Characterizing spatiotemporal information loss in sparse-sampling-based dynamic MRI for monitoring respiration-induced tumor motion in radiotherapy

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Purpose: Sparse-sampling and reconstruction techniques represent an attractive strategy to achieve faster image acquisition speeds, while maintaining adequate spatial resolution and signal-to-noise ratio in rapid magnetic resonance imaging (MRI). The authors investigate the use of one such sequence, broad-use linear acquisition speed-up technique (k - t BLAST) in monitoring tumor motion for thoracic and abdominal radiotherapy and examine the potential trade-off between increased sparsification (to increase imaging speed) and the potential loss of “true” information due to greater reliance on *a priori* information.

Methods: Lung tumor motion trajectories in the superior–inferior direction, previously recorded from ten lung cancer patients, were replayed using a motion phantom module driven by an MRI-compatible motion platform. Eppendorf test tubes filled with water which serve as fiducial markers were placed in the phantom. The modeled rigid and deformable motions were collected in a coronal image slice using balanced fast field echo in conjunction with k - t BLAST. Root mean square (RMS) error was used as a metric of spatial accuracy as measured trajectories were compared to input data. The loss of spatial information was characterized for progressively increasing acceleration factor from 1 to 16; the resultant sampling frequency was increased approximately from 2.5 to 19 Hz when the principal direction of the motion was set along frequency encoding direction. In addition to the phantom study, respiration-induced tumor motions were captured from two patients (kidney tumor and lung tumor) at 13 Hz over 49 s to demonstrate the impact of high speed motion monitoring over multiple breathing cycles. For each subject, the authors compared the tumor centroid trajectory as well as the deformable motion during free breathing.

Results: In the rigid and deformable phantom studies, the RMS error of target tracking at the acquisition speed of 19 Hz was approximately 0.3–0.4 mm, which was smaller than the reconstructed pixel resolution of 0.67 mm. In the patient study, the dynamic 2D MRI enabled the monitoring of cycle-to-cycle respiratory variability present in the tumor position. It was seen that the range of centroid motion as well as the area covered due to target motion during each individual respiratory cycle was underestimated compared to the entire motion range observed over multiple breathing cycles.

Conclusions: The authors’ initial results demonstrate that sparse-sampling- and reconstruction-based dynamic MRI can be used to achieve adequate image acquisition speeds without significant information loss for the task of radiotherapy guidance. Such monitoring can yield spatial and temporal information superior to conventional offline and online motion capture methods used

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1. INTRODUCTION

Respiratory motion management is a major challenge during the treatment of thoracic and abdominal tumors in modern radiation therapy (RT). Such motion introduces geometric and dosimetric errors in the administration of the prescribed radiation dose to the tumor target while potentially causing excessive dose-related toxicity in healthy tissue and critical organs. The current clinical standard for capturing motion-related anatomical changes is respiratory-correlated four dimensional (3D volume + time) computed tomography (4DCT), which generates a retrospectively sorted set of 3D volumes (typically 6–10) distributed over an average representative respiratory cycle.^{1–3} Typically, the extent of motion of the tumor target is assessed from 4DCT and used to create a motion-encompassing internal target volume (ITV). One of the major limitations with the 4DCT-based approach is that cycle-to-cycle irregularities such as baseline shifts, amplitude, and frequency variations are not captured adequately and can lead to significant dosimetric uncertainties, underdosing of tumors, and radiation damage to healthy tissues.^{4,5} Therefore, long-term monitoring over multiple breathing cycles is desirable to better capture and account for such variations. Rapid magnetic resonance imaging (MRI) is an attractive alternative that enables long-term soft-tissue based monitoring.^{6,7} In addition to being ionizing radiation-free (thus enabling long-term motion monitoring), MRI offers many advantages such as a rich variety of contrast mechanisms, arbitrary slice orientation, and variable spatial and temporal resolution.

The challenge in rapid MRI is that there exists a trade-off between image signal-to-noise ratio (SNR) and spatiotemporal resolution. One approach to achieve a balance between these competing objectives is to make use of techniques based on sparse-sampling and reconstruction, which make use of *a priori* information about the anatomy and its motion in order to go beyond the limits imposed by conventional rapid imaging techniques. For instance, broad-use linear acquisition speed-up technique (k - t BLAST) increases image acquisition speed by reducing k -space sampling in the phase-encoding direction by a given k - t acceleration factor.^{8,9} Reduced data are later recovered by exploiting correlations among the entire series of acquired images in both k -space and time. Therefore, high temporal resolution is achieved without significantly compromising spatial resolution and SNR. However, as this and other sparse-sampling sequences rely on progressively added *a priori* information, there is increased risk of losing “true” spatial or temporal information. To our knowledge, such loss of information with increasing sparsification has not been quantified in the context of image guided radiation therapy.

In this study, we characterize such loss of spatiotemporal information in an adaptation of a 2D image over time (2D + t) balanced fast field echo sequence (bFFE), also known as balanced steady state free precession (bSSFP) using k - t BLAST to capture the thoracic and abdominal tumor motion model and in cancer patients. The k - t acceleration factor must sufficiently incorporate the high frequency components of tumor motion while maintaining adequate spatial resolution for image-guided RT. Two main tasks were undertaken in this study. First, the true loss of motion information was estimated based on four different k - t acceleration factors (1, 2, 5, and 16) to keep track of lung tumor motion. This estimation enabled determination of the relationship between image acquisition speed and motion tracking accuracy. An in-house, programmable MRI-compatible motion platform¹⁰ [equipped with Eppendorf test tubes (1.5 ml) as fiducial markers] was employed to replicate a realistic 1D tumor motion (rigid and deformable) in the MRI scanner. Root mean square (RMS) error was used as a metric of spatial accuracy, comparing measured motion traces with “ground truth” input motion data. Finally, kidney and lung tumor motions were measured during free breathing from two patients using the same bFFE with the k - t BLAST scheme. Cycle-to-cycle variability of tumor motion area (2D cross-sectional representation of ITV) and tumor displacement were evaluated to demonstrate the presence of ITV differences between a single representative breath and multiple respiration cycles.

2. METHODS

2.A. Overview

This study consisted of two main parts: (1) In a modeling phantom study, spatiotemporal informational losses were estimated for four different k - t acceleration factors (1, 2, 5, and 16) for the application of tracking patient-recorded lung tumor motion in the superior–inferior direction. Using a custom-built MRI-compatible programmable motion platform, realistic tumor motion was evaluated in the MRI scanner (3T Philips Ingenia). This phantom study is further divided into two parts: rigid and deformable motions. The rigid phantom study strictly quantifies the spatial error between measured motion and ground truth input motion when the motion is monitored along either frequency or phase encoding direction. The deformable phantom study evaluates the additional spatial error associated to viscoelastic motion. (2) In a human subject study, the k - t BLAST imaging scheme was tested on two human subjects with kidney (H1) and lung (H2) tumors. Tumor respiratory motion patterns were captured in a single coronal image plane over multiple respiratory cycles (8 cycles with H1 and 15 cycles with H2 in 49 s). Cycle-to-

cycle respiratory motion irregularity was quantified for each subject.

2.B. Phantom study

2.B.1. CyberKnife Synchrony lung tumor motion data

Lung tumor motion data were obtained from a database created by Suh *et al.*, the CyberKnife Synchrony motion system.¹¹ We selected one representative treatment fraction from ten individual patients (M1–M10) treated with the Cyberknife Synchrony technology (G3 System with delivery software version 6.2.3, Accuray Incorporated, Sunnyvale, CA) at Georgetown University Hospital between July 2005 and January 2006.¹¹ Tumor respiratory motion data were derived using a motion prediction algorithm, which utilizes the correlation model between the patient's external chest-abdominal motion and internal tumor fiducial locations. The estimated systematic error of the internal tumor position is considered to be less than 1 mm.¹² All ten motion data sets were also visually inspected to exclude possible regions of tracking errors including large transient tumor position changes as well as long pauses. The duration of the selected motion data was a minimum of 120 s.

2.B.2. MRI-compatible motion platform

Each individual motion trace was programmed into a custom-built MRI-compatible motion platform driven by piezoceramic motors,¹⁰ as shown in Fig. 1(A). While the positioning update rate of the motion platform system was set at 50.0 Hz, the original CyberKnife Synchrony data were sampled at either 26.3 or 25.6 Hz. Therefore, input motion data were resampled at 50.0 Hz using linear interpolation of the original Synchrony data. No additional filter or smoothing was applied. The actual stroke position of the motion platform and input motion data is typically within 0.1 mm unless external resistance prevented the piezoceramic motor from driving proper motion. Deviation of the actual stroke position from input data was constantly monitored via an in-house control panel developed in LabView (National Instruments, Austin, TX). In the current study, no deviation in the stroke position

was observed. The 10 motion datasets represented the ground truth in this study.

2.C. MRI studies

2.C.1. Tracking modeled rigid tumor motion

Six conical 1.5 ml Eppendorf tubes were filled with water and placed on the motion platform. The test tubes served as fiducial markers in MR images [Fig. 1(B)]. Marker motion in superior–inferior direction within a single 2D coronal slice [field of view (FOV): $323 \times 323 \text{ mm}^2$, reconstruction matrix: 480×480 , reconstructed resolution: $0.67 \times 0.67 \text{ mm}^2$, slice thickness: 5 mm] was collected on a 3.0 T whole-body MR scanner (Ingenia, Philips, Best, Netherlands). A torso radio frequency (RF) receiver coil was mounted on a plastic spacer with the motion platform placed on the MRI table. A dynamic imaging scheme, consisting of bFFE (TE/TR minimum: 1.3/2.5 ms, flip angle: 40° , phase encoding steps: 160) in conjunction with *k-t* BLAST, allowed us to capture multiple images within a single coronal slice over a given time period. The frequency and phase-encoding directions were selected to be in superior–inferior and left–right directions, respectively. A rectangular FOV scheme was used and the frequency-encoding direction (i.e., superior–inferior direction) was reduced compared to the phase-encoding direction (rectangular FOV: $f250 \times p323 \text{ mm}^2$, acquisition matrix: $f124 \times p160$, rectangular reconstruction matrix: $f372 \times p480$). These image acquisition parameters represent typical human subject chest protocol.

The rigid phantom study was an experiment; yet the frequency and phase encoding directions were switched to examine the influence of directionality in terms of the motion tracking accuracy (TE/TR minimum: 1.4/2.7 ms, flip angle: 40° , phase encoding steps: 160, rectangular FOV: $p323 \times f250 \text{ mm}^2$, acquisition matrix: $p160 \times f124$, rectangular reconstruction matrix: $p480 \times f372$). Thus, the direction of marker motion was set along phase encoding direction.

Four *k-t* acceleration factors (1, 2, 5, and 16) were compared in randomized order; each tumor motion pattern was repeated four times and a total of 40 MRI measurements were made. Since the maximum number of images

FIG. 1. (A) The MRI-compatible motion platform used in this study. Modeled lung tumor motion data in patients were programmed into the platform, enabling replication of realistic 1D tumor motion within the MR scanner. (B) Six fiducial markers were observed in a coronal MR image, and an average motion trajectory was computed from each dynamic imaging series using affine image registration of the six fiducial markers. Two arrows represent the motion direction.

acquired during one dynamic scan was limited to 720 due to the limited scanner memory, the maximum acquisition duration was approximately 37 s with a k - t factor of 16. Each dynamic imaging series consisted of a simulated respiratory motion trace of at least 30 s in duration; image data were eliminated within the first 5 s to cope with system latency and the initial offset error of the motion platform. Therefore, the rest of the data were analyzed for 25 s; all data comparisons referred to in this paper were made during this 25 s interval. This sampling period corresponded to approximately 6–8 respiratory cycles.

Affine image registration¹³ was used to compute the transformation between the first image of each series and the remaining images, thereby characterizing the 2D motion trajectories of six fiducial markers. A total of 60 trajectories (10 traces $\times$ 6 markers) were obtained. For each dynamic image series, one average motion trajectory was also computed based on the displacement of six fiducial markers during the analysis period.

2.D. Data analysis

2.D.1. Characteristics of input ground truth tumor motion data

The characteristics of ground truth motion data from ten individuals during the 25 s analysis period are shown in Table I. The frequency spectrum (from 0 to 25.0 Hz) of each ground truth motion data was computed using a 1D Fourier transform to identify the major frequency components among the patients' lung tumor respiratory motion.

2.D.2. Sampling frame rate for each k - t acceleration factor

The image acquisition speed (i.e., sampling rate in the units of Hz) for each dynamic image, at a given k - t acceleration factor, was unknown. Thus, it was individually assessed; for each dynamic image series, the one average motion trajectory

based on the displacement of six fiducial was compared with its corresponding ground truth motion data. Two parameters, namely, the sampling frame rate and the offset time shift, were optimized by maximizing the correlation coefficient between measured motion trajectory and ground truth data during the analysis period.

2.D.3. Spatial accuracy of tumor motion tracking using k - t BLAST

Once the measured motion trajectory was aligned with the ground truth motion data in the time series, the spatial accuracy of the k - t BLAST based motion tracking scheme was determined using the RMS error. Here, error is the difference between a position measured with MRI and the corresponding ground truth input position. The number of data points equals the number of dynamic images during the analysis period.

All data are presented as mean standard deviation (SD). When data from the 10 modeled tumor motions were averaged, the SD corresponded to intertumor motion variability.

2.D.4. Tracking modeled deformable tumor motion

In addition to the rigid motion study, deformable motion was also tested to quantify the motion tracking accuracy associated to speed-dependent viscoelastic motion. The phantom module^{14,15} for the deformable tumor respiratory motion study consists of three parts: an outer shell resembling a human torso (Radiology Support Devices, Inc., Long Beach, CA), deformable latex foam inserted into the inner cavity, and diaphragm attached to the MR-compatible motion platform. As the diaphragm advances into the inner cavity of torso in superior direction, it presses against the foam, resulting in the deformable motion inside the foam. Ten water filled Eppendorf test tubes (fiducial markers) were embedded into the latex foam and additional two tubes were attached to the diaphragm to present deformable and rigid motions, respectively.

TABLE I. Characteristics of 10 ground truth lung tumor motion datasets during a 25 s analysis period. Maximum peak–trough distance corresponds to the difference between the deepest inhalation (peak) and the exhalation (trough) observed during the analysis period for each subject in the respiratory trace. Mean peak to mean trough distance corresponds to the distance between mean of peaks and mean of troughs. The respiratory rate was computed from the number of peaks and troughs during the 25-s period. The mean (SD) value over ten individual data sets is reported in the bottom row.

Subject	Maximum peak–trough distance (mm)	Mean peak to mean trough distance (mm)	Respiratory rate (breath/min)
M1	8.59	6.90	21.6
M2	8.20	7.32	15.6
M3	10.71	8.79	19.2
M4	12.55	9.22	21.6
M5	19.26	11.76	14.4
M6	10.03	8.72	14.4
M7	15.09	12.66	10.8
M8	3.27	2.84	19.2
M9	7.54	5.16	19.2
M10	8.63	5.33	14.4
Mean(SD)	10.39(4.42)	7.87(3.01)	17.0(3.6)

Three motion trajectories out of ten trajectories used for the rigid motion study were selected (M1, M6, and M10 from Table I). The current deformable phantom module limits the dynamic range of motion due to the force limitation exerted from the motion platform (5 mm inward and 10 mm outward in the foam). In addition to these three trajectories, they were also resampled and modified temporally to make the resultant input motions slower by 7.74-fold. Thus, a total of six motion trajectories were tested. It is expected that slower motion would cancel the viscoelastic term of deformable motion, resulting in the fiducial marker motion inside the latex foam being approximated to the rigid motion.

The same MRI scanner parameters used for the rigid motion study were also employed and the frequency encoding direction was set along the superior–inferior direction. K - t acceleration factors of 1 and 16 were used to monitor slow and normal speed trajectories, respectively. Hence, the number of modeled respiratory cycles over 720 acquired images with k - t factor of 16 at the normal speed was matched to that over the same 720 acquired images with k - t factor of 1 at the slower speed. The marker motion was calculated using deformable image registration (NiftyReg, University College London).¹⁶ The temporal scale of measured motion with k - t factor of 1 was readjusted to that of the original input motion for the sake of data presentation. The motion tracking errors between ground truth motion and rigid motion (2 markers $\times$ 3 trajectories $\times$ 2 k - t factors) during the 25-s analysis period were evaluated for a comparison with the rigid motion study. In addition, errors between two deformable motions at two different speeds (10 markers $\times$ 3 trajectories) were also evaluated to account for motion tracking inaccuracy associated with viscoelastic term.

2.E. Human subject study

This study was approved by the Institutional Review Board (IRB) at UT Southwestern Medical Center. Two human subjects participated after giving written informed consent and undergoing MRI safety screening. Subject H1 was an 87-yr old male kidney tumor patient, while subject H2 was a 65-yr old male lung tumor patient. MRI data were collected on the same 3.0 T whole-body scanner used for the model study. Patients underwent MRI in the supine position with a torso RF receiver coil placed directly over the chest/upper abdomen or chest following standard clinical practice. According to AAPM Task Group 76,⁴ respiratory motion management is required if a tumor moves 5 mm or more. Kidney tumor motion of subject H1 was considered to be a tumor with large degree of respiratory motion as it moved more than 5 mm in the craniocaudal direction. The lung tumor motion of subject H2 was limited at least in part due to a known paralysis of the left hemidiaphragm. This is an example of small tumor respiratory motion.

A bFFE sequence was also used in conjunction with k - t BLAST acceleration to measure the dynamic motion of a subject's abdomen/thorax part within a single coronal slice (TE/TR: 1.3/2.6 ms, flip angle: 40°, k - t acceleration factor: 10, FOV: 403 $\times$ 403 mm², reconstruction matrix: 528 $\times$ 528, resolution: 0.76 $\times$ 0.76 mm², slice thickness: 10 mm, phase

encoding steps: 200). A total of 650 consecutive dynamic images were acquired from a single scanning session lasting for 49.2 s. The corresponding sampling frame rate for this set of MRI parameters was 13.18 Hz. The sampling frame rate is within a practical frequency range (10–25 Hz) for real-time tumor respiratory motion tracking using kilo-voltage x-ray imaging system.^{11,15,17} The phase-encoding direction was selected to be in the left–right lateral direction. A rectangular FOV scheme was also used; the frequency-encoding direction was reduced (rectangular FOV: $f250 \times p403$ mm², acquisition matrix: $f124 \times p200$, rectangular reconstruction matrix: $f328 \times p528$). Subjects were asked to breathe freely during dynamic image scanning.

Two tumor respiratory motions were obtained from the kidney and the lung of subjects H1 and H2, respectively. Each target tumor was manually segmented from one representative image out of a series of dynamic images; the tumor outline was visually distinguishable. The tumor outline is a 2D cross-sectional representation of gross tumor volume (i.e., GTV). Its in-plane deformation and translation in subsequent images were computed using deformable image registration (NiftyReg). All segmentation results were visually inspected. If a segmentation error was found (i.e., a deformed outline was failed to delineate the target tumor), the object outline was manually redrawn.

2.F. Human data analysis

The target tumor area corresponded to the region encompassed by the deformed outline of a tumor in each image. The centroid position of each tumor and its displacement over time were also computed. The centroid motion trace demonstrated the overall range of tumor motion presented during the scanning session including the maximum inhalation peak and exhalation trough. Moreover, both mean inspiratory and expiratory positions were computed for each subject to show the average range of tumor motion. Finally, the smallest respiration (based on a difference between inspiratory and expiratory tumor positions from one end-expiratory state to another) among all respiratory cycles was selected for each subject to give one representative, lower end of respiration. In addition to centroid motion, the range of motion area (2D cross-sectional representation of ITV) was also computed.

The accuracy of tumor centroid motions in the superior–inferior direction was also validated using the same rigid motion protocol. The measured two tumor centroid motions were used as the ground truth motion and programmed into the motion platform. The exact same MRI parameters used for the humans study were used to monitor the motion. The errors between marker trace data and input motions were evaluated.

3. RESULTS

3.A. Model study

The maximum peak–trough distance presented in the respiratory trace of M5 was 19.26 mm, which was the greatest inhale–exhale amplitude among the 10 traces. The minimum

FIG. 2. Cumulative distributions of the tumor motion frequency spectrum from 0 to 25 Hz. The ten solid green lines represent individual distributions of 10 ground truth motion data. Solid red and blue lines represent the overall mean, $\pm$ SD calculated from ten individuals at a given frequency component. Four red broken vertical lines indicate four different frame rates 2.47, 4.67, 9.79, and 19.12 Hz, corresponding to k - t factors of 1, 2, 5, and 16, respectively, as the motion direction was set along frequency encoding direction. (See color online version.)

amplitude was observed from M8 (3.27 mm). The mean of maximum peak–trough distance (the difference between the deepest inhalation peak and exhalation trough observed during the analysis period from each subject) for each respiration was 10.39(4.42) mm. The mean respiratory rate was 17.0(3.6) breath/min, corresponding to 0.28(0.06) Hz (Table I).

Figure 2 shows the cumulative distribution of frequency components in the tumor motion. Red and blue solid lines represent the overall mean, mean + SD, and mean – SD at a given frequency over ten individual cumulative distributions, respectively. On average, 90% of tumor motion was included within a frequency of 3.88 Hz or less according to the solid red line shown in Fig. 2. As Nyquist frequency is considered, the sampling frequency must be a double of 3.88 Hz or greater.

For a given set of MRI parameters, sampling frame rates determined using ten modeled tumor motions for k - t acceleration factors of 1, 2, 5, and 16 were 2.47(0.00), 4.67(0.00), 9.79(0.01), and 19.12(0.02), respectively, as the motion direction was set along frequency encoding direction. When the motion direction was set along phase encoding direction, the four sampling frame rates were 2.29(0.00), 4.29(0.00), 9.01(0.02), 17.59(0.06) for k - t acceleration factors of 1, 2, 5, and 16, respectively. For a given k - t acceleration factor and MR parameters, there was virtually no variability in sampling frame rate.

3.B. Rigid motion study

RMS errors between ten intermarker-average data and ground truth motions for k - t factors of 1, 2, 5, and 16 were frequency encoding direction: 0.07(0.03), 0.14(0.03), 0.19(0.04), and 0.25(0.06) mm and phase encoding direction: 0.14(0.03), 0.26(0.04), 0.47(0.08), and 0.62(0.10) mm, respectively. Figure 3 shows Box and Whisker plot of errors in which

the red bar, two ends of box, and two whiskers correspond to median, first and third quartiles, minimum and maximum out of all 60 data; Fig. 3(A) gives RMS errors whereas Fig. 3(B) shows the largest error present in each trajectory during 25 s analysis period as the motion direction was set along frequency encoding direction. The increased k - t factor resulted in reduced accuracy of motion tracking. However, the worst case RMS errors at a k - t acceleration factor of 5 and 16 were 0.45 and 0.43 mm [Fig. 3(A)], which were still smaller than the pixel resolution (0.67 mm). The largest errors presented among all 60 trajectories, which represent the worst case scenarios of motion tracking, were 1.6, 2.1, 2.5, and 2.6 mm with k - t factors 1, 2, 5, and 16, respectively. It should be also noted that percentages of data points in which the absolute error exceeded 1 mm were 0.11(0.34)%, 0.06(0.18)%, 0.24(0.40)%, and 0.91(0.81)% for k - t factors of 1, 2, 5, and 16, respectively.

Figures 3(C) and 3(D) present RMS and the largest errors present in each trajectory during the same analysis period as the phase encoding direction was switched along the motion direction. The motion tracking accuracy in phase encoding direction measured as RMS and the largest errors in phase encoding direction was much worse than that in frequency encoding direction at the same given k - t acceleration factor ($p < 0.01$, repeated measures ANOVA). The increased k - t factor also resulted in reduced accuracy of motion tracking. The worst case errors presented among all 60 trajectories were 2.3, 3.4, 3.9, and 5.1 mm with k - t factors 1, 2, 5, and 16, respectively. Finally, the percentages of data points in which the absolute error exceeded 1 mm were 0.90(0.19)%, 1.60(0.16)%, 9.68(0.46)%, and 16.40(0.55)% for k - t factors of 1, 2, 5, and 16, respectively.

3.C. Deformable motion study

Figure 4(A) shows one representative MRI. There are twelve fiducial markers in the image in which ten markers present deformable motions (i.e., from 1 to 10) whereas markers present rigid motions (i.e., 11 and 12). Figure 4(B) shows input ground truth motion (M1) superimposed with the resultant rigid and deformable motions measured with k - t acceleration factor; the temporal scale was adjusted to the original input motion. It shows that the rigid motion kept track of the ground truth motion while the amplitude of deformable motion was attenuated.

3.C.1. Ground truth motion vs rigid motion (2 markers $\times$ 3 trajectories)

RMS errors between three ground truth motions and their corresponding rigid motions obtained at two different k - t factors were k - t 1: 0.08(0.01) mm and k - t 16: 0.40(0.03) mm, respectively. The maximum errors observed among a total of six motions for each k - t acceleration were k - t 1: 0.42 mm and k - t 16: 1.71 mm; thus there was no data point in which the absolute error was exceeded by 1 mm with a k - t factor of 1. The percentage of data points in which the absolute error exceeded 1 mm with k - t of 16 was 3.98(2.26)%.

FIG. 3. Box and Whisker plots of (A) RMS errors and (B) maximum errors between measured motion trajectories and ground truth displacement in frequency encoding direction at four different k - t acceleration factors, 1, 2, 5, and 16. (C) and (D) are also RMS and Maximum errors, respectively, in phase encoding direction at the same set of k - t acceleration factors. There were a total of 60 measured trajectories (10 motion traces $\times$ 6 fiducial markers). Red bar, two ends of box, and two whiskers correspond to median, first and third quartiles, minimum and maximum of errors presented in 60 motion data (mm). (See color online version.)

3.C.2. Slow motion with k - t factor of 1 vs normal motion with k - t factor of 16; rigid motion (2 markers $\times$ 3 trajectories)

The comparison between two k - t acceleration factors with regard to rigid motion was made as follows: RMS error: 0.39(0.04) mm; maximum error: 1.58 mm; and percentages of points exceeded 1 mm error: 3.45(2.33)%.

3.C.3. Slow motion with k - t factor of 1 vs normal motion with k - t factor of 16; deformable motion (10 markers $\times$ 3 trajectories)

The comparison between two k - t acceleration factors with regard to deformable motion was made as follows: RMS error: 0.35(0.10) mm; maximum error: 1.76 mm; and percentages of points exceeded 1 mm error: 1.45(2.37)%. Furthermore,

FIG. 4. Deformable motion analysis. (A) Twelve fiducial markers in a coronal imaging plane. Ten fiducial markers (from 1 to 10) were embedded in a deformable latex foam presenting deformable motion whereas additional two markers (11 and 12) were attached to a diaphragm which traces ground truth input motion. (B) Modeled tumor respiratory motion obtained from M1 motion trajectory in superior-inferior direction. Black line: ground truth motion. Green line: rigid motion presented by marker No. 11. Blue and red lines: deformable motions presented by markers No. 1 and No. 8, respectively. (See color online version.)

FIG. 5. The relationships between the amplitude of deformable motion and two measures of spatial errors [(A) RMS error and (B) maximum error]. The maximum peak–trough distance represents a distance between the deepest peak and the trough observed during the 25-s analysis period measured with k - t factor of 1. A total of 30 data points obtained from three independent motion trajectories were shown. As 30 data points were combined, the squared correlations were (A): 0.16 and (B): 0.46 for RMS error and maximum error, respectively.

the relationships between the amplitude of deformable motion (presented as the maximum peak–trough distance during the 25-s analysis period measured with k - t factor of 1) and two measures of errors (i.e., RMS errors and maximum error) are shown in Figs. 5(A) and 5(B). There are a total of 30 data points (10 deformable motions $\times$ 3 trajectories). Virtually no correlation was found between the maximum peak–trough distance and RMS error for the 30 data points [Fig. 5(A): $R^2 = 0.16$]. There was a moderate correlation between the maximum peak–trough distance and maximum error [Fig. 5(B): $R^2 = 0.46$].

FIG. 6. Centroid motion trajectory of kidney tumor obtained from subject H1. Eight breathing cycles are reported (from one end-expiratory state to another, marked with open blue circles). The original kidney tumor centroid is defined with 0 mm displacement at time = 0 s. Positive and negative signs correspond to inhalation and exhalation, respectively. Solid red line: one representative respiratory cycle showing the smallest inspiratory peak to expiratory trough difference (9.54 mm). Broken red and blue lines: mean positions for open red circles and open blue circles, respectively, i.e., mean inspiratory and expiratory centroid positions. The distance between two broken lines was 14.24 mm. The SD of inspiratory peaks around the broken red line was 3.22 mm while that of expiratory peaks around the broken blue line was 1.73 mm. Maximum range of motion: the difference between the deepest inhalation and exhalation observed during the dynamic scan was 21.29 mm. This subject took a short apnea between 25 and 35 s. (See color online version.).

3.D. Human subject study

Centroid motions in the superior and inferior directions of kidney and lung tumors from subjects H1 and H2 are given in Figs. 6 and 7, respectively; the smallest respiration cycle, determined from the smallest difference between inspiratory peak and expiratory trough positions present within a single cycle, is indicated with a solid red line for each subject. Eight and fifteen respiratory cycles (from one end-expiratory state to another) were observed during 49.2 s of dynamic imaging of H1 and H2, respectively.

H2 presented relatively regular respiratory pattern compared to H1, while H1 took a short apnea for approximately 10 s, followed by deep inspiration.

FIG. 7. Centroid motion trajectory of lung tumor obtained from subject H2. Fifteen breathing cycles are reported. The solid red line represents one respiratory cycle, indicating the smallest inspiratory peak to expiratory trough difference (1.16 mm). Broken red and blue lines are mean positions of open red circles and open blue circles, respectively, indicating mean inspiratory and expiratory positions. The distance between two broken lines was 1.86 mm. The SD of inspiratory peaks around the broken red line was 0.31 mm while that of expiratory peaks around the broken blue line was 0.18 mm. The maximum range of motion was 2.73 mm. Two inspiratory peaks at 1.5 and 47.7 s and their respective breathing cycles were eliminated from the breath-by-breath analysis because the end-expiratory state could not be determined. (See color online version.).

FIG. 8. Right kidney tumor motion within a coronal slice. (A) Abdominal image of subject H1. The image was taken at the end expiratory state, the beginning of its representative breathing cycle (solid red line in Fig. 6). Solid green outline indicates the cross section area of the kidney tumor (213.22 mm^2). (B) Range of kidney tumor motion area. The solid green outline indicates the same kidney tumor location as in panel (A). The area in red depicts the range of motion during the smallest representative breathing cycle corresponding to the solid red line in Fig. 6 (487.60 mm^2). The additional blue area indicates the whole extent covered by the kidney tumor during the entire dynamic image acquisition, i.e., 2D cross-sectional representation of ITV (731.12 mm^2). (See color online version.)

Maximum distances, namely, the difference between the deepest inhalation and exhalation observed during their respective dynamic scans, were 21.29 and 2.73 mm for patients H1 and H2, respectively. Dashed red and blue lines indicate mean inspiratory and expiratory positions (Figs. 6 and 7). Distances between these broken lines (average inspiratory peak to expiratory trough distance) were 14.24 mm for H1 and 1.86 mm for H2. The standard deviation for inspiratory and expiratory peak positions of H1 kidney tumor was equal to 3.22 and 1.73 mm, respectively (Fig. 6). Similarly, the standard deviation for inspiratory and expiratory peak positions H2 lung tumor was equal to 0.31 and 0.18 mm, respectively (Fig. 7). During their respective smallest respiration cycles indicated in solid red lines in Figs. 6 and 7, the peak to trough (i.e., inhalation to exhalation) distances of the two tumor centroids were 9.54 mm (H1 kidney tumor) and 1.16 mm (H2 lung tumor). The accuracies of tumor centroid motion were also validated using MRI-compatible motion platform with Eppendorf tubes as fiducial markers. RMS errors between marker trace data

and input motions described in Figs. 6 and 7 were H1 kidney: $0.32(0.16) \text{ mm}$ and H2 lung: $0.08(0.01) \text{ mm}$, respectively [Mean(SD) among markers]. In addition, maximum errors measured in H1 and H2 motions were 1.44 and 0.42 mm, respectively.

Motion area ranges for the H1 kidney and H2 lung tumors are also illustrated in Figs. 8 and 9, respectively. The cross-sectional areas of the kidney and lung tumors at the beginning of their respective smallest respiration (i.e., end expiratory state, solid red lines in Figs. 6 and 7) were 213.22 and 587.22 mm^2 . These areas are indicated by the green outlines in Figs. 8(A) and 9(A). Sizes of motion areas covered by the tumors during their entire respective dynamic image scans were H1: 731.12 mm^2 and H2: 690.33 mm^2 , as depicted by the blue and red areas combined [Figs. 8(B) and 9(B)]. These combined areas correspond to the cross-sectional representation of ideal ITV. Motion areas covered by the tumors during their smallest respiration cycles were 487.60 mm^2 for H1 and 643.73 mm^2 for H2, as shown by the red area in Figs. 8(B) and 9(B).

FIG. 9. Left lung tumor motion within a coronal slice. (A) Abdominal image of Subject H2. The image was taken at the end expiratory state, the beginning of its representative breathing cycle (solid red line in Fig. 7). The solid green outline represents the cross section area of the lung tumor (587.22 mm^2). (B) Range of lung tumor motion area. The solid green outline is the same lung tumor location as in panel (A). The area in red illustrates the range of motion during the smallest representative breathing cycles corresponding to the solid red line in Fig. 7 (643.73 mm^2). The additional area in blue is the full extent covered by the lung tumor during the entire dynamic image acquisition, i.e., 2D cross-sectional representation of ITV (690.33 mm^2). (See color online version.)

FIG. 10. Cumulative increases in the kidney tumor motion area recorded within each individual breath, during an entire dynamic scan. The solid black line depicts the cycle-to-cycle progressive accumulation of tumor motion area during each breath, from one end-expiratory state to another. The solid red line indicates the cumulative increase in the tumor motion area during the smallest representative breathing cycle, which corresponds to the solid red line shown in Fig. 6 (right-end value of 487.60 mm²). The solid blue line indicates the whole range of tumor motion area during a dynamic scan. The value at its right-hand end (731.12 mm²) corresponds to the combined blue and red area shown in Fig. 8(B). The broken red line illustrates the mean of eight cycle-to-cycle cumulative tumor motion areas at the end of each respiration [548.92(71.81) mm²]. (See color online version.)

and 9(B), respectively. These areas in red and blue represent two extreme scenarios of tumor respiratory motion presented during the respective dynamic image scans.

Figures 10 and 11 show increased tumor motion areas due to breathing. Solid blue lines represent the cumulative range of the tumor motion area from the first to the 650th image during their respective dynamic scan. Thus, values of cumula-

FIG. 11. Cumulative increases in the lung tumor motion area recorded within each individual breath, during an entire dynamic scan. The solid black line depicts cycle-to-cycle progressive accumulation of tumor motion area during each breath from one end-expiratory state to another. The solid red line indicates cumulative increases in the tumor motion area during the smallest representative breathing cycle, which corresponds to the solid red line shown in Fig. 7 (right-end value of 487.60 mm²). The solid blue line illustrates the whole range of the tumor motion area during the dynamic scan. The value at its right-hand end (690.34 mm²) corresponds to the blue and red area shown in Fig. 9(B). The broken red line indicates the mean of eight cycle-to-cycle cumulative tumor motion areas at the end of each respiration [652.59 (9.44) mm²]. (See color online version.)

tive areas at their respective right-hand-ends correspond to the entire range of tumor motion areas. Values are 731.12 mm² for H1 and 690.33 mm² for H2 as shown by the blue and red areas in Figs. 8(B) and 9(B). Solid black lines show the underlying progressive accumulation of the tumor motion area during each breath cycle. Therefore, its right-end value corresponds to the range of tumor motion area during each breath. The inter-respiration mean (and SD) of the tumor motion areas over eight respiratory cycles from the H1 kidney tumor was 548.92(71.81) mm². Likewise, the value for lung tumor motion was 652.59(9.44) mm² over fifteen breathing cycles.

4. DISCUSSION

The major findings of the present model study using a 2D balanced fast field echo with *k-t* BLAST imaging scheme are as follows: (1) the image acquisition rate is accelerated up to 19 Hz, which was adequately fast enough to incorporate most of the frequency components in tumor respiratory motion measured using fluoroscopic system (Fig. 2); (2) spatial inaccuracy of motion monitoring, measured as RMS error, was less than 1 mm and lower than the reconstructed MRI pixel resolution, as the frequency encoding direction was set along the principal motion direction [Fig. 3(A)]. Such accuracy is adequate for radiotherapy image guidance as the expected tracking error is smaller than ITV-to-PTV margin surrounding the target tumor (3–15 mm).^{4,18–20} We also tested the same imaging scheme to monitor the actual patient's tumor respiratory motion. This enabled motion monitoring over multiple respiratory cycles, allowing us to evaluate breath-by-breath variation (Figs. 6–11).

Normal frequency of human respiratory motion at rest is 12–18 breaths/min (i.e., 0.20–0.30 Hz).^{21,22} Respiratory motion does not have a perfect sinusoidal waveform; it is also composed of additional frequency components to form its complex shape. Respiratory irregularities in frequency and magnitude result in various different components in a frequency spectrum and are difficult to be characterized. In addition to the actual breathing motion, cardiac motion, which is typically about 1.4 Hz ranging from 0.1 to 1.0 mm,²³ also partly contributes to tumor motion.

In our present model study, the respiratory rate measured from the 10 ground truth respiratory motions was 17.0(3.6) breaths/min [i.e., 0.28(0.06) Hz]. In addition to the main frequency component of tumor respiratory motion, we also analyzed its frequency spectrum ranging from 0 to 25 Hz. For instance, on average, 90% of the tumor motion component was 3.88 Hz or less over multiple respiratory cycles obtained from 10 individual motion models. In other words, as Nyquist frequency is considered, the sampling frame rate must be at least double of 3.88 Hz or higher to keep track of high frequency components in tumor motion. Thus, a sampling frequency of approximately 8 Hz is considered adequate for the tumor respiratory motion data used in the present study. The *k-t* BLAST approach was able cover the most frequency components in tumor respiratory motion measured using CyberKnife Synchrony system. It should be noted that the original CyberKnife Synchrony data were sampled at

approximately 25 Hz; thus, the high frequency component above 13 Hz could have been underestimated.

In the clinical situation, kilo-voltage x-ray imaging system for real time tumor motion tracking uses the sampling frequency between 10 and 25 Hz.^{11,15,17} This is, indeed, taking a safety margin for high frequency components. This safety margin would serve to monitor the respiratory irregularity of which the real frequency components are hard to be assessed. It should be noted the frequency of 3.88 Hz is more than double the human cardiac motion. Therefore, the sampling frequency of 8 Hz or above may contain motion noise, which does not represent a physiological motion.

Earlier studies by Palthow *et al.* monitored lung tumor mobility in 2D thoracic images at 3 frames/s using true FISP sequence with a GRAPPA acceleration factor of 2.^{24,25} Cai *et al.* investigated the reproducibility of the probability density function (PDF) of tumor location as a function of sampling frame rate up to 10 Hz.^{26,27} The study showed that PDF reproducibility improved as the frame rate became faster. However, it converged into an equilibrium state as the frame rate was increased to 2 Hz.²⁷ In our model study, we have tested four different k - t acceleration factors, 1, 2, 5, and 16, and their corresponding sampling frame rates were 2.47, 4.67, 9.79, and 19.12 Hz, respectively, as frequency encoding direction was set along superior–inferior direction. In the case that the sampling frame rate of 8 Hz is to be employed, a k - t acceleration factor of 5 or above needs to be selected for tumor motion monitoring with a given TR and the number of phase encoding steps. If the sampling rate is set to the speed of real time monitoring used for kV fluoroscopy, the greater k - t acceleration factor needs to be selected. It should be noted that the sampling frame rate is not proportional to the k - t acceleration factor; it plateaus off as the acceleration factor increases.

We have also shown that spatial inaccuracy measured using the RMS error was elevated as the k - t acceleration factor increased [Fig. 3(A)]. In other words, as image acquisition speed increases, spatial information is lost to some degree. There is a known relationship between SNR and image acquisition time in which SNR is proportional to the square root of the acquisition time (i.e., 1/sampling frame rate).²⁸ Lutz *et al.* concluded that k - t factor of two is to be used to monitor cardiac motion; however, the higher acceleration should be avoided due to substantial degradation in the motion pattern.²⁹ On the other hand, Hsu *et al.* demonstrated that k - t factor of five could be used for contrast-enhanced lung perfusion measurement.³⁰ Thus, the selection of k - t acceleration factor must be based on the level of tolerance in the motion error as well as the image degradation for a specific purpose. The focus of present study is the application of k - t BLAST based dynamic MRI for the motion management for radiation treatment. In this study as the motion direction was set along the frequency encoding direction, the overall average of RMS error with k - t acceleration factor of 16 was 0.25 mm, which was less than half of the reconstructed image pixel resolution (0.67 mm). The magnitude of average error is considered to be negligible in terms of quality for image guided radiation treatment since it is the order of magnitude smaller than the ITV-to-PTV margin

surrounding the target tumor (3–15 mm).^{4,18–20} In other words, the average degradation in spatial information measured as RMS error of motion displacement was still negligible even with the k - t factor of 16. In terms of the percentage of data points (i.e., time) in which the error exceeds ± 1 mm, only less than 1% of data points met this criterion with the k - t factor of 16. The slight improvement in this metric from the k - t factor of 1–2 (k - t factor of 1: 0.11%, k - t factor of 2: 0.06%) might suggest that the sampling frame rate of 2.47 Hz was not sufficient to monitor high frequency component of cycle-to-cycle variation in the tumor respiratory motion. However, it should be noted that ± 1 mm error occurred in only one out of ten motion tracking experiments with the k - t factors of 1 and 2. In addition, the difference in 5-basis-point might not be the substantial difference. Finally, the largest error presented among all 10 motion traces $\times$ 6 markers with the k - t factor of 16 was 2.6 mm. Even with the worst case scenario, it is still smaller than the ITV-to-PTV margin. The true image resolution should be based on MRI acquisition matrix, which was 3×3 times greater than the reconstructed pixel resolution in the model study, i.e., 2 mm. The reconstruction algorithm preinstalled in the scanner also contributed the accuracy. For the purpose of RT guidance, we have considered that the reconstructed resolution is more relevant to our clinical application.

As the motion direction was set along phase encoding direction, the accuracy of motion tracking was significantly reduced compared to that set along frequency encoding direction. This is expected as k - t sparse-sampling occurs in phase encoding direction. The result suggests that the principal direction of tumor respiratory motion must be set along frequency encoding direction to minimize the tumor tracking error. MRI is capable of arbitrarily selecting an imaging plane. For the clinical application, the selection of imaging plane based on a prior knowledge of tumor motion direction is essential. If the phase encoding direction needs to be set along the principal direction of tumor motion and the RMS and maximum errors should be kept below the sizes of reconstructed MRI pixel resolution and ITV-to-PTV margin, respectively, k - t factor of 5 or above should be avoided.

In addition to the evaluation of rigid motion tracking accuracy with regard to the different k - t acceleration factors, the additional spatial error associated to deformable motion was also estimated. First of all, the comparison between the ground truth motion and measured rigid motion with k - t factor of 1 suggests that the combination of slow input motion and no k - t sparse-sampling enabled the virtually error free motion tracking. The measured marker location with k - t factor of 1 is likely to represent the true marker location with the average RMS error of 0.08 mm, which is an order of magnitude smaller than the pixel resolution. Based on this assumption, the comparison between measured deformable motions with k - t factors of 1 and 16 reveals the possible motion tracking error associated with speed dependent viscoelastic term of motion when the motion is measured with the greater k - t factor; the average RMS and maximum errors were 0.35 and 1.76 mm, respectively. These error values were similar to the errors between the measured rigid motion with k - t factor of 16 and its corresponding ground truth motion and the measured rigid

motion with k - t factor of 1. If the magnitude of deformable motion error depends on the amplitude of marker motion, it would be possible that the contribution of deformable motion in the gross error to be more pronounced when the amplitude of motion is small (Fig. 5). However, the important implication from this result in regards to respiratory motion management during RT is that even though deformable motion is added, RMS error was still smaller than the reconstructed pixel resolution (0.67 mm) and the maximum error was less than ITV-to-PTV margin (3–15 mm).

4.A. Comparison between rigid and deformable phantom studies

For the deformable motion phantom study, the error measures between the ground truth motion and measured motion with k - t factor of 16 were as follows: RMS error: 0.40(0.03) mm, maximum error: 1.71 mm, and the percentage of data points in which the absolute error exceeded 1 mm: 3.98(2.26)%. The data indicated that the tracking accuracy was worse in the deformable motion phantom study than those measured in the rigid motion phantom study for the same three motion trajectories (M1, M6, and M10); RMS error: 0.24(0.05) mm, maximum error: 1.41 mm, and the percentage of data points in which the absolute error exceeded 1 mm: 0.38(0.42)%. These elevations in error measures between rigid and deformable phantom studies would be partially rooted from the difference in the image analysis techniques used to compute marker motion from image data; the affine transformation and nonrigid deformable image registration techniques were used for rigid and deformable phantom studies, respectively. It would be expected that additional flexibility associated with local control of deformable image registration would give an additional motion tracking error. Since the same image registration method (i.e., NiftyReg) was used to compute tumor centroid motions in the human study, extra caution should be taken for the motion tracking accuracy especially when texture of measured object is homogeneous.

4.B. Human studies

We also monitored tumor motion from two patients with kidney and lung tumors, respectively. The same balanced fast field echo sequence was used in conjunction with k - t BLAST, which was tested during the model study. The sampling frame rate was 13.18 Hz, which is considered to be adequately efficient to capture the high frequency component of tumor respiratory motion and a practical sampling frequency used for real-time tumor respiratory motion tracking with kilovoltage x-ray imaging system.^{11,15,17} Based on the validation study using MRI-compatible motion platform, the estimated RMS motion tracking error was less than the reconstructed pixel resolution in both patients. The maximum error was also smaller than the estimated ITV-to-PTV margin. The present human study showed that breath-by-breath variation of tumor respiratory motion was evident during a total scan time of 49.2 s (Figs. 4–9). The result showed that the range of tumor motion areas (2D cross-sectional representation of

ITV) observed during an entire scan exceeded the average of those over multiple breaths (Fig. 8, H1 kidney tumor: during a whole scan time 731.12 mm², mean of 8 breaths 548.92 mm²; Fig. 9, H2 lung tumor: during a whole scan time 690.34 mm², mean of 15 breaths 652.59 mm²). Therefore, one representative average respiratory tumor motion is not sufficient to account for all possible ranges of tumor motion. It is crucial to determine ITV based on tumor motion over multiple breathing cycles rather than one average respiration. Also, respiratory motion management is required if a tumor moves 5 mm or more based on the current recommendation for clinical procedure.⁴ In other words, motion management was required for the kidney tumor of patient H1 (Fig. 4), but not in the case of the lung tumor of subject H2 (Fig. 5). Tumor motion of 5 mm or more depends on various factors including location²⁴ and connection to major anatomical structures.²¹ Therefore, each tumor needs individual assessment. Conventional tumor respiratory motion monitoring using 4DCT presents some shortcomings, including soft tissue contrast, temporal resolution, long-term monitoring ability over multiple breathing cycles, and fixed imaging slice orientation.^{31,32} The 4DCT technique typically reconstructs ten thoracoabdominal volumetric images over one average respiratory cycle. Therefore, the effective sampling frame rate is considered to be approximately 2.5 Hz. One average respiratory motion is not sufficient to account for cycle-to-cycle variability.⁵ Moreover, the present study suggests that the sampling rate may not be adequate to incorporate the high frequency component of tumor motion. Finally, the orientation of CT imaging slices is not suited to monitor tumor motion; it is fixed on an axial plane while the greatest tumor motion is usually seen along the superior–inferior direction, which is a through-plane direction of the axial plane.^{21,24} Compared to 4DCT, the present study showed that dynamic MRI had the advantages such as adding capabilities of soft-tissue contrast, rapid image acquisition up to approximately 20 Hz over multiple respiratory cycles, and arbitrary slice selection. Since CT provides better spatial fidelity and spatial resolution than MRI for a static structural image, a cross-modality approach using both CT and MRI techniques would leverage the best-of-both-worlds for image guided radiotherapy.

Efforts have been made to develop dynamic 3D MRI sequences. However, the typical frame rate is approximately 1 Hz, i.e., 1 frame/s.^{31,33–35} Blackall *et al.* demonstrated dynamic 3D MRI sequence at a frame rate of 3 Hz.³⁶ The same group showed that imaging sequence compromised image quality to a great extent.³⁶ Hardware and software improvements are needed to achieve dynamic 3D MRI with high spatial resolution and tissue contrast.³⁶ In addition, sophisticated, multislice excitation using the parallel transmission technique needs to be addressed for the rapid 3D MRI while reducing the specific absorption rate (SAR).³⁷ Another 3D + time approach is known as retrospective 4DMRI; multiple 2D MR images, acquired at different slice locations and time points, are retrospectively sorted based on respiratory phases measured using a respiratory surrogate device. However, the main focus of this approach is still limited to obtain one representative 4D respiratory model, which is similar to conventional 4DCT.^{38–41}

The retrospective sorting technique can be further developed to incorporate more than one respiratory pattern. In the course of dynamic 3D MRI development, it is also necessary to develop an MRI-compatible deformable motion phantom to repeatedly mimic patient torso motion for validation.¹⁵

4.C. Limitations

Although we have shown several advantages of adapting a dynamic MRI technique to tumor respiratory monitoring during RT, limitations are still present in our study design. First, we only demonstrated tumor respiratory motion monitored within a single 2D coronal plane. Thus, motion in the anterior–posterior direction was not measured. Second, MRI cannot measure electron density distribution, which is crucial for radiation dose calculation. Therefore, dynamic MRI technique will not compete with or replace the conventional CT approach.

We believe that the MRI technique will complement technical shortfalls presented by the 4DCT technique (e.g., one average respiratory cycle, lack of spatial resolution in superior–inferior direction, etc.). In this scenario dynamic MRI can be exclusively used to monitor the relatively large scale tumor respiratory motion with erratic cycle-to-cycle variation to determine the range of ITV and the interfractional tumor monitoring. A 2D imaging plane and its frequency-encoding direction were placed along the principal motion direction. Additional sagittal imaging plane would incorporate motions in both superior–inferior and anterior–posterior directions where most of the respiration-induced motion takes place.⁴⁰ The multislice approach would be benefitted from the rapid dynamic imaging scheme. If the maximum sampling rate is substantially faster than the frequency component of tumor respiratory motion, the redundancy in the temporal domain can be utilized to obtain the additional slice. Three dimensional dynamic MRI is more suited to model the entire thoracoabdominal motion. Technical difficulties still need to be overcome in both hardware and software to achieve much faster sampling frame rate.

Additional potential criticisms would be related to the difference in the mechanical properties between the latex foam and real biological tissue, as well as the limitation in the motion driving range of MRI-compatible motion platform. Our future work is going to consist of the implementation of more realistic MRI-compatible deformable phantom which mimics a patient's tumor motion as well as the external chest motion.

The current MRI system presents additional disadvantages. First, the MRI scanner has a memory constraint limiting the number of acquired images up to about 800 for a given file size. SAR deposition also limits the number of MRI acquisitions from patients during a single scanning session. Therefore, total duration is limited to the number of images taken. Second, additional time is needed for reconstruction, which is approximately 10 min for all 800 acquired images. A current trade-off exists between sampling frame rate and total scan time; the faster the frame rate, the shorter the scan time. Since image reconstruction takes a long time even after completion of the

entire image acquisition, real-time tumor motion monitoring is currently difficult to achieve. However, these limitations can be easily addressed by improving the computational processing power.

5. CONCLUSION

Spatiotemporal information losses were empirically determined in an adaptation of dynamic MRI for monitoring tumor respiratory motion in patients, using an in-house, programmable, MRI-compatible motion platform system. In order to observe a wide frequency spectrum of tumor motion, balanced fast field echo sequence with the k - t BLAST enables capturing of a 2D image within a single imaging plane as fast as 20 Hz, with less than 1 mm root mean square error.

Using the same dynamic imaging scheme, we also monitored actual kidney and lung tumor respiratory motions in two human subjects. The range of tumor motion during one average respiration cycle and the motion area was underestimated as the entire motion range observed over multiple breathing cycles was taken into account.

The present study demonstrates that dynamic MRI can complement technical deficits presented by conventional 4DCT for tumor respiratory management during radiation therapy. MRI enables rapid image acquisition over multiple respiratory cycles to monitor cycle-to-cycle respiratory variation. Future work will involve dynamic volumetric imaging (3D + time) and multimodality integration to develop patient-specific tumor and respiratory organ models which will be used for motion management during RT.

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CONFLICT OF INTEREST DISCLOSURE

The authors have no COI to report.

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