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Reducing scan angle using adaptive prior knowledge for a limited-angle intrafraction verification (LIVE) system for conformal arc radiotherapy

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Abstract

The purpose of this study is to develop an adaptive prior knowledge guided image estimation technique to reduce the scan angle needed in the limited-angle intrafraction verification (LIVE) system for 4D-CBCT reconstruction.

The LIVE system has been previously developed to reconstruct 4D volumetric images on-the-fly during arc treatment for intrafraction target verification and dose calculation. In this study, we developed an adaptive constrained free-form deformation reconstruction technique in LIVE to further reduce the scanning angle needed to reconstruct the 4D-CBCT images for faster intrafraction verification. This technique uses free form deformation with energy minimization to deform prior images to estimate 4D-CBCT based on kV-MV projections acquired in extremely limited angle (orthogonal 3°) during the treatment. Note that the prior images are adaptively updated using the latest CBCT images reconstructed by LIVE during treatment to utilize the continuity of the respiratory motion.

The 4D digital extended-cardiac-torso (XCAT) phantom and a CIRS 008A dynamic thoracic phantom were used to evaluate the effectiveness of this technique. The reconstruction accuracy of the technique was evaluated by calculating both the center-of-mass-shift (COMS) and 3D volume-percentage-difference (VPD) of the tumor in reconstructed images and the true on-board images. The performance of the technique was also assessed with varied breathing signals against scanning angle, lesion size, lesion location, projection sampling interval, and scanning direction.

In the XCAT study, using orthogonal-view of 3° kV and portal MV projections, this technique achieved an average tumor COMS/VPD of 0.4 ± 0.1 mm/ $5.5 \pm 2.2\%$, 0.6 ± 0.3 mm/ $7.2 \pm 2.8\%$, 0.5 ± 0.2 mm/ $7.1 \pm 2.6\%$, 0.6 ± 0.2 mm/ $8.3 \pm 2.4\%$, for baseline drift, amplitude variation, phase shift, and patient breathing signal variation, respectively. In the CIRS phantom study, this technique achieved an average tumor COMS/VPD of 0.7 ± 0.1 mm/ $7.5 \pm 1.3\%$ for a 3 cm lesion and 0.6 ± 0.2 mm/ $11.4 \pm 1.5\%$ for a 2 cm lesion in the baseline drift case. The average tumor COMS/VPD were 0.5 ± 0.2 mm/ $10.8 \pm 1.4\%$, 0.4 ± 0.3 mm/ $7.3 \pm 2.9\%$, 0.4 ± 0.2 mm/ $7.4 \pm 2.5\%$, 0.4 ± 0.2 mm/ $7.3 \pm 2.8\%$ for the four real patient breathing signals, respectively. Results demonstrated that the adaptive prior knowledge guided image estimation technique with LIVE

system is robust against scanning angle, lesion size, location and scanning direction. It can estimate on-board images accurately with as little as 6 projections in orthogonal-view 3° angle.

In conclusion, adaptive prior knowledge guided image reconstruction technique accurately estimates 4D-CBCT images using extremely-limited angle and projections. This technique greatly improves the efficiency and accuracy of LIVE system for ultrafast 4D intrafraction verification of lung SBRT treatments.

Keywords

intrafraction verification; prior knowledge; free form deformation; cone beam computed tomography; image reconstruction

1. Introduction

Lung cancer is the leading cause of cancer death and is the second most common type of cancer in both males and females. In 2016, estimated deaths of lung cancer in the United States are more than those of colon, breast, and prostate cancers combined (American Cancer Society 2016). Hypo-fractionated treatment regimens, such as stereotactic body radiation therapy (SBRT), are becoming emerging and effective treatment paradigms in radiation therapy to treat early stage non-small cell lung cancer (NSCLC) patients with very promising early clinical outcome (Chang *et al* 2015). Compared to traditional fractionated radiotherapy, SBRT delivers much higher radiation dose per fraction with no more than five fractions (Wulf *et al* 2004, Fakiris *et al* 2009). Accurate target localization is especially critical for SBRT treatments, due to its high fractional dose, tight PTV margin, and long treatment time. Introduction of advanced image-guidance systems, such as kilovoltage (kV) cone-beam computed tomography (CBCT) (Siewerdsen and Jaffray 2001, Jaffray *et al* 2002, Letourneau *et al* 2005), megavoltage (MV) CBCT (Morin *et al* 2006, Pouliot 2007), and digital tomosynthesis (DTS) (Dobbins and Godfrey 2003, Godfrey *et al* 2006, Wu *et al* 2011, Gomi 2011, Zhang *et al* 2013a, 2015a), enabled us to localize the tumor in 3D to minimize target misalignment during radiation therapy (Sonke and Belderbos 2010). However, these 3D imaging techniques may not be adequate for localizing the lung tumor, due to the uncertainties caused by the respiratory motion of the tumor.

4D imaging techniques have been developed to improve the localization accuracy of moving targets, such as 4D-CBCT (Sonke *et al* 2005, Dietrich *et al* 2006, Lu *et al* 2007) and 4D-DTS (Maurer *et al* 2008, 2010, Ren *et al* 2008). Compared with 3D imaging techniques, the 4D capacity of these techniques enables us to capture the trajectory of the moving targets for 4D localization, which can lead to better target alignment as well as better target delineation. However, current 4D-CBCT reconstructed by the Feldkamp–Davis–Kress (FDK) algorithm (Feldkamp *et al* 1984) suffers from poor image quality, long scanning time, high imaging dose, and limited mechanical clearance. In contrast, 4D-DTS only acquires limited-angle projection data for reconstruction, leading to shorter scanning time, less imaging dose and better mechanical clearance. However, 4D-DTS suffers from degraded resolution along the plane-to-plane direction without full volumetric information due to missing of depth information caused by the limited angle scan. This degraded resolution leads to severe tumor

and soft tissue distortions, which can affect the target localization accuracy. Other novel image reconstruction techniques using compressed sensing, such as the prior image constrained compressed sensing (PICCS) technique (Chen *et al* 2008), have been proposed for 4D CT/CBCT image reconstruction using under sampled data acquired over a full scan angle. However, when the projections are acquired in limited scan angle, the scanning angle requirement of PICCS to reconstruct the individual time frames using undersampled projections cannot be fulfilled. As a result, PICCS has similar organ distortion and degradation of plane-to-plane resolution as DTS, due to the missing of depth information in the limited angle acquisition.

A limited-angle intrafraction verification (LIVE) system has been developed previously to address the limitations of 4D-CBCT and 4D-DTS (Ren *et al* 2014). The LIVE system acquires only limited angle orthogonal kV and beam's eye view (BEV) MV projections to reconstruct high quality 4D-CBCT images based on prior knowledge and a motion modeling and free-form deformation (MM-FD) technique (Zhang *et al* 2013b, 2015b). Preliminary studies demonstrated that the LIVE system can reconstruct the target volume accurately when using kV and MV projections acquired in orthogonal-view 30° scan angles. LIVE can potentially provide fast volumetric target verification on-the-fly during arc treatment with minimal imaging dose and little interruption to the treatment (Ren *et al* 2014). However, due to the requirement of 30° scan angle, LIVE still requires the scan time of a few breathing cycles, which limits the efficiency of the intrafraction verification. The accuracy of the LIVE system can also be affected when patients have breathing pattern changes during the 30° scan, such as tumor baseline shift, motion amplitude change, or phase shift.

To address the limitations of the LIVE system to achieve faster and more accurate intrafraction verification of the lung tumor position during the treatment, we developed an adaptive prior knowledge guided image estimation technique for LIVE to further reduce the scanning angle needed for image estimation to accelerate the system. The adaptive prior knowledge guided image estimation technique uses adaptive prior images and deformation models to estimate on-board CBCT images based on extremely limited angle, e.g. orthogonal 3°, kV-MV projections. It considers each phase of the new on-board image as a deformation of the prior image at the same phase of the previous adjacent respiratory cycle. The deformation field is solved by deforming the prior images based on the on-board 2D kV cone-beam projections and portal BEV MV projections acquired in a single respiratory cycle. Note that in arc treatments, limited-angle portal MV projections are acquired from the exit fluence of the treatment beam with no extra MV imaging dose introduced. The technique was evaluated through simulation studies using the 4D digital extended-cardiac-torso (XCAT) phantom (Segars *et al* 2010) and experimental studies using the CIRS 008 A dynamic thoracic phantom (Computerized Imaging Reference Systems, Norfolk, VA).

2. Methods and materials

2.1. Adaptive prior knowledge guided image estimation

We aim to accelerate the LIVE system to reconstruct 4D-CBCT images for each respiratory cycle throughout the treatment. Unlike conventional 4D imaging where all the projections over many cycles are used together for reconstruction, LIVE reconstructs 4D images on a

per cycle basis, which corresponds to per cluster in figure 1. We will describe below how the image acquisition and reconstruction are performed for a specific phase x . The same process will be repeated for other phases to generate 4D-CBCT with all phases for each respiratory cycle. Figure 1 shows the kV-MV acquisition scheme of the adaptive prior knowledge guided image estimation technique, where $\alpha_n(x)$ is the scan angle to acquire kV-MV projections for a specific phase x in respiratory cycle n . Note that kV and BEV MV projections are concurrently acquired with orthogonal 90° angle in each cycle.

The flowchart of the adaptive prior knowledge guided image estimation technique is shown in figure 2. To reconstruct CBCT images at a specific phase (e.g. phase x) in the current cycle, the CBCT images reconstructed for phase x in the previous adjacent respiratory cycle are used as the prior images. The CBCT images for phase x at the current respiratory cycle are considered as a deformation of the prior images, as shown in equation (1).

$$\text{CBCT}_n(x) = \text{Deform}(\text{CBCT}_{n-1}(x), \mathbf{D}_n(x)), \quad (1)$$

where $n = 1, 2, 3 \dots$ is the respiratory cycle number; $x = 1, 2 \dots, 10$ is the phase number. $\text{CBCT}_{n-1}(x)$ and $\text{CBCT}_n(x)$ are CBCT images at the same respiratory phase x in adjacent respiratory cycles. $\mathbf{D}_n(x)$ is the deformation field map (DFM) that deforms $\text{CBCT}_{n-1}(x)$ to $\text{CBCT}_n(x)$, and it can be solved using the extremely-limited angle on-board kV and BEV MV projections acquired in the current respiratory cycle based on the data fidelity constraint and energy constraint. Once $\mathbf{D}_n(x)$ is solved, $\text{CBCT}_n(x)$ can be obtained by deforming $\text{CBCT}_{n-1}(x)$ based on $\mathbf{D}_n(x)$. These newly reconstructed CBCT images at the current respiratory cycle are then used to update the prior images for reconstruction of CBCT images at the next respiratory cycle, as shown in figure 2. Note that the pretreatment CBCT images reconstructed by our MM-FD method at phase x are used as the initial $\text{CBCT}_{\text{prior}}$ to begin with. Different from previous methods, this adaptive update of the prior images minimizes the differences between the prior images and the current images to be reconstructed, which allow us to further reduce the projection number and scanning angle needed to accelerate the LIVE system.

Details about solving the $\mathbf{D}_n(x)$ based on the data fidelity constraint and energy constraint are explained below. The data fidelity constraint requires the digitally reconstructed radiographs (DRRs) of $\text{CBCT}_n(x)$ to match with the on-board limited angle kV and portal MV projections acquired at phase x for n th breathing cycle.

$$\text{Project}(\text{CBCT}_n(x)) = \text{On board projections at phase } x. \quad (2)$$

For real clinical images, the data fidelity constraint in equation (2) may not be satisfied due to errors caused by the gray level difference between DRRs and on-board kV and portal MV projections. To solve this problem, we use normalized cross correlation (NCC) as the metric for the data fidelity constraint instead of the sum of squared differences (SSD) used in our

previous studies (Zhang *et al* 2013b). Equation (2) is then substituted by the following equation:

$$\text{NCC}(\text{Project}(\text{CBCT}_n(x)), \text{On board projections at phase } x) = 1 - \varepsilon, \quad (3)$$

where $\text{CBCT}_n(x)$ is a function of $\text{CBCT}_{n-1}(x)$ and deformation field map $\mathbf{D}_n(x)$ as shown in equation (1). Once the deformation vector field $\mathbf{D}_n(x)$ is solved, the on-board images $\text{CBCT}_n(x)$ can be obtained by deforming the adaptive prior image $\text{CBCT}_{n-1}(x)$ based on $\mathbf{D}_n(x)$. ε here accounts for the fact that DRRs cannot be exactly matched to on-board projections even when the DFMs are perfect. This is due to the existence of data inconsistencies such as imaging artifacts and noise, spectral and other hardware differences between prior image and on-board image.

The NCC calculation in the data fidelity constraint in equation (3) is further developed by introducing weightings in the target region, as shown in equation (4).

$$\text{NCC} = (1 - w) * \text{NCC}_{\text{global}} + w * \text{NCC}_{\text{ROI}}$$

Where $\text{NCC}_{\text{global}}$ is the normalized cross correlation calculated using the entire image (typically with detector size of 512×384 pixels), NCC_{ROI} is the normalized cross correlation calculated using ROI (around the tumor with irregular shape), and w is the weighting factor. w varies between 0 and 1 for kV projections, but is 1 for MV projections as the BEV MV projections only capture images of the ROI around the tumor. The weighted NCC gives extra freedom for adjusting weightings for different regions to optimize the estimation accuracy of the region of most clinical interest. For the ROI selection in the on-board projections and DRRs, internal target volume (ITV) was first contoured based on the maximum intensity projection (MIP) images of the initial 4D-CT, and PTV was generated by expanding the ITV by 5 mm on lateral direction and 7 mm on longitudinal direction. Then the PTV was expanded by 5 mm in all directions and projected to the detector as binary ROI masks using the same acquisition parameters as on-board projections. Note that the ROI masks are dynamically changed as the projection angle changes.

A free-form deformation (FD) model is used to get the deformation field map— $\mathbf{D}_n(x)$. It deforms the voxels independently from each other to satisfy the data fidelity constraint (equation (3)). To maintain the smoothness of the deformation vector field, the FD method minimizes the field deformation energy $E(\mathbf{D})$ defined by Lu *et al* (2004) during reconstruction.

$$E(\mathbf{D}) = \sum_{i=1}^{n_i} \sum_{j=1}^{n_j} \sum_{k=1}^{n_k} \sum_{m=1}^3 \left(\left(\frac{\partial D_m(i, j, k)}{\partial x} \right)^2 + \left(\frac{\partial D_m(i, j, k)}{\partial y} \right)^2 + \left(\frac{\partial D_m(i, j, k)}{\partial z} \right)^2 \right) \quad (5)$$

Where $\mathbf{D}_m$ represents the deformation fields along the three canonical directions of the Cartesian coordinate system, n_i , n_j , and n_k represent the voxel numbers along x, y, and z directions, respectively. Now the optimization problem turns into

$$D = \arg \min E(D) \quad (6)$$

subject to the data fidelity constraint in equation (3).

To solve this constraint optimization problem, an adaptive steepest descent free-form deformation (ASD-FD) algorithm (Zhang *et al* 2013b) is used similar to the ASD-POCS algorithm used in Sidky and Pan (2008). Figure 3 shows the flowchart of the ASD-FD algorithm with pseudo codes. The data fidelity constraint increases the deformation energy in equation (5) while reducing the data fidelity error in equation (4). During the optimization process, the deformation energy minimization and data fidelity constraint are enforced consecutively through gradient descent optimization with adaptive control of the step size of the deformation energy minimization to reach final convergence.

2.2. XCAT phantom study

A digital anthropomorphic phantom, extended-cardiac-torso, was used in this study to simulate the prior 4D-CBCT set, on-board 4D-CBCTs, on-board kV and portal MV projections. XCAT uses non-uniform rational B-spline surfaces to model detailed human anatomy based on databases from the National Library of Medicine and patient datasets (Segars *et al* 2010). It can generate 4D images based on anatomical and respiratory parameters inputted by the user.

2.2.1. Prior 4D-CBCT simulation—First, a lung 4D-CBCT was simulated for use as the initial prior volumes. A spherical lesion of 30 mm diameter was simulated in the middle of the lung. The respiratory motion of both the body and lesion can be controlled separately by two respiratory curves: the diaphragm curve and the chest wall curve. The diaphragm curve mainly determines the motion in the superior–inferior (SI) direction, and the chest wall curve mainly controls the motion in the anterior–posterior (AP) direction. Sinusoidal curves with a respiratory cycle of 5 s were used to simulate both the diaphragm and chest wall curves for body and lesion motions. The peak-to-peak amplitudes of the diaphragm curve and the chest wall curve were set to 2 cm and 1.2 cm, respectively. The 4D-CBCT volume of each phase was composed of $256 \times 256 \times 150$ voxels, with each voxel measuring $1.67 \times 1.67 \times 1.67$ mm in dimension. The end-inspiration phase of the simulated prior 4D-CBCT was selected as CBCT_{prior} and only end-inspiration phase on-board CBCT images were reconstructed for each respiratory cycle in this study.

2.2.2. ‘Ground-truth’ on-board CBCT images, kV and portal MV projections simulation—To evaluate the effects of potential breathing change during the treatment, four breathing pattern scenarios were simulated for the on-board 4D-CBCT sets:

1. Baseline drift: body and lesion move according to the same diaphragm curve and chest wall curve, but lesion baseline shifts 2 mm along SI direction after every respiratory cycle for 5 cycles.

2. Phase shift: body and lesion move according to the same diaphragm curve and chest wall curve, but the lesion having 5% phase shift relative to the body volume after every respiratory cycle for 5 cycles.
3. Amplitude variation: body and lesion move according to the same diaphragm curve and chest wall curve, but the peak-to-peak amplitudes of the diaphragm curve and chest wall curve increase 16.7% (1/6) along both SI and AP directions after every respiratory cycle for 5 cycles.
4. Patient breathing signal: the real-time position management (RPM) signal from a patient was imported to XCAT to simulate the diaphragm curve and chest wall curve, these curves are used to control the body motion, the lesion moves with the body according to the same diaphragm curve and chest wall curve.

These on-board 4D-CBCT images were used as the ‘ground-truth’ on-board CBCT images to evaluate the accuracy of the estimated CBCT using the adaptive prior knowledge guided image estimation technique. Two monochromatic energies were used to generate on-board image volumes: 40 keV to simulate on-board kV imaging and 1 MeV to simulate on-board MV imaging. Full fan on-board kV and portal BEV MV projections were simulated by the ray-tracking technique (Siddon 1985) based on the keV and MeV imaging volumes. The source to isocenter distance was set to 100 cm, and the isocenter to detector distance was set to 50 cm. Each projection contains 512×384 pixels, with each pixel size of 0.78×0.78 mm. The projections were simulated with an angular sampling interval of 0.3° /projection, assuming a gantry rotation speed of 6° s^{-1} and projection acquisition frame rate of 20 fps. The MV scan started from the PA direction (corresponding kV started from left lateral) and rotated in the clockwise direction. The scheme of the kV-MV acquisition was explained in figure 1. Based on the respiratory cycle (5 s) and gantry rotation speed (6° s^{-1}), it can be calculated that the projection scan directions of the same respiratory phase (of consecutive respiratory cycles) were 30° apart as shown in table 1. The new on-board image volume was reconstructed by the adaptive prior knowledge guided image estimation method using adaptive prior CBCT images and simulated on-board kV-MV projections with the imaging angle sets showed in table 1.

2.2.3. Effect of scanning angle—To determine the effects of different scan angles on the estimation results of the adaptive prior knowledge guided image estimation technique, single-view 3° , orthogonal-view 1° , 2° and 3° projections were simulated for the end-inspiration phases. The single-view here means the projections were acquired only with the kV scan angle and direction, and the orthogonal-view means the projections are acquired within two orthogonal scan angles, which were at, respectively, the kV and the MV directions in our study. The angular spacing between projections was set to 0.3° for all the different acquisition angles.

2.2.4. Effect of lesion size—Lesion sizes of 2 cm, 3 cm and 4 cm in diameter were simulated for all scenarios listed in II.B.2 to investigate the robustness of the adaptive prior knowledge guided image estimation technique against different lesion sizes. The lesion location was set in the middle of lung, and the angular spacing between projections was set to 0.3° .

2.2.5. Effect of lesion location—Three different lesion locations in the lung were simulated using the XCAT phantom: one with the lesion in the middle of the lung (MOL), one with the lesion near the chest wall (CHW), and one with the lesion near the mediastinum (MS). For the MOL case, the tumor was in the middle of the lung without any adjacent critical structures. For the CHW case, the lesion edge was attached to the chest wall and the lesion was close to the spinal cord. For the MS case, the lesion was in the right lung and close to the mediastinum. The tumor size was 3 cm, and the angular spacing between projections was 0.3° .

2.2.6. Sampling interval study—To investigate how the sparseness of projection affects the adaptive prior knowledge guided image estimation technique, different numbers of projections were simulated for the orthogonal-view 3° -each scan angle. In this study, 20, 10, 6, 4 and 2 projections were simulated and used in evaluation, which corresponds to a sampling interval of 0.3° /projection, 0.6° /projection, 1° /projection, 1.5° /projection, and 3° /projection, respectively.

2.2.7. Effect of scanning direction—The reconstruction accuracy of the adaptive prior knowledge guided image estimation technique was also evaluated for different scanning directions. In this study, three different scanning directions were simulated for kV imaging starting angles of 90° , 210° , and 300° , respectively. Correspondingly, the orthogonal MV imaging starting angles were 180° , 300° , and 30° , respectively. The results from different scanning directions were compared.

2.3. CIRS phantom study

Experiments were performed using the CIRS 008A dynamic thoracic phantom to further assess the efficacy of the adaptive prior knowledge guided image estimation technique. The CIRS phantom is a precision instrument that provides known, accurate and reproducible target motion inside a tissue equivalent phantom for investigating the impact of tumor motion inside the lung. A lung equivalent rod containing a spherical target is inserted into the lung equivalent lobe of the phantom to mimic the target. The insert is driven by a motion actuator and moves according to user-specified respiratory profiles.

2.3.1. CIRS phantom study using simulated respiratory signals—In our experiments, a GE LightSpeed RT scanner (GE Healthcare, Waukesha, WI) was used to acquire 4D-CT scans in cine mode using 120 kVp, 192 mAs per rotation. The MIP was then generated from the 4D-CT for the binary ROI masks described in II.A. The 4D-CT volume of each phase was composed of $512 \times 512 \times 144$ voxels, with each voxel measuring $0.98 \times 0.98 \times 1.25$ mm in dimension. A 3 cm-diameter and soft tissue-equivalent (density: 1.06 g cc^{-1}) spherical insert was placed inside the phantom to simulate a tumor and was programmed to move based on a $\cos^4(x)$ curve in SI direction with 5 s/cycle and 2 cm peak-to-peak amplitude. Similar to ROI selection in section 2.1, internal target volume (ITV) was contoured based on the maximum intensity projection (MIP) images of the 4D-CT, and PTV was generated by expanding the ITV by 5 mm on lateral direction and 7 mm on longitudinal direction.

A dynamic conformal arc plan was made after the 4D-CT scan in Eclipse using 6 MV beam to deliver $12.5 \text{ Gy} \times 4$ to the PTV. The MLC aperture in the plan was generated by adding a 5 mm margin to the PTV in all directions. True beam (Varian Medical Systems, Palo Alto, CA) research mode was used for treatment delivery and simultaneous kV-MV acquisition. The MLC positions were exported from the plan made in Eclipse and used for specifying the MLC locations in the xml file used for research mode delivery. The MV projections were acquired by enabling MV cine ('Continuous' mode, $\sim 6 \text{ frames s}^{-1}$) acquisition during treatment, which acquires portal MV projections every $\sim 1^\circ$. The kV projections were acquired by enabling intermittent kV projection ('DynamicGain' mode, $\sim 13 \text{ frames s}^{-1}$, 120 kVp, 80 mA, 25 ms, full-fan scan) acquisition, which acquires kV projections every $\sim 0.5^\circ$ during the treatment.

To simulate the tumor motion pattern change during the beam delivery, the peak-to-peak amplitude of the tumor was gradually increased from 2 cm to 4 cm in 5 respiratory cycles, with 0.4 cm increasing after each cycle. The end inspiration phase of the 4D-CT with 2 cm amplitude was used as the initial prior image, and on-board images at the end inspiration phase were reconstructed by the adaptive prior knowledge guided image estimation method for each respiratory cycle using the kV and portal MV projections collected in the experiment. Five 4D-CT scans were acquired separately with peak-to-peak amplitudes of 2.4 cm, 2.8 cm, 3.2 cm, 3.6 cm, and 4.0 cm to be used as ground truth, respectively. The same study was carried out with a 2 cm tumor to investigate the robustness of the method against different tumor sizes.

2.3.2. CIRS phantom study using real patient respiratory signals—In real patient scenarios, the pretreatment 4D-CBCT reconstructed by the conventional FDK method may suffer from various artifacts, such as scatter, beam hardening or truncation artifacts. These artifacts can potentially affect the accuracy of the LIVE system, as it uses pretreatment 4D-CBCT as prior images in this study. To address this issue, we propose to generate the pre-treatment high quality 4D-CBCT imaging set from the prior 4D-CT using the structural motion modeling and weighted free-form deformation (SMM-WFD) method developed previously (Harris *et al* 2017). To investigate the accuracy of this proposed clinical workflow, a 3 cm-diameter tumor was placed inside the phantom and moved with 5 s cycle and 3 cm amplitude during the prior 4D-CT acquisition. A 2 cm-diameter tumor was placed inside the phantom and moved with 5 s cycle and 2 cm amplitude during the pre-treatment 4D-CBCT acquisition to simulate tumor shrinkage and breathing amplitude change from CT to pre-treatment CBCT scans. The pretreatment 4D-CBCT was reconstructed based on the 4D-CT using the SMM-WFD method, and then used as the initial prior images for adaptive LIVE reconstruction during the arc treatment delivery. Different patient breathing variations during the treatment delivery were studied by importing four RPM signals from different patients into the CIRS software to control the CIRS lesion motion. The motion amplitudes were between 5 mm and 15 mm as shown in figure 4.

2.4. Evaluation methods

The lesions were automatically contoured based on a threshold voxel value in both estimated images and 'ground-truth' CBCT images for comparison. Two metrics were defined to

quantify the accuracy of the estimated tumor volume: center-of-mass-shift (COMS) (equation (7)) and volume percentage-difference (VPD) (equation (8)).

$$\text{COMS} = \sqrt{\Delta x^2 + \Delta y^2 + \Delta z^2} \quad (7)$$

x , y , z are center-of mass distances from V to V_0 .

$$\text{VPD} = \frac{|V \cup V_0 - V \cap V_0|}{V_0} * 100\% \quad (8)$$

V is the lesion volume contoured in the estimated image and V_0 is that contoured in the 'ground-truth' image. COMS indicates the tumor location accuracy and VPD indicates the tumor shape accuracy.

3. Results

3.1. XCAT results

Figure 5 shows an example of the ROI chosen within a kV projection at 0° and concurrently acquired portal MV projection at 90° . For MV portal projection, the BEV was chosen as the ROI, as the other region is blocked by the multi leaf collimator (MLC).

3.1.1. Image comparison and geometric accuracy of the estimated lesion—

Figure 6 shows the coronal views of the reconstructed images using the prior knowledge guided image estimation technique with and without the adaptive update of the prior images. The images were reconstructed at the end-inspiration phase using orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3° in the baseline drift scenario (XCAT scenario 1). Tumor contours from the ground-truth images were overlaid onto the reconstructed images to evaluate their accuracy. Table 2 shows the average COMS and VPD of the four XCAT scenarios described in II.B.2 with and without the adaptive technique using kV and portal MV projections acquired in orthogonal 3° scanning angle. Both the COMS and VPD were computed for the reconstruction of the end-inspiration phase of the on-board imaging volume. 2D–2D rigid registrations in the ROI region with mutual information (MI) were also performed to the orthogonal projections at the intervals without reconstructing CBCT for comparison. As shown in table 2, 2D–2D matching has larger localization errors than the LIVE adaptive method. This is mainly because 2D imaging does not provide the volumetric information of the patient. As a result, all the anatomical structures are overlaid in the 2D imaging, making it prone to registration errors especially when the small tumors typically seen in SBRT treatments are overshadowed by bony structures in the 2D images. In addition, 2D imaging cannot localize any deformations of the patient due to the missing of volumetric information. For these reasons, 2D imaging is typically used only for bony structure alignment in the initial patient set up, followed by verifications of target location using CBCT. In comparison, LIVE generated patient 4D images for 4D target verification with higher precisions than 2D imaging.

3.1.2. Effects of scanning angle—Table 3 shows the image estimation results from the adaptive prior knowledge guided image estimation technique using single-view 3°, orthogonal-view 1°, orthogonal-view 2°, and orthogonal-view 3° scan angle acquisition for all XCAT scenarios. It can be observed that orthogonal-view 1° achieved substantially better results than single-view 3° even with less total scanning angle (2° versus 3°).

3.1.3. Effects of lesion size—Figure 7 shows the reconstruction results over 5 respiratory cycles for 2 cm tumor, 3 cm tumor and 4 cm tumor using the adaptive prior knowledge guided image estimation technique. It can be observed that the COMS results from this technique are consistent for different sizes of tumor, and the VPDs from 2 cm tumor is larger than those from 3 cm tumor and 4 cm tumor because of the sensitivity of VPD to the actual tumor size.

3.1.4. Effects of lesion location in lung—Table 4 lists the reconstruction results from the adaptive prior knowledge guided image estimation technique for different tumor locations. The localization accuracy of adaptive prior knowledge based image estimation technique is slightly location-dependent, with the target near the chest wall and mediastinum demonstrate slightly better reconstruction accuracy compared to those in the middle of lung.

3.1.5. Effects of sampling interval—Figure 8 shows the reconstruction results from the adaptive prior knowledge guided image estimation technique using different number of projections for orthogonal-view 3° scan angle acquisition. For the 2 projections scheme, the kV image was acquired at the anterior–posterior view (0°) and the corresponding portal MV image was acquired at the left-lateral view (90°). It can be observed that 6 (1° angular-sampling-interval) and 10 (0.6° angular-sampling-interval) projections provide similar estimation accuracy. 20 (0.3° angular-sampling-interval) projections also provide similar estimation accuracy as using 6 and 10 projections.

3.1.6. Effects of scanning direction—Table 5 shows the reconstruction accuracy of the adaptive prior knowledge guided image estimation using orthogonal-view 3° of different scanning directions. It can be clearly seen that the estimation accuracy is very robust to the variations of scan directions.

3.2. CIRS phantom results

Figure 9 shows an example of (a) raw kV image and (b) raw MV portal image acquired during the arc treatment delivery, while (c) and (d) are the projections after blank scan normalization and $-\log$ transformation.

3.2.1. Image comparison and geometric accuracy of the estimated lesion—

Figure 10 shows the image estimation results from the adaptive prior knowledge guided image estimation technique using orthogonal-view 3° kV and portal MV projections acquired in the CIRS phantom study for 3 cm tumor. The projection sampling frequency was $\sim 0.5^\circ/\text{projection}$ for kV imaging and $\sim 1^\circ/\text{projection}$ for portal MV imaging. Table 6 shows the COMS and VPD results for each respiratory cycle in CIRS phantom study. It can be seen that the adaptive prior knowledge guided image estimation technique achieved accurate

reconstruction. The mean COMS and VPD among all respiratory cycles for orthogonal-view 3° was 0.7 ± 0.1 mm and $7.5 \pm 1.3\%$.

3.2.2. Effects of lesion size—Table 7 shows the COMS and VPD for each respiratory cycle in CIRS phantom study for 2 cm tumor. The mean COMS and VPD among all respiratory cycles for orthogonal-view 3° was 0.6 ± 0.2 mm and $11.4 \pm 1.5\%$.

3.2.3. CIRS results from the real patient RPM signals—Figure 11 shows the pre-treatment 4D-CBCT images reconstructed from the SMM-WFD method using orthogonal 30° kV projections acquired in the CIRS phantom study. The target size was changed from 3 to 2 cm in diameter, and target amplitude also had 1 cm change. SMM-WFD method achieved accurate reconstruction and the reconstructed pre-treatment 4D-CBCT images were used in the adaptive prior knowledge guided image reconstruction technique as the initial input of prior images.

Table 8 shows the COMS and VPD for the intrafractional target volume reconstructed by LIVE for each respiratory cycle of the different patient RPM signals. The mean COMS/VPD among all respiratory cycles for different scenarios with orthogonal-view 3° were 0.5 ± 0.2 mm/ $10.8 \pm 1.4\%$, 0.4 ± 0.3 mm/ $7.3 \pm 2.9\%$, 0.4 ± 0.2 mm/ $7.4 \pm 2.5\%$, 0.4 ± 0.2 mm/ $7.3 \pm 2.8\%$, respectively.

4. Discussions

This study investigates the feasibility of using an adaptive prior knowledge guided estimation technique to obtain high quality 4D-CBCT images with extremely limited-angle and extremely limited projections acquired during the arc treatment delivery. XCAT simulation and CIRS phantom studies showed that the adaptive prior knowledge guided image estimation technique can reconstruct target volume accurately using orthogonal-view 3° scanning angle.

4.1. Adaptive prior knowledge guided image estimation technique versus MM-FD technique

Compare with MM-FD technique, the adaptive prior knowledge guided image estimation technique enables to capture intra-treatment tumor variations between consecutive respiratory cycles. This technique is innovative in that it uses the adaptive prior knowledge to do image estimation and allows reconstructing a set of CBCT images within a single respiratory cycle. The adaptive prior knowledge guided image estimation technique can improve the accuracy of the 4D-CBCT estimation substantially, especially when using extremely small scan angles or low number of projections. This allows us to achieve real-time CBCT imaging for intrafraction verification to improve the localization accuracy as shown in figure 6 and table 2, which is especially critical for SBRT treatments, considering high dose of SBRT and the respiratory variation happens often during the treatment. Figure 6 and results in table 2 showed that the adaptive prior knowledge guided image estimation technique greatly reduced the COMS and VPD by deforming the tumor in the prior image to the correct locations and size for each respiratory cycle in XCAT phantom study. Figure 10 and results in tables 6–8 showed that the CBCT estimations from the adaptive prior

knowledge guided image estimation technique achieved accurate tumor localization for each respiratory cycle in CIRS phantom study.

4.2. Effects of scanning angles, lesion sizes, lesion locations, projection numbers, and scanning directions

Table 3 showed that orthogonal-view 3° scan angle yielded more accurate estimation than single-view 3° scan angle. Reducing the scan angle to orthogonal-view 1°, this technique was still able to achieve less than 1.2 mm COMS and 13% VPD for all XCAT scenarios. Orthogonal-view achieved substantially better results than single-view even with less total scanning angle.

Figure 7, tables 6 and 7 showed that the adaptive prior knowledge guided image estimation technique is very robust against different lesion sizes. In figure 7, the COMS from 2 cm tumor and 4 cm tumor are consistent with the results from 3 cm tumor at different respiratory cycles. The VPDs from 2 cm tumor are consistently large than those from 3 cm and 4 cm tumors, as the VPD is inversely proportional to the tumor volume V_0 as showed in equation (8).

Results in table 6 demonstrated that the image estimation accuracy of this technique is slightly location-dependent, with the target near the chest wall and mediastinum demonstrate slightly better reconstruction accuracy compared to those in the middle of lung, probably due to the tumor motion near the chest wall and mediastinum is less than the motion in middle of the lung.

Figure 8 showed that more accurate estimation can be achieved using as few as 6 projections with orthogonal-view 3° scan angle (equal to 1° angular-sampling-interval). Reducing the projection number to 4 degraded the accuracy slightly, while reducing the projection to 2 (only 1 kV projection and 1 MV portal projection) degraded the estimation accuracy substantially.

Results from table 5 demonstrated that the image estimation accuracy is less affected by the scanning directions. COMS and VPDs from different scanning directions are almost same.

4.3. Effects of breathing irregularity

Patients' breathing irregularities include long progressive changes, such as baseline drift and amplitude change commonly seen in patients, and short sudden sporadic changes. Previous results demonstrated the accuracy of the LIVE system in localizing tumor motions with various progressive changes, as shown in the patient RPM signals. However, it's unclear about the system's performance under circumstances where there might be large sudden sporadic respiration changes between consecutive cycles. To investigate this, in the following XCAT simulation, the respiratory amplitudes were gradually changed at the first two respiratory cycles. Then at the third cycle, the amplitudes were increased dramatically by 5/6 in AP and SI directions (increased from 1.2 cm to 2.2 cm in AP direction and from 2.0 cm to 3.7 cm in SI direction) to simulate a sudden large breathing change. After the third cycle, the breathing pattern becomes normal and gradually decreased by 1/6 (16.7%) after each respiratory cycle for the rest of cycles as shown in figures 12(a) and (b). Figures 12(c)

and (d) show the image estimation results from the adaptive prior knowledge guided image estimation technique using orthogonal-view 3° kV and portal MV projections. It can be seen that the large sudden breathing change only affected the localization accuracy of LIVE for the third cycle when it occurred. The LIVE system was able to achieve sub-mm accuracy immediately after the cycle with the large sudden breathing change, as the results shown in figure 12. This demonstrated the technique's ability to auto-correct reconstruction errors caused by large sporadic breathing irregularities.

From a dosimetry point of view, breathing irregularities with long progressive changes have a major impact on the total dose delivery in SBRT, since it can cause the tumor to move outside PTV for long period of time to cause large delivery errors for the accumulated dose. In comparison, the short sudden sporadic change will have minimal effects on the total delivered dose as its lasting period is much shorter than the total delivery time of SBRT. As results showed that LIVE is able to localize the target accurately during long progressive changes and also within only one respiratory cycle after a large sporadic change, it can be anticipated that LIVE is adequate to prevent treatment errors that have clinically significant dosimetric effects on the treatments. However, further dosimetric studies are warranted to quantify the improvements of the dose delivery accuracy achieved with LIVE verification.

4.4. Clinical implementation and significance

In practice, the intrafraction verification by LIVE can be fully automated without therapists' intervention. During daily clinical implementation, pretreatment 4D-CBCT images can first be generated by deforming the planning CT images using the prior knowledge based reconstruction method (Harris *et al* 2017). The pretreatment 4D-CBCT images generated in this approach essentially have the same image quality as planning CT images, and are adequate to be used as prior images for LIVE image reconstruction. LIVE can then generate intrafraction 4D-CBCT images by deforming the pretreatment 4D-CBCT images using the adaptive method proposed in this study, as demonstrated in the experimental study in section 2.3.2. Since target volume contour is always available in the planning CT images, the target volume contour in pretreatment 4D-CBCT can be automatically generated by deforming the contour in CT based on the deformation field solved in the reconstruction. Subsequently, the target volume contours in the LIVE 4D-CBCT images can be automatically generated from the contour in the pretreatment 4D-CBCT using the same approach. These target volume contours in LIVE images can be automatically compared with the planned PTV volume to verify if the target is still within the PTV. A threshold value can be set to automatically stop the radiation delivery when the target is outside PTV for certain amount of time. This verification process mainly involves deformation of contours based on deformation fields solved by LIVE and comparison between target contour and PTV, which can be fully automated with minimal processing time.

The current studies focused on the applications of the LIVE verification for dynamic conformal arc therapies. For rapid arcs, as the MV field will be partially blocked during the delivery, the MV cine images may not be adequate for LIVE reconstruction, depending on the complexities of the leaf motions. As an alternative, we can acquire limited angle kV and MV projections between the deliveries of different arcs for LIVE 4D verification. Note that

the MV projections will still be confined to the target region, similar as in the BEV MV case. The extra MV imaging dose to the target can potentially be accounted for in the planning process by incorporating the imaging dose in the plan (Alaei *et al* 2010). For 3D/IMRT cases, limited angle kV and MV projections are acquired as gantry rotates from one static beam to the next. Again, similar approach for MV imaging confinement and dose compensation can be taken in this scenario. On another note, based on our own institutional experiences, around 70% of lung SBRT patients have been effectively treated with the 3D planning technique in the past. All 3D treatments can be effectively planned with dynamic conformal arcs to achieve equivalent or even better dosimetric distribution. Therefore, potentially dynamic conformal arcs can be used for ~70% of lung SBRT patients in the future with the extra benefits of LIVE verification during the arc delivery.

To the best of our knowledge, in current practice, there are no intrafraction 4D verification tools that can localize the target during the treatment to minimize the treatment errors caused by intrafractional respiratory motion change or patient position change. As a result, ITV to PTV margin of 5 mm or larger is needed, partially to account for any intrafractional localization errors. The LIVE system addressed this problem by providing 4D intrafraction verification of the target during the treatment delivery. Our previous developments required orthogonal-30° scan angles for the LIVE reconstruction, which limits the efficiency of the intrafraction verification (Ren *et al* 2014). This work reduces the scanning angle to orthogonal-3° while keep the similar accuracy, which allows more frequent cycle by cycle verification throughout the arc treatment delivery. This improvement of localization accuracy by LIVE can potentially further enhance the tumor control and reduce the normal tissue toxicities, paving the roads to further margin reduction and dose escalation in SBRT.

4.5. Limitation of this study

The adaptive prior knowledge guided image estimation technique uses the NCC similarity metric in the data fidelity constraint, which is more robust against the intensity mismatches between DRRs and on-board projections. However, the intensity mismatches between DRRs and real kV/MV projection data caused by imaging artifact, such as scattering, beam hardening, and gray level mismatch due to kV-MV energy differences, can still cause differences within the NCC, which may affect the data fidelity value and optimization of the algorithm. This can be potentially solved using modeling/correction of image artifacts and kV-MV conversion techniques mentioned in previous studies (Yin *et al* 2005, Ren *et al* 2012, 2014, 2016). Another option is to explore the feasibility of using mutual information as the similarity matrix, which could be more robust than NCC.

Currently, with 30 iterations, the image estimation takes approximately 74 s^{-1} for 10 projections for a volume of $256 \times 256 \times 150$ voxels on a single GPU device with NVIDIA CUDA toolbox. A profile summary has been shown in table 9. DRR forward projections were called 112 times during the optimization and took more than 80% of the computation time. This can be potentially reduced by using multiple GPUs in the future, as the forward projection time is dramatically reduced to 1/8 if only one DRR projection is calculated. The NCC and backward projection time can also be reduced accordingly using multiple GPUs and parallel computing. In addition, using algorithm optimization, the iteration number and

the line search steps in each iteration can be further reduced to further accelerate the speed of the system. With all the acceleration strategies implemented, we anticipate that the total reconstruction time of LIVE can be reduced to seconds.

The current studies have validated the LIVE system using the XCAT simulation and the CIRS phantom. Simulation and phantom studies provide us the unique opportunities to simulate different patient and image acquisition scenarios to evaluate the robustness of the system against each scenario. Besides, ground-truth images are always available in these studies to evaluate the accuracy of the system. However, the anatomical structures in XCAT and CIRS phantom are simpler than the real patient anatomy, and further patient studies are warranted to fully evaluate the efficacy of LIVE. One challenge with the patient study is to obtain the ground truth images, as currently there are no imaging techniques that can provide 4D images of the patient for each respiratory cycle. One possible option is to acquire another 4D-CBCT scan shortly after the pre-treatment 4D-CBCT scan, and use the second 4D-CBCT scan as the ground-truth images.

5. Conclusion

We have developed an adaptive prior knowledge guided image estimation technique for the LIVE system to reconstruct 4D volumetric images using kV and portal MV projections acquired in extremely-limited angles for intrafraction verification. This technique greatly improves the efficiency and accuracy of the LIVE system for ultrafast 4D intrafraction verification of lung SBRT treatments.

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Figure 1.
kV-MV acquisition scheme of the adaptive prior knowledge guided image estimation technique.

Figure 2.
Flowchart of the adaptive prior knowledge guided image estimation technique.

Figure 3.
Flowchart of the ASD-FD algorithm with pseudo codes and parameter values used.

Figure 4.
Different patient RPM signals used to control the lesion motion in the CIRS phantom study.

Figure 5.

An example of the ROI selected within projection images. (a) Selected ROI within a kV projection at 0° . (b) Selected ROI within a concurrently acquired portal MV projection at 90° . The weightings would be applied for the ROI within the data fidelity constraint of the adaptive free-form deformation model.

Figure 6.

CBCT images reconstructed without and with the adaptive technique using the prior knowledge guided image estimation technique. The lesion baseline was simulated to shift by 2 mm along SI direction after every respiratory cycle for 5 cycles (scenario 1). The lesion contours in the ground-truth images are overlaid onto the reconstructed images for comparison (red contours). The baseline of the lesion is shown with yellow lines. Orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3° were used in this reconstruction.

Figure 7.

COMS and VPD comparison of the CBCT images reconstructed with the adaptive prior knowledge guided image estimation technique between 2 cm, 3 cm and 4 cm tumors after each respiratory cycle for different scenarios in section 2.2.2. The reconstruction used orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3° .

Figure 8.

Comparison of image estimation COMS results from the adaptive prior knowledge guided image estimation technique for orthogonal-view 3° -each scan angle acquisition of different angular sparseness. The results were calculated based on the estimated and ground-truth 4D-CBCT end-inspiration phase images. The reconstruction used orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3° .

Figure 9.

An example of kV and portal MV image acquired during the arc treatment. (a) Raw kV image acquired at 102° . (b) Raw MV portal image acquired concurrently at 192° . (c) kV image after blank scan normalization and $-\log$ transformation. (d) MV portal image after blank scan normalization and $-\log$ transformation.

Figure 10.

CBCT images reconstructed with the adaptive technique using orthogonal-view 3° kV and portal MV projections acquired in the CIRS phantom study. The lesion amplitude was simulated to increase by 20% (1/5) after every respiratory cycle for 5 cycles from 2 cm to 4 cm. The lesion contours in the ground-truth images are overlaid onto the reconstructed images for comparison (red contours). The baseline of the lesion is shown with yellow lines.

Figure 11.

Pre-treatment 4D-CBCT images reconstructed by SMM-WFD method using orthogonal 30° kV projections in the CIRS phantom study. FDK reconstruction using full sampled projections in 200° are also shown as a reference.

Figure 12.

Simulated breathing curves and CBCT reconstruction results using the prior knowledge guided image estimation technique in irregular breathing study case. The arrows point to the time where the irregularity happens. The reconstruction used orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3°. (a) Irregular breathing, (b) irregular breathing, (c) reconstructed result, (d) reconstructed result.

Table 1

Five imaging angle sets for respiratory cycles 1–5 simulated in this study.

Acquisition set	1	2	3	4	5
kV scan angle	90°–93°	120°–123°	150°–153°	180°–183°	210°–213°
MV scan angle	180°–183°	210°–213°	240°–243°	270°–273°	300°–303°

Table 2

Average COMS and VPD of five respiratory cycles simulated in XCAT with different scenarios in section 2.2.2. The prior data, 2D–2D rigid registration in ROI region, and reconstruction without adaptive method are also shown for comparison. The reconstruction used orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3°.

XCAT scenario		Prior	2D-2D	LIVE without adaptive	LIVE with adaptive
1	COMS (mm)	6.0 ± 3.2	4.1 ± 2.1	3.5 ± 2.7	0.4 ± 0.1
	VPD	57.9% ± 29.5%	—	30.6% ± 22.5%	5.5% ± 2.2%
2	COMS (mm)	6.8 ± 3.3	4.3 ± 2.2	4.7 ± 3.1	0.6 ± 0.3
	VPD	63.8% ± 30.3%	—	40.5% ± 25.1%	7.2% ± 2.8%
3	COMS (mm)	3.8 ± 2.0	1.0 ± 0.5	1.8 ± 1.3	0.5 ± 0.2
	VPD	35.5% ± 18.5%	—	17.2% ± 11.8%	7.1% ± 2.6%
4	COMS (mm)	4.8 ± 2.4	1.2 ± 0.6	2.6 ± 1.9	0.6 ± 0.2
	VPD	45.0% ± 22.5%	—	23.5% ± 16.9%	8.3% ± 2.4%

Table 3

Average COMS and VPD of five respiratory cycles simulated in XCAT with different scenarios in section 2.2.2 using different scanning angles. Angular sampling intervals of kV and portal MV projections were both 0.3°.

XCAT scenario		Single-view 3° (kV-only)	Orthogonal-view 1°	Orthogonal-view 2°	Orthogonal-view 3°
1	COMS (mm)	2.2 ± 0.7	0.6 ± 0.2	0.5 ± 0.2	0.4 ± 0.1
	VPD	21.7% ± 6.9%	8.0% ± 2.9%	7.2% ± 3.0%	5.5% ± 2.2%
2	COMS (mm)	3.6 ± 1.9	1.1 ± 0.5	0.8 ± 0.4	0.6 ± 0.3
	VPD	32.3% ± 15.0%	11.6% ± 4.1%	9.3% ± 3.2%	7.2% ± 2.8%
3	COMS (mm)	1.4 ± 0.8	0.9 ± 0.4	0.7 ± 0.3	0.5 ± 0.2
	VPD	14.4% ± 6.8%	10.4% ± 3.4%	9.2% ± 3.0%	7.1% ± 2.6%
4	COMS (mm)	1.9 ± 1.0	1.1 ± 0.4	0.9 ± 0.3	0.6 ± 0.2
	VPD	17.7% ± 7.3%	12.8% ± 4.5%	11.0% ± 3.7%	8.3% ± 2.4%

Table 4

Average COMS and VPD of five respiratory cycles simulated in XCAT with different scenarios in section 2.2.2 for different target locations. The reconstruction used orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3°.

XCAT scenario		Chest wall	Mediastinum	Middle of lung
1	COMS (mm)	0.6 ± 0.2	0.5 ± 0.2	0.4 ± 0.1
	VPD	$7.2\% \pm 2.6\%$	$6.9\% \pm 2.4\%$	$5.5\% \pm 2.2\%$
2	COMS (mm)	0.3 ± 0.1	0.7 ± 0.2	0.6 ± 0.3
	VPD	$4.8\% \pm 1.1\%$	$7.9\% \pm 2.7\%$	$7.2\% \pm 2.8\%$
3	COMS (mm)	0.6 ± 0.3	0.4 ± 0.1	0.5 ± 0.2
	VPD	$7.8\% \pm 2.9\%$	$5.2\% \pm 1.3\%$	$7.1\% \pm 2.6\%$
4	COMS (mm)	0.4 ± 0.1	0.4 ± 0.2	0.6 ± 0.2
	VPD	$7.2\% \pm 1.5\%$	$5.0\% \pm 2.2\%$	$8.3\% \pm 2.4\%$

Table 5

Average COMS and VPD of five respiratory cycles for the adaptive prior knowledge guided image estimation using orthogonal kV and portal MV projections acquired along different scanning directions in the XCAT phantom study. The reconstruction used orthogonal-view 3° kV and portal MV projections with an angular sampling interval of 0.3°.

		<u>kV: 90°–240°</u>	<u>kV: 210°–0°</u>	<u>kV: 300°–90°</u>
XCAT scenario		MV: 180°–330°	MV: 300°–90°	MV: 30°–180°
1	COMS (mm)	0.4 ± 0.1	0.4 ± 0.1	0.3 ± 0.1
	VPD	5.5% ± 2.2%	5.7% ± 3.7%	5.0% ± 1.4%
2	COMS (mm)	0.6 ± 0.3	0.6 ± 0.1	0.7 ± 0.3
	VPD	7.2% ± 2.8%	7.0% ± 1.1%	7.7% ± 2.6%
3	COMS (mm)	0.5 ± 0.2	0.5 ± 0.2	0.7 ± 0.2
	VPD	7.1% ± 2.6%	6.7% ± 1.1%	7.9% ± 2.1%
4	COMS (mm)	0.6 ± 0.2	0.7 ± 0.2	0.7 ± 0.1
	VPD	8.3% ± 2.4%	8.9% ± 2.5%	9.3% ± 1.9%

COMS and VPD results for each respiratory cycle in CIRS phantom study for 3 cm tumor. The difference between prior images and on-board images is also shown for comparison. *Prior* is the difference between prior image and the ground truth image, *estimated* is the difference between estimated image from LIVE and the ground truth image. The reconstruction used orthogonal-view 3° kV and portal MV projections acquired at different angles for different cycles. The projection sampling frequency was ~0.5°/projection for kV imaging and ~1°/projection for portal MV imaging.

Table 6

Respiratory cycle	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
Prior					
COMS (mm)	2.0	4.0	6.0	8.0	10.0
VPD	19.7%	39.3%	58.3%	76.7%	94.9%
Estimated					
COMS (mm)	0.5	0.7	0.8	0.6	0.7
VPD	5.8%	7.7%	9.0%	6.7%	8.3%

COMS and VPD results for each respiratory cycle in CIRS phantom study for 2 cm tumor. The difference between prior images and on-board images is also shown for comparison. *Prior* is the difference between prior image and the ground truth image, *estimated* is the difference between estimated image from LIVE and the ground truth image. The reconstruction used orthogonal-view 3° kV and portal MV projections acquired at different angles for different cycles. The projection sampling frequency was ~0.5°/projection for kV imaging and ~1°/projection for portal MV imaging.

Table 7

Respiratory cycle		Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
Prior	COMS (mm)	2.0	4.0	6.0	8.0	10.0
	VPD	28.8%	57.6%	84.2%	109.6%	136.5%
Estimated	COMS (mm)	0.7	0.8	0.4	0.6	0.7
	VPD	11.5%	13.8%	9.9%	10.6%	11.3%

Table 8

COMS and VPD results for each respiratory cycle in CIRS phantom study for 2 cm tumor for different patient RPM signals. The reconstruction used orthogonal-view 3° kV and portal MV projections acquired at different angles for different cycles. The projection sampling frequency was ~0.5°/projection for kV imaging and ~1°/projection for portal MV imaging.

Respiratory cycle		Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
Respiratory curve 1	COMS (mm)	0.3	0.6	0.5	0.4	0.8
	VPD	9.5%	12.4%	10.4%	9.7%	12.1%
Respiratory curve 2	COMS (mm)	0.3	0.2	0.1	0.6	0.7
	VPD	5.7%	5.3%	4.6%	10.5%	10.4%
Respiratory curve 3	COMS (mm)	0.3	0.5	0.6	0.5	0.2
	VPD	4.6%	9.2%	10.1%	8.1%	4.9%
Respiratory curve 4	COMS (mm)	0.1	0.3	0.5	0.4	0.6
	VPD	2.8%	6.2%	9.6%	8.6%	9.2%

Table 9

Time profile summary of the free-form deformation algorithm in this study.

Function	Calls	Time (s)
Total_time	—	74
Forward_projection	112	62
FDK_backprojection	30	3
NCC	111	3
Energy	62	3
Others	—	3