Lung surface deformation prediction from spirometry measurement and chest wall surface motion

Joubin Nasehi Tehrani

Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, Texas 75235-8808

Alistair McEwan

School of Electrical and Information Engineering, University of Sydney, New South Wales 2006, Australia

Jing Wang^{a)}

Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, Texas 75235-8808

(Received 25 April 2016; revised 26 August 2016; accepted for publication 29 August 2016; published 15 September 2016)

Purpose: The authors have developed and evaluated a method to predict lung surface motion based on spirometry measurements, and chest and abdomen motion at selected locations.

Methods: A patient-specific 3D triangular surface mesh of the lung region was obtained at the end expiratory phase by the threshold-based segmentation method. Lung flow volume changes were recorded with a spirometer for each patient. A total of 192 selected points at a regular spacing of 2×2 cm matrix points were used to detect chest wall motion over a total area of 32×24 cm covering the chest and abdomen surfaces. QR factorization with column pivoting was employed to remove redundant observations of the chest and abdominal areas. To create a statistical model between the lung surface and the corresponding surrogate signals, the authors developed a predictive model based on canonical ridge regression. Two unique weighting vectors were selected for each vertex on the lung surface; they were optimized during the training process using all other 4D-CT phases except for the test inspiration phase. These parameters were employed to predict the vertex locations of a testing data set.

Results: The position of each lung surface mesh vertex was estimated from the motion at selected positions within the chest wall surface and from spirometry measurements in ten lung cancer patients. The average estimation of the 98th error percentile for the end inspiration phase was less than 1 mm (AP = 0.9 mm, RL = 0.6 mm, and SI = 0.8 mm). The vertices located at the lower region of the lung had a larger estimation error as compared with those within the upper region of the lung. The average landmark motion errors, derived from the biomechanical modeling using real surface deformation vector fields (SDVFs), and the predicted SDVFs were 3.0 and 3.1 mm, respectively.

Conclusions: Our newly developed predictive model provides a noninvasive approach to derive lung boundary conditions. The proposed system can be used with personalized biomechanical respiration modeling to derive lung tumor motion during radiation therapy from noninvasive measurements.

© 2016 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4962479>]

Key words: lung deformation, tumor motion prediction, finite element modeling, surrogate signals, canonical correlation analysis

1. INTRODUCTION

There has been growing interest in developing real-time tumor tracking methods in current radiation therapy settings. Real-time tumor tracking may reduce exposure to benign tissue using smaller margins in advanced beam delivery techniques, such as gated or tumor tracking delivery. Direct access to tumor motion information is either challenging or unfeasible; hence the interest in real-time tumor tracking methods. These techniques can be classified into two main groups: (1) image-based tracking and (2) tumor motion modeling.

Image-based tracking uses patient images taken in real-time with the aid of a fluoroscopic video,^{1–5} cone beam CT (CBCT),^{6–8} or magnetic resonance (MR).^{9–11} Image-based tracking also requires real-time image segmentation and motion detection.^{12–14} However, these approaches (except

for MRI) may involve exposure of normal tissue to additional radiation increasing the risk of stochastic biological effects. Although MRI provides high contrast for soft tissues, the acquisition speed for 3D volumetric imaging is limited for this method. Additionally, most of these methods require the invasive implantation of fiducial markers to monitor motion, adding a level of risk and inconvenience.

In tumor motion modeling, a correlation fitting model is implemented to estimate target motion during treatment. Current surrogate signals include spirometry flow monitoring^{15,16} or surface displacements of the body. Surface displacement of the body can be monitored by sensors such as strain gauge¹⁷ or electromagnetic sensors.^{18,19} While this class of methods does not involve any additional radiation exposure typical of image-based tracking, tumor motion prediction is often less accurate as it is only based on a correlation model.^{20,21}

FIG. 1. Flowchart of the proposed lung surface motion prediction method.

Finite element method-based biomechanical modeling has been widely explored for simulating respiratory motion of the lung and tumors.^{22–27} In biomechanical modeling, tissue deformation is simulated according to physical causes and biomechanical properties of the tissue. However, the development of an accurate model relies on the accuracy of boundary condition displacement and biomechanical properties associated with each element. In previous studies, we evaluated the sensitivity of tumor motion simulation accuracy to lung biomechanical properties and developed an optimization-based method to estimate patient-specific optimal biomechanical parameters.^{28,29} However, for our biomechanical modeling we assumed having direct access to lung surface deformation obtained by deformable image registration of the planning 4D-CT.

The purpose of this study was to develop and evaluate a method to predict lung surface motion for biomechanical respiration modeling based on spirometry measurements and chest wall motion at selected locations. The flowchart of the proposed method is illustrated in Fig. 1. The estimated deformation vector fields (DVFs) of the lung surface can be used as boundary conditions for finite element modeling, providing the motion behavior of the entire lung volume during radiation treatment. The chest and abdomen surfaces of ten lung cancer patients were monitored concurrently with the acquisition of the spirometer flow volume during 4D-CT imaging. Preprocessing techniques such as QR factorization with column pivoting (QCRP) were employed to remove redundant observations of the chest and abdominal areas. Surrogate signals and lung surface deformation vector fields (SDVFs) were used to build a predictive model based on the canonical ridge regression (CRR) algorithm. The

predictive model was then used to estimate lung surface motion from spirometry measurements and chest wall motion at preselected locations. Finally, the estimated SDVFs were used in patient-specific biomechanical respiration modeling to calculate landmark and tumor residual motion errors.

2. MATERIALS AND METHODS

2.A. Triangular surface lung mesh

4D-CT images from ten lung cancer patients were used for this study. Lung characteristics of each patient are summarized in Table I. The images were acquired by a Philips Brilliance Big Bore CT-simulator (Philips Healthcare, Cleveland, OH). The resolution of CT images varied from $0.9 \times 0.9 \times 1.5$ mm to $1.2 \times 1.2 \times 2.5$ mm. The 4D-CT images were sampled at 10 or 14 equal respiratory cycle intervals, with the initial and final breathing states taken at end-expiration (EE) and end-inhalation (EI), respectively. For each patient, a number of anatomical landmarks were identified by radiation oncologists at prominent inner lung vascular and bronchial bifurcations. The landmarks in the center of each lung, by the borders and close to the tumor, were about 20, 15, and 10, respectively. The average number of landmarks for each patient was 77. These landmark motions were used to quantify the prediction accuracy of the biomechanical modeling described in Sec. 2.F. The 3D triangular surface mesh of the lung region at the EE was obtained by threshold-based segmentation using ITK-SNAP.³⁰ The level of thresholding was selected manually and set to 300 HU.

The magnified texture of the triangular lung mesh is indicated by the red square in Fig. 2. The mesh was

TABLE I. Lung characteristics of each patient.

#Patient	#Vertices	#Elements	#Landmarks left/right of lung	Lung volume (cm ³)	AP landmark motion range (mm) (mean $\pm$ SD)	RL landmark motion range (mm) (mean $\pm$ SD)	SI landmark motion range (mm) (mean $\pm$ SD)
1	553 268	1 106 696	35/35	2786.9	2.1 $\pm$ 2.1	3.1 $\pm$ 1.9	5.5 $\pm$ 3.7
2	280 652	561 460	35/45	2035.2	0.9 $\pm$ 0.8	1.6 $\pm$ 1.4	5.6 $\pm$ 7.0
3	361 880	724 216	44/35	1883.6	1.6 $\pm$ 1.4	1.4 $\pm$ 1.2	6.7 $\pm$ 4.5
4	239 802	479 804	35/45	1450.6	1.8 $\pm$ 1.4	2.6 $\pm$ 2.1	5.8 $\pm$ 4.8
5	365 314	730 784	34/45	2495.2	1.8 $\pm$ 1.4	5.3 $\pm$ 2.2	2.7 $\pm$ 3.7
6	239 442	479 032	45/35	1473.4	1.4 $\pm$ 0.9	4.1 $\pm$ 1.9	5.3 $\pm$ 2.1
7	244 724	489 576	35/45	1449.0	2.2 $\pm$ 1.9	2.4 $\pm$ 1.7	4.2 $\pm$ 3.4
8	338 316	676 792	35/45	2723.5	2.0 $\pm$ 1.3	3.1 $\pm$ 2.6	6.8 $\pm$ 6.2
9	355 578	711 288	41/33	2930.7	0.8 $\pm$ 0.7	1.3 $\pm$ 1	4.4 $\pm$ 2.9
10	256 688	513 664	35/45	1578.1	1.8 $\pm$ 1.6	2.3 $\pm$ 1.8	8.8 $\pm$ 6.9

FIG. 2. Triangular lung surface mesh for patient 1. (See color online version.)

first segmented and created using ITK-SNAP. To improve the triangular surface of the mesh we performed surface remeshing and morphologic operations to smooth irregular boundaries of the mediastinum, using the open source code MeshLab project.³¹ A sample of the triangular surface mesh before and after the preprocessing step is shown in Fig. 3. The number of vertices for each patient depends on the complexity of the lung structure. Following preprocessing, the average numbers of the lung vertices and faces were 323 566 and 647 331, respectively.

For each patient, the nonrigid Demons registration algorithm^{32,33} was used to create lung SDVFs in different respiration phases. The standard deviation of the Gaussian regularization kernel of the algorithm was set to 1. The accuracy of this algorithm in estimating lung motion from 4D-CT was previously reported with an average 3D error of 1.6 mm.³⁴ The algorithm was developed in MATLAB (Ref. 35) and run on a personal computer (PC) (CPU: Intel:Core i7, 2.4 GHz; 16 GB DDR3 RAM).

2.B. Surrogate signals

In this study, we used combinations of motion signals detected from the chest surface and spirometry measurements to predict lung surface motion. First, we used a spirometer (VMM-400, Interface Associates, Laguna Niguel, CA) to measure lung flow volume changes for each patient during

4D-CT imaging. Second, we probed 192 selected points at a regular spacing of 2×2 cm matrix over a total area of 32×24 cm on the chest and abdomen surfaces to monitor motion during 4D-CT imaging. The displacements (i.e., Euclidean distance change) of the selected points at different respiration phases were calculated based on the corresponding reference grid located on top of the chest as illustrated in Fig. 4(a). The initial points on the chest are indicated by the red points in Fig. 4(b).

An observation matrix was constructed from the surrogate signals with rows corresponding to either 8 or 12 respiratory phases (10 or 14 4D-CT phases minus the reference and the test phase CT) and the 193 columns corresponding to the number of surrogate observations per phase—the spirometer flow volume and the 192 selected chest surface points. A normalized sample diaphragm motion curve (Fig. 5) indicated that the rate of increase to the maximum was similar to the spirometer signal, chest marker 1 (a sample marker on abdomen area) and chest marker 2 (a sample chest marker on chest surface area). However, the decreased rate of the diaphragm marker from its maximum was faster than other signals. This figure also shows that the diaphragm marker motion does not perfectly match the spirometry flow volume in later respiratory phases.

An example of surface motion around the chest and the abdomen between phases 0% and 50% is provided in Fig. 6(a). The color bar shows the displacement range from light blue to red (0–22 mm). The distance between respiratory phases 0% and 50% was calculated using the Hausdorff distance sampling.³⁶ The acquired spirometry flow volumes for all ten patients during 4D-CT imaging are shown in Fig. 6(b).

2.C. QRCP

In Sec. 2.B, we described the method to construct the matrix for surrogate signals. The signals acquired from the chest surface contained redundant and collinear observations and needed to be removed from the training set.³⁷ During the training stage, the measurements of one respiration phase were removed and used as a test dataset for predictive algorithm evaluation. A well-known technique that creates low-rank approximations of dense observation matrices is the house-holder QRCP.³⁸

FIG. 3. (a) Example of the triangular surface mesh extracted from 4D-CT images using ITK-SNAP. (b) The same segment after surface remeshing contained more homogenous triangle elements. The selected region is part of Fig. 2 (indicated by the arrow and square).

FIG. 4. (a) The horizontal reference plane shows the 2-cm spaced matrix points; (b) points of interest chosen on the chest surface of patient 1. (See color online version.)

A $m \times n$ ($m \geq n$) matrix A is an observation matrix where m is the number of selected points on the chest plus the spirometer value, and n is the number of the phases minus 2 (phase 0 as a reference phase and phase 50 as a test phase). The objective of QR factorization is to find a $n \times n$ permutation matrix E so that

$$AE = QR, \quad (1)$$

where R is an $m \times n$ upper-triangular matrix, and Q is an orthogonal $n \times n$ unitary matrix. E is selected so that the matrix R is partitioned into $R = (R_1, R_2)$, where the upper-triangular $m \times b$ matrix R_1 is well-conditioned with

$$|\hat{r}_{11}| \geq |\hat{r}_{22}| \geq \dots \geq |\hat{r}_{bb}|. \quad (2)$$

The rank estimation tolerance t is equal to the number of $|\hat{r}_{ii}|$, $1 \leq i \leq b$, greater than $|\hat{r}_{11}| \times 10^{-10}$, and the selected observation columns are taken as $E(1:t)$. The final selections, after removing the collinearities from the surrogate data, are the points on the chest with independent motion patterns ($y_1, y_2, \dots, y_M$) and the spirometry measurement (y_s).

2.D. Lung surface motion

We have developed a method to predict lung surface motion from the chest wall surface motion and spirometry

FIG. 5. Normalized sample of the chest signal from two separate locations and normalized spirometer flow volume for patient 1. The normalized marker motion on the diaphragm in the SI direction is indicated by the black line.

measurements. To build the prediction model for a 3D lung surface we constructed a matrix H , which contained the information on the displacement of the vertices on the triangular lung surface mesh,

$$H = [AP_1, RL_1, SI_1, AP_2, RL_2, SI_2, \dots, AP_p, RL_p, SI_p]^T, \quad (3)$$

where the matrix dimension is $N_H = 3 \times p$. Here, p is the number of anatomical points on the triangular lung surface mesh described in Sec. 2.A. AP_i , RL_i and SI_i are

(a)

(b)

FIG. 6. (a) Surface displacement plot between phase 0 and phase 50% in patient 1; (b) spirometer signals in all ten patients. (See color online version.)

the displacements of the i th point in the anterior–posterior (AP), right–left (RL), and superior–inferior (SI) directions, respectively. The phase at time t is described by the sampling matrix of surface vertices H_t and the selected surrogate signal. The displacement in each phase is the distance between the current vertex locations and the corresponding locations in the reference phase.

2.E. Fitting model based on CRR

Canonical correlation analysis (CCA) has been explored to create a statistical model between the lung tumor location and the corresponding dense image deformation of the high contrast lung surface.^{39–41} In this study, we implemented a regularized CCA called CRR (Ref. 42) to predict lung surface motion. The main reason to use CRR is to avoid the singularity problem that may occur in the cross-correlation matrices of CCA. CRR is a statistical method that obtains stable canonical correlation estimation for data sets with some degree of collinearity. A motion model of each lung surface mesh vertex was re-expressed in terms of the weighting factors selected for surrogate signals during the training process (Fig. 7).

We assumed two sets of variables, H and Y , located in the x and y coordinates, as described in Sec. 2.C. We estimated w and u to maximize the correlation between $H_{\text{proj},w}$ and $Y_{\text{proj},u}$,

$$H_{\text{proj},w} = \langle w, H \rangle = \frac{w * H'}{\|w\|_2^2 * w}, \quad Y_{\text{proj},u} = \langle u, Y \rangle = \frac{u * Y'}{\|u\|_2^2 * u}. \quad (4)$$

The maximization function is shown by the following equation:

$$\begin{aligned} \rho &= \max_{w,u} \text{cor}(H_{\text{proj},w}, Y_{\text{proj},u}) \\ &= \max_{w,u} \frac{E[H_{\text{proj},w} Y_{\text{proj},u}]}{\sqrt{E(H_{\text{proj},w}^2) E(Y_{\text{proj},u}^2)}} \\ &= \max_{w,u} \frac{w' E[HY'] u}{\sqrt{w' E[HH'] w u' E[YY'] u}}, \end{aligned} \quad (5)$$

$$Y_t = [y_{1,t}, y_{2,t}, \dots, y_{M,t}, y_{S,t}]$$

$$H_t = [AP_{1,t}, RL_{1,t}, SI_{1,t}, AP_{2,t}, RL_{2,t}, SI_{2,t}, \dots, AP_{p,t}, RL_{p,t}, SI_{p,t}]^T$$

t is respiratory phases = {2,3,4,6,7,8,9,10}, p is the vertex number

FIG. 7. Block diagram of CRR training for the vertices. The $y_1, \dots, y_M$ parameters represent the Euclidean displacement of the chest markers, while M is the number of independent chest points in the observation. The y_S parameter indicates the spirometry value in each t phase.

where $E[\cdot]$ is the empirical expectation of the random variable. To avoid the collinearity problem, Eq. (5) is replaced by the following equation:

$$\begin{aligned} \rho(k_1, k_2) &= \max_{w,u} \frac{w' E[HY'] u}{[w' (E[HH'] + k_1 I) w]^{1/2} [u' (E[YY'] + k_2 I) u]^{1/2}}. \end{aligned} \quad (6)$$

The weighting vectors w and u are unique for each vertex and are optimized with respect to Eq. (6). These parameters are employed to predict the vertex locations of the testing data set. In Eq. (6), $k_1 = 0.1$, $k_2 = 0.1$ are the regularization parameters for H and Y ;⁴² I is the identity matrix.

A motion model of each lung surface mesh vertex was expressed in terms of weighting factors selected for the surrogate signals during the training process (Fig. 7). During the training process, we removed one respiration phase (30%, 50%, or 70%) from the training datasets to test the algorithm. The weighting vectors w and u were unique for each vertex. The vectors were optimized using all other 4D-CT phases except for the test phase. These parameters were employed to predict the vertex locations of a testing data set.

2.F. Evaluating the predicted SDVFs

In this study, one of the respiratory phases (30%, 50%, or 70%) was considered as testing data. The predicted SDVFs were compared to the vertex motion determined from the 4D-CT images through the Demons deformable registration. The prediction vertex error was calculated on the lung surface for ten lung cancer patients along the AP, RL, and SI directions. For each patient, the percentage of vertices with errors less than 1 mm and the 98th percentile error were calculated. The vertices on the lung surface were further grouped based on their location. The lung was divided into three equal regions along the SI direction. The vertices by the diaphragm region were grouped under the lower lung region, the vertices in the middle of the lung were grouped under the middle region, and those close to the lung apex were grouped under the upper region. Vertices gathered within each group were used separately to evaluate the lung motion estimation error in that specific area.

We also used the estimated SDVFs as boundary conditions for patient-specific lung biomechanical respiration modeling.²⁸ In this approach, the uncoupled Mooney–Rivlin material model was used, and the whole lung was simulated as homogenous material. The incompressibility of the whole lung (k -factor in last column of Table V) was optimized iteratively for each patient to minimize the overall landmark errors. We performed two simulations for each patient. One simulation was conducted with the direct calculation of the SDVFs from the nonrigid Demons registration, while the other was performed with the predicted SDVFs using the method described in Sec. 2.E. The simulation motion error of the selected landmarks and tumor was used to quantify the influence of the predicted lung SDVFs.

FIG. 8. Examples of independent chest surface moving points from three patients after QRCP.

3. RESULTS

Using the QRCP method described in Sec. 2.C, we reduced the 192 monitored points on the chest surface to a small group of points with an independent motion pattern. Samples of selected point sets are reported for three patients (Fig. 8). The red points depict the monitoring points selected during treatment based on the patient’s independent respiratory motion styles. The selected points on the chest are mostly located in the abdomen area and are patient-specific. The correlation between the selected points for each patient is shown in Table II. These results show that the selected points are highly patient-dependent.

We found that 98% of the mesh vertices showed an error lower than 1.8 mm for each patient in the AP, RL, and SI directions at phase 50% (Table III and Fig. 9 histograms). The estimation of the maximum 98th percentile motion error in testing data was observed for patient 3 with errors of 1.8, 1.0, and 1.4 mm in the AP, RL, and SI directions, respectively. Patient 3 had a large tumor close to the mediastinum that affected the accuracy of the lung triangular surface mesh. This may have caused the large motion prediction error observed in this patient. The average 98th percentile error was less than 1 mm (AP=0.9 mm, RL=0.6 mm, and SI=0.8 mm). The mean percentage of error less than 1 mm is shown for the vertices and was more than 98% in three directions (Table III). The histogram for vertex motion prediction in each direction is shown for patient 10 as an example (Fig. 9).

To further evaluate the stability of the proposed method, we also used phases 30% and 70% as test data. Table IV summarizes the 98th percentile error of the predicted lung

SDVFs at phases 30% and 70% for each patient. The mean 98th percentile errors were all less than 1 mm in the AP, RL, and SI directions.

The Euclidean distance error between the estimated vertices and the ground truth of different parts of the lung is illustrated in Fig. 10. As expected, the error in different regions was proportional to the absolute motion of the vertices in the same region. The minimum error related to the vertices was located in the upper region.

The landmark errors between respiration phases 0% and 50% using a biomechanical modeling approach are summarized in Table V.²⁸ The optimized incompressibility factors of the lung material during biomechanical simulation are shown in the last column. The Euclidean landmark motion errors, derived from the biomechanical modeling using the real SDVFs (by deformable registration of 4D-CT) and the predicted SDVFs, are shown in the third and fourth columns, respectively (Table V). The mean landmark motion errors were 3.0 and 3.1 mm for real SDVFs and predicted SDVFs, respectively. The Wilcoxon signed-rank test showed there was no significant difference in the mean landmark Euclidean error between the real SDVFs and the predicted SDVFs (p -value = 0.64). These results were expected because the SDVFs extracted from the deformable registration were used as the input during the training stage of the CCA. Thus, for a testing phase, we expected the predicted SDVFs to be similar to the SDVFs extracted from the deformable registration.

TABLE II. Correlation coefficients between selected points for each patient.

Patient #	1	2	3	4	5	6	7	8	9	10
1	1	0.087	0.087	0.043	0.053	0.053	0.053	0.161	0.053	0.056
2		1	0.043	0.087	0.053	0.053	0.053	0.053	0.053	0.056
3			1	0.087	0.053	0.053	0.053	0.161	0.053	0.047
4				1	0.053	0.053	0.053	0.053	0.053	0.056
5					1	0.066	0.022	0.111	0.111	0.101
6						1	0.066	0.066	0.022	0.016
7							1	0.111	0.022	0.101
8								1	0.022	0.101
9									1	0.016
10										1

TABLE III. Percentage of error less than 1.0 mm and 98th percentile error at phase 50% for each patient in the AP, RL, and SI directions.

Patient #	Percentage of error less than 1 mm (%)			98th percentile error (mm)			Independent vectors + spirometer
	AP	RL	SI	AP	RL	SI	
1	96.8	98.5	97.3	1.2	0.9	1.1	8
2	100	100	100	0.5	0.3	0.4	8
3	93.3	97.7	93.6	1.8	1.0	1.4	8
4	99.9	100	98.9	0.7	0.5	0.9	8
5	99.5	98.6	99.6	0.7	0.9	0.8	12
6	100	100	99.4	0.5	0.5	0.7	12
7	100	100	100	0.1	0.1	0.1	12
8	97.0	99.2	95.2	1.3	0.7	1.2	12
9	94.1	98.3	99.8	1.4	0.9	0.7	12
10	96.2	99.2	98.0	1.3	0.8	1.0	12
Mean	98.3	99.2	98.0	0.9	0.6	0.8	12

FIG. 9. Lung vertex prediction error in the AP, RL, and SI directions at phase 50%. Patient 10 was selected as an example.

Table VI shows the tumor center of mass (TCM) motion range for each patient and the TCM simulation error using the predicted SDVFs as the boundary condition for phase 50%. The average TCM simulation Euclidean error for 10 patients was below 2.0 mm.

TABLE IV. The 98th percentile error for each patient in the AP, RL, and SI directions at phases 30% and 70%.

Patient #	98th percentile error (mm) phase 30%			98th percentile error (mm) phase 70%		
	AP	RL	SI	AP	RL	SI
1	0.5	0.8	0.5	1.0	0.9	1.0
2	0.4	0.5	0.4	0.4	0.5	0.4
3	0.7	1.0	1.1	0.4	0.7	0.5
4	0.7	1.0	0.9	0.7	1.0	0.8
5	0.6	1.0	0.7	0.9	0.7	0.8
6	0.2	0.2	0.3	0.5	0.5	0.7
7	0.5	0.4	0.5	0.1	0.1	0.1
8	0.4	0.8	0.6	0.7	1.1	1.2
9	0.9	1.1	1.1	0.9	1.2	0.7
10	0.1	0.1	0.2	0.8	1.1	1.0
Mean	0.5	0.7	0.6	0.6	0.8	0.7

4. DISCUSSION

A predictive model can be created based on the relationship between internal organ motion and respiratory surrogate signals. Two well-known examples of these signals are surface chest displacement via an IR camera or a laser-based distance sensor, and tidal air volume measured by a spirometer. Respiratory motion has a random, nonlinear behavior and is completely patient-specific. Hence the challenge to create a robust and precise lung respiration model.^{19,43,44} Previous studies have shown that the motion signals detected from the chest surface have greater phase discrepancy and upward drift to diaphragm or internal target motion, as compared with spirometry signals.^{15,20,45–47} In this work, we combined the chest and abdomen wall surface motion and spirometry measurements to predict lung surface motion induced by respiration.

As the motions on the chest and abdomen wall surface are highly correlated, we propose using only a limited number of observations as surrogate signals during 4D-CT imaging, by minimizing the matrix of observation to an independent set

FIG. 10. Estimated error at different sections the lung: lower, middle, and upper regions.

TABLE V. Overall landmark errors based on lung biomechanical modeling of using estimated DVFs and real DVFs between phases 0% and 50%.

Patient #	Land marks motion range (mm)	Mean and S.D. Euclidean error (mm) real SDVFs	Mean and S.D. Euclidean error (mm) predicted SDVFs	K-factors for lung
1	6.7 ± 4.6	2.9 ± 1.6	3.1 ± 1.7	15.32
2	5.9 ± 7.2	3.3 ± 3.0	3.3 ± 3.0	5.86
3	7.0 ± 4.9	2.9 ± 1.7	2.7 ± 1.9	1.29
4	6.6 ± 5.5	3.2 ± 2.8	3.3 ± 2.8	0.72
5	6.5 ± 4.5	2.8 ± 1.7	2.8 ± 1.7	2.91
6	6.8 ± 4.5	3.0 ± 1.9	3.1 ± 2.0	3.27
7	5.3 ± 4.3	3.0 ± 2.2	3.0 ± 2.2	5.18
8	7.7 ± 6.9	3.1 ± 2.1	3.3 ± 2.1	8.74
9	4.7 ± 3.1	1.9 ± 1.5	2.3 ± 1.4	6.22
10	8.3 ± 7.3	4.0 ± 3.4	4.0 ± 3.5	14.13
Mean	6.5 ± 5.3	3.0 ± 2.2	3.1 ± 2.2	6.36

of either 10 or 14 components (depending on the number of respiratory phases in 4D-CT). The monitored points around the abdominal region exhibited larger amplitude and greater variation as compared to those in the chest area. For this reason, more abdomen-related points were selected as compared to chest-related points by the QRCF. This study indicated that a small number of selected observations are sufficient to accurately model the 3D lung surface motion.

From respiratory surrogate signals, including spirometry measurements and surface motion, we could also directly estimate the entire lung deformation vector fields. However, this procedure is deterministic in estimating lung motion: any uncertainties in the observation signals will directly affect the final estimated lung DVFs and tumor motion. Instead of directly estimating the lung volumetric DVFs, we propose to estimate lung surface deformation from surrogate signals first and then use the estimated lung surface DVFs as the boundary condition to derive lung volumetric deformation through biomechanical modeling. Our proposed strategy may be more robust to uncertainties of observation signals as it generates biomechanically realistic simulations by finite element analysis.

In this study, the lung SDVFs extracted from the Demons deformable registration were used to evaluate the prediction accuracy of the proposed strategy. However, the uncertainty of

the Demons deformable registration is between 1 and 2 mm,³⁴ which may negatively affect the evaluation accuracy of the proposed strategy. To avoid the influence of deformable image registration uncertainty, a dedicated MR tagging technique may be employed to directly measure lung motion.⁴⁸

The computation time for our model depends on the number of selected vertices on the lung surface during the training step (the average number of vertices was 323 566). Our proposed method also involves a deformable registration algorithm that registers the different respiratory phases to obtain lung SDVFs to train the predictive model. Volume-deformable image registration takes approximately 15 min on a PC. However, patient 4D-CT imaging is always conducted several days before treatment. Thus sufficient time is available to create the motion model from 4D-CT. In our current implementation, we predicted the motion of each vertex (average 323 566 vertices) sequentially with a total time less than 3 min, including the training and predicting steps. However, the calculation time for testing data after the training step was less than 1 s. If we use GPU programming for parallel estimation of the vertex motion, this approach could be used as a real-time monitoring technique during treatment.

The robustness and accuracy of our approach has only been evaluated based on the respiratory motion occurring within a single treatment fraction. Sensitivity to irregular

TABLE VI. TCM motion range between phase 0% and 50% and TCM simulation error.

Patient #	TCM motion range AP (mm)	TCM motion range RL (mm)	TCM motion range SI (mm)	TCM Euclidean range (mm)	TCM simulation error AP (mm)	TCM simulation error RL (mm)	TCM simulation error SI (mm)	TCM Euclidean error (mm)
1	1.2	2.4	1.1	2.9	0.5	1.0	0.7	1.3
2	0.6	1.2	0.3	1.3	0.6	0.6	0.3	0.9
3	1.6	1.6	4.3	4.9	0.7	0.8	1.4	1.8
4	1.5	3.7	12.0	12.7	0.4	1.1	2.1	2.4
5	1.2	2.9	0.4	3.2	0.3	0.8	0.4	1.0
6	1.5	5.0	3.3	6.1	1.0	2.3	1.3	2.8
7	1.4	0.9	1.5	2.2	0.4	0.8	0.5	1.0
8	1.1	1.7	5.7	6.0	0.4	0.5	1.8	1.9
9	0.8	0.7	5.4	5.5	0.4	0.5	1.2	1.4
10	0.7	2.5	14.2	14.5	0.3	1.0	2.2	2.5
Mean	1.2	2.2	4.8	5.9	0.5	0.9	1.2	1.7

breathing patterns, variations during treatment fractions, and nonrespiratory motion artifacts have not yet been considered. As we use the complimentary information from both surface motion and spirometry measurement, we expect that our proposed method is more robust to irregular respiration as compared with methods relying on a single respiratory surrogate signal. Nevertheless, further evaluation on more patients is required to test the stability of the proposed strategy.

5. CONCLUSION

We have developed a model to predict patient-specific lung surface motion induced by respiration in a 3D space using respiratory surrogate signals. The surrogate signals included two noninvasive measurements: (1) chest/abdomen surface motion at selected locations and (2) spirometry measurements. The 98th error percentile was calculated for ten lung cancer patients with an average error less than 1 mm. The predicted lung surface motion can be used as the boundary condition for respiration biomechanical modeling. This will not only allow us to derive the tumor position but also to evaluate the whole lung status during radiotherapy.

ACKNOWLEDGMENTS

The authors acknowledge funding support from the American Cancer Society (Grant No. RSG-13-326-01-CCE), the U.S. National Institutes of Health (Grant No. R01 EB020366), and the Cancer Prevention and Research Institute of Texas (Grant Nos. RP130109 and RP110562-p2). The authors would like to thank Dr. Daniel Low, Dr. Wei Lu, and Dr. Rene Werner for providing 4D-CT images with spirometry measurements. The authors also thank Dr. Damiana Chiavolini for editing the paper.

CONFLICT OF INTEREST DISCLOSURE

The authors have no COI to report.

^{a)} Author to whom correspondence should be addressed. Electronic mail: Jing.Wang@utsouthwestern.edu

- ¹G. S. Mageras, E. Yorke, K. Rosenzweig, L. Braban, E. Keatley, E. Ford, S. A. Leibel, and C. C. Ling, "Fluoroscopic evaluation of diaphragmatic motion reduction with a respiratory gated radiotherapy system," *J. Appl. Clin. Med. Phys.* **2**, 191–200 (2001).
- ²T. Lin, L. I. Cervino, X. Tang, N. Vasconcelos, and S. B. Jiang, "Fluoroscopic tumor tracking for image-guided lung cancer radiotherapy," *Phys. Med. Biol.* **54**, 981–992 (2009).
- ³Q. Xu, R. J. Hamilton, R. A. Schowengerdt, B. Alexander, and S. B. Jiang, "Lung tumor tracking in fluoroscopic video based on optical flow," *Med. Phys.* **35**, 5351–5359 (2008).
- ⁴H. Teske, P. Mercea, M. Schwarz, N. H. Nicolay, F. Sterzing, and R. Bendl, "Real-time markerless lung tumor tracking in fluoroscopic video: Handling overlapping of projected structures," *Med. Phys.* **42**, 2540–2549 (2015).
- ⁵H. Shirato, S. Shimizu, K. Kitamura, T. Nishioka, K. Kagei, S. Hashimoto, H. Aoyama, T. Kunieda, N. Shinohara, and H. Dosaka-Akita, "Four-dimensional treatment planning and fluoroscopic real-time tumor tracking radiotherapy for moving tumor," *Int. J. Radiat. Oncol., Biol., Phys.* **48**, 435–442 (2000).
- ⁶M. Wang, G. C. Sharp, S. Rit, V. Delmon, and G. Wang, "2D/4D marker-free tumor tracking using 4D CBCT as the reference image," *Phys. Med. Biol.* **59**, 2219–2233 (2014).

- ⁷J.-J. Sonke, L. Zijp, P. Remeljeij, and M. van Herk, "Respiratory correlated cone beam CT," *Med. Phys.* **32**, 1176–1186 (2005).
- ⁸Y. Zhang, F.-F. Yin, T. Pan, I. Vergalasova, and L. Ren, "Preliminary clinical evaluation of a 4D-CBCT estimation technique using prior information and limited-angle projections," *Radiother. Oncol.* **115**, 22–29 (2015).
- ⁹L. I. Cervino, J. Du, and S. B. Jiang, "MRI-guided tumor tracking in lung cancer radiotherapy," *Phys. Med. Biol.* **56**, 3773–3785 (2011).
- ¹⁰S. Crijns, B. Raaymakers, and J. Lagendijk, "Proof of concept of MRI-guided tracked radiation delivery: Tracking one-dimensional motion," *Phys. Med. Biol.* **57**, 7863–7872 (2012).
- ¹¹J. J. Lagendijk, B. W. Raaymakers, A. J. Raaijmakers, J. Overweg, K. J. Brown, E. M. Kerkhof, R. W. van der Put, B. Hårdemark, M. van Vulpen, and U. A. van der Heide, "MRI/linac integration," *Radiother. Oncol.* **86**, 25–29 (2008).
- ¹²S. Vedam, P. Keall, V. Kini, and R. Mohan, "Determining parameters for respiration-gated radiotherapy," *Med. Phys.* **28**, 2139–2146 (2001).
- ¹³L. Xing, J. Siebers, and P. Keall, "Computational challenges for image-guided radiation therapy: Framework and current research," *Semin. Radiat. Oncol.* **17**, 245–257 (2007).
- ¹⁴E. Rietzel, G. T. Chen, N. C. Choi, and C. G. Willet, "Four-dimensional image-based treatment planning: Target volume segmentation and dose calculation in the presence of respiratory motion," *Int. J. Radiat. Oncol., Biol., Phys.* **61**, 1535–1550 (2005).
- ¹⁵W. Lu, D. A. Low, P. J. Parikh, M. M. Nystrom, I. M. El Naqa, S. H. Wahab, M. Handoko, D. Fooshee, and J. D. Bradley, "Comparison of spirometry and abdominal height as four-dimensional computed tomography metrics in lung," *Med. Phys.* **32**, 2351–2357 (2005).
- ¹⁶H. D. Kubo, P. M. Len, S.-i. Minohara, and H. Mostafavi, "Breathing-synchronized radiotherapy program at the University of California Davis Cancer Center," *Med. Phys.* **27**, 346–353 (2000).
- ¹⁷H. D. Kubo and B. C. Hill, "Respiration gated radiotherapy treatment: A technical study," *Phys. Med. Biol.* **41**, 83–91 (1996).
- ¹⁸A. Schweikard, H. Shiomi, and J. Adler, "Respiration tracking in radio-surgery," *Med. Phys.* **31**, 2738–2741 (2004).
- ¹⁹J. D. Hoisak, K. E. Sixel, R. Tirona, P. C. Cheung, and J.-P. Pignol, "Correlation of lung tumor motion with external surrogate indicators of respiration," *Int. J. Radiat. Oncol., Biol., Phys.* **60**, 1298–1306 (2004).
- ²⁰D. A. Low, P. J. Parikh, W. Lu, J. F. Dempsey, S. H. Wahab, J. P. Hubenschmidt, M. M. Nystrom, M. Handoko, and J. D. Bradley, "Novel breathing motion model for radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **63**, 921–929 (2005).
- ²¹D. Yang, W. Lu, D. A. Low, J. O. Deasy, A. J. Hope, and I. El Naqa, "4D-CT motion estimation using deformable image registration and 5D respiratory motion modeling," *Med. Phys.* **35**, 4577–4590 (2008).
- ²²K. K. Brock, M. B. Sharpe, L. A. Dawson, S. M. Kim, and D. A. Jaffray, "Accuracy of finite element model-based multi-organ deformable image registration," *Med. Phys.* **32**, 1647–1659 (2005).
- ²³T. Zhang, N. P. Orton, T. R. Mackie, and B. R. Paliwal, "Technical note: A novel boundary condition using contact elements for finite element based deformable image registration," *Med. Phys.* **31**, 2412–2415 (2004).
- ²⁴M. Li, E. Castillo, X. L. Zheng, H. Y. Luo, R. Castillo, Y. Wu, and T. Guerrero, "Modeling lung deformation: A combined deformable image registration method with spatially varying Young's modulus estimates," *Med. Phys.* **40**, 081902 (10pp.) (2013).
- ²⁵A. Al-Mayah, J. Moseley, M. Velec, and K. K. Brock, "Sliding characteristic and material compressibility of human lung: Parametric study and verification," *Med. Phys.* **36**, 4625–4633 (2009).
- ²⁶J. Eom, X. G. Xu, S. De, and C. Shi, "Predictive modeling of lung motion over the entire respiratory cycle using measured pressure-volume data, 4DCT images, and finite-element analysis," *Med. Phys.* **37**, 4389–4400 (2010).
- ²⁷R. Werner, J. Ehrhardt, R. Schmidt, and H. Handels, "Patient-specific finite element modeling of respiratory lung motion using 4D CT image data," *Med. Phys.* **36**, 1500–1511 (2009).
- ²⁸J. N. Tehrani, Y. Yang, R. Werner, W. Lu, D. Low, X. Guo, and J. Wang, "Sensitivity of tumor motion simulation accuracy to lung biomechanical modeling approaches and parameters," *Phys. Med. Biol.* **60**, 8833–8849 (2015).
- ²⁹J. N. Tehrani and J. Wang, "Mooney-Rivlin biomechanical modeling of lung with Inhomogeneous material," *Conf Proc IEEE Eng Med Biol Soc.*, pp. 7897–7900, 2015.

- ³⁰P. A. Yushkevich, J. Piven, H. C. Hazlett, R. G. Smith, S. Ho, J. C. Gee, and G. Gerig, "User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability," *NeuroImage* **31**, 1116–1128 (2006).
- ³¹P. Cignoni, M. Corsini, and G. Ranzuglia, "MeshLab: An open-source 3D mesh processing system," *ERCIM News* **73**(45–46), 6 (2008).
- ³²D. J. Kroon and C. H. Slump, *Proceedings IEEE International Symposium on Biomedical Imaging: from nano to macro*, pp. 963–966, 2009.
- ³³J. P. Thirion, "Image matching as a diffusion process: An analogy with Maxwell's demons," *Med. Image Anal.* **2**, 243–260 (1998).
- ³⁴X. Gu, H. Pan, Y. Liang, R. Castillo, D. Yang, D. Choi, E. Castillo, A. Majumdar, T. Guerrero, and S. B. Jiang, "Implementation and evaluation of various demons deformable image registration algorithms on a GPU," *Phys. Med. Biol.* **55**, 207–219 (2010).
- ³⁵S. Lynch, "A tutorial introduction to MATLAB," in *Dynamical Systems with Applications using MATLAB®* (Springer International Publishing, Switzerland, 2014), pp. 1–14.
- ³⁶D. P. Huttenlocher, G. Klanderman, and W. J. Rucklidge, "Comparing images using the Hausdorff distance," *IEEE Trans. Pattern Anal. Mach. Intell.* **15**, 850–863 (1993).
- ³⁷T. Mary, I. Yamazaki, J. Kurzak, P. Luszczek, S. Tomov, and J. Dongarra, "Performance of random sampling for computing low-rank approximations of a dense matrix on GPUs," in *Proceedings of the International Conference for High Performance Computing, Networking, Storage and Analysis* (ACM, Austin, Texas, 2015), pp. 1–11.
- ³⁸P. Businger and G. H. Golub, "Linear least squares solutions by Householder transformations," *Numer. Math.* **7**, 269–276 (1965).
- ³⁹J. McClelland, "Estimating internal respiratory motion from respiratory surrogate signals using correspondence models," in *4D Modeling and Estimation of Respiratory Motion for Radiation Therapy* (Springer, Berlin Heidelberg, 2013), pp. 187–213.
- ⁴⁰X. Liu, I. Oguz, S. M. Pizer, and G. S. Mageras, "Shape-correlated deformation statistics for respiratory motion prediction in 4D lung," *Proc. SPIE* **7625**, 76252D (2010).
- ⁴¹G. Gao, J. McClelland, S. Tarte, J. Blackall, and D. Hawkes, *Proceeding of 1st International Workshop on Pulmonary Image Analysis at MICCAI 2008*, pp. 145–154, 2008.
- ⁴²H. D. Vinod, "Canonical ridge and econometrics of joint production," *J. Econometrics* **4**, 147–166 (1976).
- ⁴³A. S. Beddar, K. Kainz, T. M. Briere, Y. Tsunashima, T. Pan, K. Prado, R. Mohan, M. Gillin, and S. Krishnan, "Correlation between internal fiducial tumor motion and external marker motion for liver tumors imaged with 4D-CT," *Int. J. Radiat. Oncol., Biol., Phys.* **67**, 630–638 (2007).
- ⁴⁴C. Plathow, H. Zimmermann, C. Fink, R. Umathum, M. Schöbinger, P. Huber, I. Zuna, J. Debus, W. Schlegel, and H.-P. Meinzer, "Influence of different breathing maneuvers on internal and external organ motion: Use of fiducial markers in dynamic MRI," *Int. J. Radiat. Oncol., Biol., Phys.* **62**, 238–245 (2005).
- ⁴⁵T. Zhang, H. Keller, M. J. O'Brien, T. R. Mackie, and B. Paliwal, "Application of the spirometer in respiratory gated radiotherapy," *Med. Phys.* **30**, 3165–3171 (2003).
- ⁴⁶Q.-S. Chen, M. S. Weinhaus, F. C. Deibel, J. P. Ciezki, and R. M. Macklis, "Fluoroscopic study of tumor motion due to breathing: Facilitating precise radiation therapy for lung cancer patients," *Med. Phys.* **28**, 1850–1856 (2001).
- ⁴⁷G. Li, M. Caraveo, J. Wei, A. Rimner, A. J. Wu, K. A. Goodman, and E. Yorke, "Rapid estimation of 4DCT motion-artifact severity based on 1D breathing-surrogate periodicity," *Med. Phys.* **41**, 111717 (9pp.) (2014).
- ⁴⁸J. Cai, G. W. Miller, T. A. Altes, P. W. Read, S. H. Benedict, E. E. de Lange, G. D. Cates, J. R. Brookeman, J. P. Mugler III, and K. Sheng, "Direct measurement of lung motion using hyperpolarized helium-3 MR tagging," *Int. J. Radiat. Oncol., Biol., Phys.* **68**, 650–653 (2007).