DCT images and the PICCS-4DCBCT images at two different phases. The top row shows 4DCT images, and from the 2nd row to the bottom are PICCS-4DCBCT images when breathing periods are 2, 3, 4, 5, and 6 s, respectively. From left to right are the end-inspiration and the end-expiration phase, respectively.

FIG. 6. Comparisons of the motion trajectories of the tumor centroid from the original 4DCT images and PICCS reconstructed ones from the simulated 4DCBCT dataset along three directions. The displacement values are relative to the end-expiration phase. “bp” indicates breathing period.

In all three directions, motion trajectories from PICCS-4DCBCT images agree well with those from 4DCT images. The RMSEs and the MaxEs of motion trajectories from PICCS images at different breathing periods are listed in Table III. For all simulated breathing periods, the RMSEs are less than 0.6 mm, and the MaxEs are less than 1 mm in all three directions (the pixel size is 0.88 mm in comparison). Within a sufficiently wide range of breathing periods, PICCS-4DCBCT shows no sensitivity to the breathing period.

V.D. Human subject study

Figure 7 shows PICCS-4DCBCT images at two respiratory phases. This patient has a large tumor located at the top of the diaphragm on the right side. In the axial slice, the tumor can be seen moving in and out of the plane. In the coronal slice, it is observed that the tumor and the diaphragm reach different heights at different respiratory phases. The observed motion is quantified by deformable registration and shown in Fig. 8. The motion trajectories from PICCS images

indicate that the tumor motion is primarily in the superior/inferior (SI) direction, which shows good agreement with visual observation of the images. The SI motion amplitude is about 7 mm and the AP motion amplitude is about half of that. The LR motion shows an amplitude of approximately a single pixel size; considering the RMSE evaluation in the physical phantom study, the tumor is likely to experience negligible motion in that direction. These results demonstrate that it is feasible to apply PICCS-4DCBCT and deformable registration to clinical subjects for faithful delineation of tumor motion.

VI. DISCUSSION AND CONCLUSIONS

In this paper, the feasibility of motion trajectory extraction from the PICCS-4DCBCT method was validated using a 4DCBCT scan of a physical motion phantom, and a simulated 4DCBCT data acquisition from a 4DCT data set. The ground truth for both validation methods is known, and thus the performance of the PICCS-4DCBCT method can be

TABLE III. Motion quantification errors for the 4DCT based validation on PICCS-4DCBCT images when different breathing periods are simulated (the image pixel size is 0.88 mm.)

Breathing period	Anterior-posterior		Left-right		Superior-inferior	
	RMSE (mm)	MaxE (mm)	RMSE (mm)	MaxE (mm)	RMSE (mm)	MaxE (mm)
2 s	0.11	0.19	0.06	0.11	0.18	0.28
3 s	0.18	0.29	0.15	0.30	0.31	0.46
4 s	0.15	0.25	0.20	0.34	0.32	0.52
5 s	0.14	0.27	0.25	0.43	0.29	0.46
6 s	0.12	0.27	0.33	0.51	0.52	0.81

FIG. 7. PICCS-4DCBCT images (top row: axial slices; bottom row: coronal slices) at two respiratory phases (left column: the end-expiration phase; right column: the end-inspiration phase). The display window is $[0, 0.03] \text{ mm}^{-1}$. The arrows point to the tumor location and the dashed lines are drawn to aid the visualization of the motion.

quantified by calculating the average and maximum errors in extracted motion trajectories. In this study, a free-form deformable registration method was used to extract motion trajectories from PICCS-4DCBCT images. The success of the deformable registration method is heavily dependent on 4DCBCT image quality which is often degraded due to the under-sampling artifacts and limited contrast to noise ratio

(CNR). Using the PICCS reconstruction algorithm, it has been demonstrated in this paper that high quality 4DCBCT image can be reconstructed from highly under-sampled data acquired with a 1-min CBCT data acquisition. This is in stark contrast to other multiple minute data acquisition schemes in which 4DCBCT image quality is still limited for deformable registration to generate motion fields.

After the motion trajectories for targeted tumors are extracted from the PICCS-4DCBCT image volumes, they can be compared with the motion trajectories obtained from 4DCT in the treatment stage. The difference of the tumor motion trajectories can be used to triage further clinical actions. If there is any significant change to tumor motion, such as baseline shift and amplitude change, the patient may need to be repositioned, or the treatment may need to be replanned to reduce treatment errors.

As demonstrated in a previous study,³³ high temporal resolution 4D images can be obtained by PICCS-4DCBCT because narrower phase bins can be used to generate high quality images without contamination of the under-sampling streaking artifacts. In the second validation study and the human subject study, 20 phases of images were reconstructed. The first validation used only 10 phases, but that is limited by the fact that the original 4D dataset contains only 10 phases. In general, PICCS-4DCBCT can generate 20 or more phase images free of under-sampling caused streak artifacts. The more phases within a breathing cycle, the

FIG. 8. Motion trajectories extracted from 20 phases of 4DCBCT images of the human subject reconstructed by FBP and PICCS. (a)–(c) show motion trajectories projected onto AP, LR, and SI directions, respectively. (d) shows the 3D motion trajectories of the tumor.

higher temporal resolution the motion trajectories have. Higher temporal resolution motion trajectories may provide more faithful delineation of tumor motion and more room for treatment margin reduction.

In conclusion, PICCS-4DCBCT has been validated to provide accurate delineation of respiratory motion when the standard 1-min gantry rotation scheme is used. PICCS-4DCBCT also enables the use of a deformable registration method to extract a 3D motion field of the image object. The PICCS-4DCBCT method provides a feasible way to adaptively incorporate respiratory motion into radiotherapy treatment. However, more patient studies are needed to fully demonstrate its clinical benefits.

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- ¹E.C. Ford *et al.*, "Respiration-correlated spiral CT: A method of measuring respiratory-induced anatomic motion for radiation treatment planning," *Med. Phys.* **30**(1), 88–97 (2003).
- ²D. A. Low *et al.*, "A Method for the Reconstruction of Four-Dimensional Synchronized CT Scans Acquired During Free Breathing," *Med. Phys.* **30**(6), 1254–1263 (2003).
- ³S. S. Vedam *et al.*, "Acquiring a Four-Dimensional Computed Tomography Dataset Using an External Respiratory Signal," *Phys. Med. Biol.* **48**(1), 45–62 (2003).
- ⁴P. Keall, "4-dimensional computed tomography imaging and treatment planning," *Semin. Radiat. Oncol.* **14**(1), 81–90 (2004).
- ⁵T. Pan *et al.*, "4D-CT imaging of a volume influenced by respiratory motion on multi-slice CT," *Med. Phys.* **31**(2), 333–340 (2004).
- ⁶E. Rietzel, T. Pan, and G.T.Y. Chen, "Four-dimensional computed tomography: Image formation and clinical protocol," *Med. Phys.* **32**(4), 874–889 (2005).
- ⁷S. Krininski *et al.*, "Respiratory correlated cone-beam computed tomography on an isocentric C-arm," *Phys. Med. Biol.* **50**(22), 5263–5680 (2005).
- ⁸J.-J. Sonke *et al.*, "Respiratory correlated cone beam CT," *Med. Phys.* **32**(4), 1176–1186 (2005).
- ⁹J. Chang *et al.*, "Integrating respiratory gating into a megavoltage cone-beam CT system," *Med. Phys.* **33**(7), 2354–2361 (2006).
- ¹⁰L. Dietrich *et al.*, "Linac-integrated 4D cone beam CT: first experimental results," *Phys. Med. Biol.* **51**(11), 2939–2952 (2006).
- ¹¹T. Li *et al.*, "Four-dimensional cone-beam computed tomography using an on-board imager," *Med. Phys.* **33**(10), 3825–3833 (2006).
- ¹²J. C. Park *et al.*, "Four-dimensional cone-beam computed tomography and digital tomosynthesis reconstructions using respiratory signals extracted from transcutaneously inserted metal markers for liver SBRT," *Med. Phys.* **38**(2), 1028–1036 (2011).
- ¹³J.-J. Sonke *et al.*, "Frameless Stereotactic Body Radiotherapy for Lung Cancer Using Four-Dimensional Cone Beam CT Guidance," *Int. J. Radiat. Oncol., Biol., Phys.* **74**(2), 567–574 (2009).
- ¹⁴T. Li, A. Koong, and L. Xing, "Enhanced 4D cone-beam CT with inter-phase motion model," *Med. Phys.* **34**(9), 3688–3695 (2007).
- ¹⁵T. Li and L. Xing, "Optimizing 4D cone-beam CT acquisition protocol for external beam radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **67**(4), 1211–1219 (2007).
- ¹⁶J.-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).

- ¹⁷J. Lu *et al.*, "Four-dimensional cone beam CT with adaptive gantry rotation and adaptive data sampling," *Med. Phys.* **34**(9), 3520–3529 (2007).
- ¹⁸F. Bergner *et al.*, "Autoadaptive phase-correlated (AAPC) reconstruction for 4D CBCT," *Med. Phys.* **36**(12), 5695–5706 (2009).
- ¹⁹T. G. Purdie *et al.*, "Respiration correlated cone-beam computed tomography and 4DCT for evaluating target motion in stereotactic lung radiation therapy," *Acta Oncol.* **45**(7), 915–922 (2006).
- ²⁰F. Bergner *et al.*, "An investigation of 4D cone-beam CT algorithms for slowly rotating scanners," *Med. Phys.* **37**(9), 5044–5053 (2010).
- ²¹J.-P. Bissonnette *et al.*, "Quantifying interfraction and intrafraction tumor motion in lung stereotactic body radiotherapy using respiration-correlated cone beam computed tomography," *Int. J. Radiat. Oncol., Biol., Phys.* **75**(3), 688–695 (2009).
- ²²R. B. Case *et al.*, "Inter- and intrafraction variability in liver position in non-breath-hold stereotactic body radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **75**(1), 302–308 (2009).
- ²³R. B. Case *et al.*, "Interfraction and intrafraction changes in amplitude of breathing motion in stereotactic liver radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **77**(3), 918–925 (2010).
- ²⁴S. Leng *et al.*, "Streaking artifacts reduction in four-dimensional cone-beam computed tomography," *Med. Phys.* **35**(10), 4649–4659 (2008).
- ²⁵Z. Zheng *et al.*, "Fast 4D cone-beam reconstruction using the McKinnon-Bates algorithm with truncation correction and nonlinear filtering," *Proc. SPIE* **7961**, 79612U (2011).
- ²⁶Q. Zhang *et al.*, "Correction of motion artifacts in cone-beam CT using a patient-specific respiratory motion model," *Med. Phys.* **37**(6), 2901–2909 (2010).
- ²⁷S. Rit *et al.*, "On-the-fly motion-compensated cone-beam CT using an a priori model of the respiratory motion," *Med. Phys.* **36**(6), 2283–2296 (2009).
- ²⁸G.-H. Chen, J. Tang, and S. Leng, *Prior Image Constrained Compressed Sensing (PICCS)* (SPIE, CA, 2008).
- ²⁹G.-H. Chen *et al.*, "High temporal resolution cardiac cone-beam CT using a slowly rotating C-arm gantry," *Proc. SPIE*, **7258**, 72580C (2009).
- ³⁰T. P. Szczykutowicz and G.-H. Chen, "Dual Energy CT Using Slow kVp Switching Acquisition and Prior Image Constrained Compressed Sensing," *Phys. Med. Biol.* **55**(21), 6411–6429 (2010).
- ³¹G.-H. Chen, J. Tang, and S. Leng, "Prior image constrained compressed sensing (PICCS): A method to accurately reconstruct dynamic CT images from highly undersampled projection data sets," *Med. Phys.* **35**(2), 660–663 (2008).
- ³²J. C. Ramirez-Giraldo *et al.*, "Nonconvex prior image constrained compressed sensing (NCPICCS): Theory and simulations on perfusion CT," *Med. Phys.* **38**(4), 2157–2167 (2011).
- ³³S. Leng *et al.*, "High temporal resolution and streak-free four-dimensional cone-beam computed tomography," *Phys. Med. Biol.* **53**(20), 5653 (2008).
- ³⁴L. A. Feldkamp, L. C. Davis, and J. W. Kress, "Practical cone-beam algorithm," *J. Opt. Soc. Am. A* **1**(6), 612–619 (1984).
- ³⁵A. H. Andersen and A. C. Kak, "Simultaneous algebraic reconstruction technique (SART): A superior implementation of the ART algorithm," *Ultrason. Imaging* **6**(1), 81–94 (1984).
- ³⁶W. Press *et al.*, *Numerical Recipes in C*, 2nd ed. (Cambridge University Press, Cambridge, United Kingdom, 1992).
- ³⁷J. Modersitzki, *Numerical Methods for Image Registration* (Oxford University Press, New York, 2004).
- ³⁸M. L. Kessler, "Image registration and data fusion in radiation therapy," *Br. J. Radiol.* **79**(1), S99–S108 (2006).
- ³⁹J. P. Thirion, "Image matching as a diffusion process: an analogy with Maxwell's demons," *Med. Image Anal.* **2**(3), 243–260 (1998).
- ⁴⁰H. Wang *et al.*, "Validation of an accelerated 'demons' algorithm for deformable image registration in radiation therapy," *Phys. Med. Biol.* **50**(12), 2887–2905 (2005).
- ⁴¹B. K. P. Horn and B. G. Schunck, "Determining optical flow," *Artif. Intell.* **17**(1–3), 185–203 (1981).
- ⁴²K. K. Brock *et al.*, "Accuracy of finite element model-based multi-organ deformable image registration," *Med. Phys.* **32**(6), 1647–1659 (2005).
- ⁴³W. Lu *et al.*, "Fast free-form deformable registration via calculus of variations," *Phys. Med. Biol.* **49**(14), 3067–3087 (2004).
- ⁴⁴W. Lu *et al.*, "Deformable registration of the planning image (kVCT) and the daily images (MVCT) for adaptive radiation therapy," *Phys. Med. Biol.* **51**(17), 4357–4374 (2006).
- ⁴⁵T. Zhang, N. P. Orton, and W. A. Tome, "On the automated definition of mobile target volumes from 4D-CT images for stereotactic body radiotherapy," *Med. Phys.* **32**(11), 3493–3502 (2005).
- ⁴⁶R. L. Siddons, "Fast calculation of the exact radiological path for a three-dimensional CT array," *Med. Phys.* **12**(2), 252–255 (1985).