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Towards Non-invasive Lung Tumor Tracking Based on Patient Specific Model of Respiratory System

Hamid Ladjal, Michael Beuve, Philippe Giraud and Behzad Shariat (member IEEE)

Abstract—The goal of this paper is to calculate a complex internal respiratory and tumoral movements by measuring respiratory air flows and thorax movements. In this context, we present a new lung tumor tracking approach based on a patient-specific biomechanical model of the respiratory system, which takes into account the physiology of respiratory motion to simulate the real non-reproducible motion. The behavior of the lungs, is directly driven by the simulated actions of the breathing muscles, i.e. the diaphragm and the intercostal muscles (the rib cage). In this paper, the lung model is monitored and controlled by a personalized lung pressure/volume relationship during a whole respiratory cycle. The lung pressure and rib kinematics are patient specific and obtained by surrogate measurement.

The rib displacement corresponding to the transformation which was computed by finite helical axis method from the end of exhalation (EE) to the end of inhalation (EI). The lung pressure is calculated by an optimization framework based on inverse finite element analysis, by minimizing the lung volume errors, between the respiratory volume (respiratory airflow exchange) and the simulated volume (calculated by biomechanical simulation). We have evaluated the model accuracy on five public datasets. We have also evaluated the lung tumor motion identified in 4D CT scan images and compared it with the trajectory that was obtained by finite element simulation. The effects of rib kinematics on lung tumor trajectory were investigated. Over all phases of respiration, our developed model is able to predict the lung tumor motion with an average landmark error of 2.0 ± 1.3mm. The results demonstrate the effectiveness of our physics-based model. We believe that this model can be potentially used in 4D dose computation, removal of breathing motion artifacts in positron emission tomography (PET) or gamma prompt image reconstruction.

Index Terms—Respiratory motion - Biomechanics modeling - Finite Element Method, Radiation therapy

I. INTRODUCTION

One of the major difficulties in radiation therapy is the treatment of moving tumours. The modern external beam radiotherapy techniques are available for cancer treatment, including Three-Dimensional Conformal Radiation Therapy (3D-CRT), Intensity Modulated Radiation Therapy (IMRT), Helical Tomotherapy (HT) and Hadron Therapy (HTH). The HTH has been the subject of growing interest, primarily due to the favorable ballistic properties of ion-matter interactions, which allow for a high degree of dose conformality in the tumor while minimizing the dose in the healthy tissue. Unfortunately, in many cases the advantage of the increased dose conformity is severely compromised due to organ motion. The internal anatomy of the patient can undergo intrafractional and inter-fractional deformation and displacement [1], [2]. Moreover, in the case of Hadron Therapy (HTH), apart the ballistic problem caused by the target motion, the organs density variations due to respiratory motion affect the particle range which can lead to unwanted dose distributions [3], [4], overshoot to critical organs or beam undershoot to tumor. The error due to density changes depends the position of the tumour and the beam direction and may exceed 1 or 2 cm [5]. The effects of density variations that occur along the beam path on dose distribution are more important in the case of HTH than in the case of conventional radiotherapy [40]. In this paper we are going to focus on breathing-induced intrafractional motion. Respiration is the most important source of intra-fractional motion in the patient’s body. Lung tumour displacement can range up to more than 2 cm, while lung volume was being varied by about 25% during respiration [7], [8]. In this context, various intra-fractional motion mitigation techniques have been developed. One solution is to reduce the organ motion of the patient using abdominal compression or partial/complete stop of the patient respiration [9]. However, these techniques would substantially increase the patient setup time as well as the associated clinical workload. Moreover, the abdominal compression methods can be hard to reproduce. Breath hold level and breathing patterns can drift between time of simulation and treatment or even within a treatment session as the patient becomes more relaxed. Other existing solutions consist on beam gating or beam tracking. The beam gating refer to the irradiation during a selected period of the breathing cycle known as the gating window [10], [11]. This technique has the major disadvantage that the treatment time is prolonged due to the frequent interruptions of the beam delivery. Moreover, the beam gating, as well as mitigation techniques, are based on previously acquired images and therefore cannot take into consideration the variations of the patient’s breathing pattern. An example of a beam tracking system used in the clinical environment is the robotic Cyberknife Synchrony system applied to x-ray radiosurgery [12], [13]. This technique increases dose to the patient from imaging and is an invasive procedure [8]. Furthermore, the density changes along the beam path cannot
be properly determined which is essential in the case of HTH. Other existing solutions consist of tracking by implantation of fiducial markers. These solutions are either intrusive or invasive and there is a risk of infection and pneumothorax [8], [14].

An ideal solution would continuously adapt the beam to the variation of the tumour position. An alternative solution is to use a motion model that is able to model the correspondence between the internal displacement and deformations of the organs and respiratory surrogate signals such as spirometry and deformation of the skin surface. Moreover, in the case of four dimensional radiotherapy treatment planning that aims to estimate the evolution of the dose distribution during the respiratory cycle on one hand the position of the organs, on the other hand the displacements and the deformations of the tissues throughout the respiratory cycle need to be estimated. Breathing is a dynamic and a complex process in which the respiratory motion is non-reproducible [8]. As shown by many studies, the breathing periodicity and amplitude of patients can vary during a single imaging or treatment session [15], [16]. Furthermore, lung tumors can even present hysteresis in their trajectories [17], making them more difficult to locate with precision.

Methods to estimate respiratory organ motions can be divided into 4 major categories; deformable image registration[18], [19], biomechanical models [20], [21], [22], [23], [24], [19], hybrid models with biomechanics and deformable image registration [25], [26] and statistical models including or not the machine learning techniques [27], [28], [29]. Currently, the existing methods do not explicitly take into account the information related to breathing physiology and physical properties of organ tissues, and all those methods assume a reproducible motion of the respiratory system and cannot fully take into account the variability of the respiratory motion. Recently, the authors in [22] have proposed a generative lung biomechanical model for half respiration cycle, where the motion is not constrained by any fixed boundary condition. The authors have used 4 and 16 pressure zones on the sub-diaphragm and thoracic cavity, respectively. However, this method, could hardly be correlated with respiratory surrogate signals during treatment. In order to overcome these limitations, the aim of this study is to propose a non-invasive approach for lung tumor tracking based on a patient-specific model of the respiratory system, which can be used during External Beam Radiation Therapy (EBRT).

In order to overcome these limitations, the aim of this study is to propose a non-invasive approach for lung tumor tracking based on a patient-specific model of the respiratory system, which can be used during External Beam Radiation Therapy (EBRT). Fig.1 illustrates our global methodology to predict and track the internal motion (lung tumor motion), from external measurable parameters, such as spirometry and Real-time Position Management (RPM), during treatment. In this study, we have developed a lung tumor tracking approach based on a patient-specific biomechanical model of the respiratory system, which takes into account the physiology of respiratory motion to simulate the real non-reproducible breathing motion. The behavior of the lungs, is driven directly by simulated actions of the breathing muscles, i.e. the diaphragm and the intercostal muscles (the rib cage). The lung model is monitored and controlled by a personalized lung pressure/volume relationship (lung compliance) during a whole respiratory cycle. The lung pressure and diaphragmatic forces are patient-specific, and calculated for different breathing states. However, as these parameters are not directly measurable, we have used the volume of the lungs, which is a measurable parameter, and through a personalized compliance pressure/volume curve, to estimate the lung pressure and to calculate diaphragmatic forces at different respiratory states. In this order, we have developed an optimization framework based on inverse finite element analysis, by minimizing the lung volume errors, between the respiratory volume (measured respiratory airflow exchange) and the simulated volume (calculated by biomechanical simulation)[14]. Finally, our model is controlled by
two physiological parameters: the respiratory volume and the ribs displacement. The respiratory volume can be replaced by surrogate signal such as spirometry during treatment and the ribs displacement by Real-time Position Management (RPM) system. In the context of HTH, our model takes into account the density variations due to breathing. However, in this paper, we do not address the real time challenging issues but we focus on modeling aspects. First, in section 2, we present the patient-specific anatomical and biomechanical model, as well as the lung-pressure/diaphragm-force optimization algorithms based on inverse finite element. Then, in section 3, a qualitative and quantitative analysis and an experimental validation of our approach are presented. Finally, we give some concluding remarks and directions for future work.

II. MATERIALS AND METHODS

A. Anatomy and physiology of the respiratory system

The lung is a passive organ which is divided into two halves, the right and left lung. It is situated in the thorax on either side of the heart. The pleural cavity is surrounded by the chest wall on the sides, and the diaphragm on the bottom. This space contains pleural fluid which facilitates near frictionless sliding at this boundary. The diaphragm is a dome-shaped musculofibrous membrane concave toward the lungs which separates the thorax from the abdominal cavity. It is composed of a peripheral part (muscular fibre) and a central part (tendon). Lungs are linked to the diaphragm and to the ribs through the pleura. The mechanics of human breathing involves two steps that alternate with each other: inhalation (inspiration) and exhalation (expiration). Negative pressure in the pleural cavity (natural breathing) initiates the diaphragm muscles and rib kinematics, as well as the boundary conditions which are used in our model. Then, we present the developed automatic tuning and optimization algorithm, to calculate the personalized physiological parameters diaphragm forces and the lungs pressure during the whole respiratory cycle.

B. Patient-specific anatomical model of respiratory system

One of the major difficulties of the finite element method applied to computational biomechanics is the complexity associated with the building of patient-specific geometrical models. In this order, we have developed previously a global strategy to generate patient-specific anatomical 3D models of the respiratory system from medical images (CT scan data) for finite element simulation [32], [36], [14]. For this, after segmentation, a 3D surface mesh is created for each volume, using the marching cubes algorithm. Due to the excessive number of nodes and large number of bad quality elements, which are common features in mesh-based models, a CAD-based approach has been developed: the meshes are rebuilt as a solid using a procedure of semi-automatic surface creation with Non-Uniform Rational Basis Splines (NURBS). Using the resulting smooth surface, a quality mesh with four-node tetrahedral elements is generated using ABAQUS packages. In this paper, we did not focus on the anatomical geometry reconstruction that do not constitute the core of this contribution.

C. Patient-specific biomechanical model of the respiratory system

First, we describe the biomechanics of the respiratory system including the mechanical behavior of the lung tissue, the diaphragm muscles and rib kinematics, as well as the boundary conditions which are used in our model. Then, we present the developed automatic tuning and optimization algorithm, to calculate the personalized physiological parameters diaphragm forces and the lungs pressure during the whole respiratory cycle.

1) Respiratory system and boundary conditions: Our anatomical model of the respiratory system comprises the lungs, tumor, thorax (rib kinematics), diaphragm behavior, skin and mediastinum. The boundary conditions (BC) are inferred from the anatomy and identified by medical experts. For the diaphragm, we have considered the direction of muscle forces to the direction of muscle fibers (Fig.5(a)). The force is applied to the muscular part of the diaphragm...
and simple homogeneous Dirichlet boundary condition is applied to the lower part of the diaphragm and the Lagrange multiplier method is used for the contact model. To simulate the sliding of the lungs, a surface-to-surface contact model is applied to the lung-chest cavity (Fig.5(b)). The frictionless contact surfaces are used to simulate the pleural fluid behavior. The rib cage kinematics have been applied as displacement boundary conditions during the whole respiratory cycle. Then, we have used the personalized compliance to apply pressure boundary conditions to the surface of the lung model. The lung model is monitored directly by simulated actions of the breathing muscles: the diaphragm and the intercostal muscles (the rib cage). In our work the amplitude of the lung pressure and diaphragm force are patient-specific, determined at different respiratory states by an optimization framework based on inverse FE analysis methodology, using lung volume variations. We have segmented the respiratory system at end expiration (EE, the reference state). Also, we have segmented lungs at all states for a full cycle (10 states from DIR-Lab Dataset [30]). Based on personalized pressure-volume curve (Fig 5(c)), we can estimate the lung pressure for each patient as:

\[ P_{\text{lung}(i)} = -K \frac{V_i - V_0}{V_0} = -\frac{E}{3(1-2\nu)} \frac{V_i - V_0}{V_0}, \]  

where \( P_{\text{lung}(i)} \) presents the lung elastic pressure at each intermediate respiratory state. The \( K, E \) and \( \nu \) are bulk modulus, Young Modulus and Poisson ratio respectively. \( V_0 \) is the initial lung volume at each intermediate respiratory state and \( V_i \) represents the current lung volume.

2) Rib kinematics: In our study, the thoracic cage model includes all skeletal structures: ribs and associated costal cartilages, the sternum and the thoracic vertebrae (Fig.5(a)). The ribs are considered as articulated rigid bodies. The motion of a rigid body between two positions can be characterized by an Euclidean transformation. Several authors have investigated the ribs kinematics. In [37], human ribs displacement were studied and the transformation parameters have been defined using planes attached to the ribs. In our previous works [39], [34], we have presented a methodology to study rib kinematics, using the finite helical axis method. The idea is to predict, from the transformation, the evolution the ribs position and orientation parameters with time. Each rib transformation parameters are automatically computed between the initial and final state (Fig.5(b)). As the rotation angle is small, a linear interpolation between the two states is applied to predict the rib motion at any intermediate breathing states. For more details about finite helical axis method, one can refer to [38], [39].

3) Lung and diaphragm Behaviors: Based on the results published [14], the Saint-Venant Kirchhoff (SVK) hyperelastic model can describe the mechanical behavior of the lung tissue. Then, we have used the personalized pressure-volume curve to apply pressure boundary conditions to the surface of the lung model based on our computational framework presented in section II-C4. The muscles of the diaphragm are skeletal muscle type, and their action has the effect of shortening or lengthening the muscles along their fiber direction. The muscles of the diaphragm are considered as compressible isotropic hyperelastic materials (SVK) [34], [36] and the tendon part is considered as linear elastic behavior (Fig.5(a)). For an isotropic elastic material, the elastic energy, noted \( W \), can be written as:

\[ W(E) = \frac{\lambda}{2} (trE)^2 + \mu tr(E^2) \]  

where \( E \) is the Green-Lagrange strain tensor, \( \lambda \) and \( \mu \) are the Lame’s coefficients. For small deformations, the Green-Lagrange strain tensor is linearized into the infinitesimal strain tensor \( \epsilon \):

\[ \epsilon = \frac{1}{2} (\text{grad}U + \text{grad}^T U) \]  

With \( U \): Young’s modulus, \( \nu \): Poisson’s ratio, and \( I \) is the identity matrix. Other expression can be written, introduce Lame’s constants, where \( \mu \): shearing coefficient and \( \lambda \): compression coefficient.

\[ \mu = \frac{E}{2(1+\nu)}, \quad \lambda = \nu \frac{E}{(1-2\nu)(1+\nu)} \]  

For the non-linear hyper elastic behavior, the Saint-Venant Kirchhoff law extends the Hooke’s law for large displacement. The relation between the second Piola-Kirchhoff stress tensor, the Green-Lagrange strain tensor and the rate effect leads to:

\[ S = \lambda (trE) I + 2\mu E \]  

\( S \) is the 2nd Piola-Kirchhoff stress tensor, can be derived from the relation: \( S = \frac{dW}{dE} \). For the dynamic simulation of the respiratory system, the equation of motion of a vertex \( v \) of the model can be written:

\[ M^v \{ \ddot{u}_v \} + \gamma^v \{ \dot{u}_v \} + \sum_{\tau \in V_v} \left( F^\text{int}_v \right) = F^\text{ext}_v \]  

Where \( M^v \), \( \gamma^v \) are respectively the mass and damping coefficients of each vertex. The \( V_v \) is the neighborhood of vertex \( v \) (i.e. the tetrahedra \( \tau \) containing node \( v \)). The \( F^\text{int}_v \) are the internal forces calculated by FE method and the \( F^\text{ext}_v \) are the imposed forces calculated by our developed algorithm based on inverse FE. To solve the dynamic system, and for more stability, the implicit finite scheme has been chosen. In our work, the mass density of each tissue is patient-specific, calculated and determined directly from CT scan images, based on density mapping algorithm defined and
developed in our last work [40]. First, organs tetrahedral meshes are generated from segmented CT scanner images. Next, the Hounsfield values issued from CT scanner images are converted into density values that are mapped to these mesh nodes, respecting the principles of mass conservation (Fig.3). For more information related to density mapping algorithm, one may refer to [6], [40].

![Fig. 3. Density mapping from regular voxel grid to our irregular tetrahedral elements.](image)

**III. Results and experimental validation**

In order to demonstrate the validity of our patient specific biomechanical model, a quantitative and qualitative analysis of simulations were conducted. We have compared the results...
Fig. 5. The boundary conditions (BC) of our patient specific biomechanical model of the respiratory system, including (a) diaphragm behavior: heterogeneous tissue with the muscles in peripheral part and the tendon in central part, (b) rib kinematics using the finite helical axis method, and (c) personalized compliance calculated for each patient.

**TABLE I**

M ECHANICAL PROPERTIES OF BREATHING SYSTEM: E YOUNG'S MODULUS AND $\nu$ POISSON RATIO (FROM [25], [41], [36], [14]), $\rho$ VOLUMETRIC DENSITY (CALCULATED FROM CT IMAGES).

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Mechanical behavior</th>
<th>$E$ (MPa)</th>
<th>$\nu$</th>
<th>$\rho$ (t/mm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lungs</td>
<td>HSVK</td>
<td>3.74x10$^{-3}$</td>
<td>0.3</td>
<td>3.0x10$^{-10}$</td>
</tr>
<tr>
<td>Lung tumor</td>
<td>LE</td>
<td>49</td>
<td>0.4</td>
<td>1.5x10$^{-9}$</td>
</tr>
<tr>
<td>Mediastinum</td>
<td>LE</td>
<td>5.87x10$^{-3}$</td>
<td>0.4</td>
<td>1.0x10$^{-10}$</td>
</tr>
<tr>
<td>Diaphragm muscle</td>
<td>HSVK</td>
<td>5.32</td>
<td>0.33</td>
<td>1.0x10$^{-9}$</td>
</tr>
<tr>
<td>Diaphragm tendon</td>
<td>LE</td>
<td>33</td>
<td>0.33</td>
<td>1.0x10$^{-9}$</td>
</tr>
<tr>
<td>Ribs</td>
<td>LE</td>
<td>5000</td>
<td>0.4</td>
<td>1.5x10$^{-9}$</td>
</tr>
<tr>
<td>Cartilage</td>
<td>LE</td>
<td>49</td>
<td>0.3</td>
<td>1.0x10$^{-9}$</td>
</tr>
<tr>
<td>Sternum</td>
<td>LE</td>
<td>11500</td>
<td>0.3</td>
<td>1.5x10$^{-9}$</td>
</tr>
<tr>
<td>Vertebra</td>
<td>LE</td>
<td>9860</td>
<td>0.4</td>
<td>1.5x10$^{-9}$</td>
</tr>
<tr>
<td>Skin</td>
<td>LE</td>
<td>5.32</td>
<td>0.4</td>
<td>1.0x10$^{-6}$</td>
</tr>
</tbody>
</table>

**TABLE II**

FIVE SELECTED PATIENTS FROM DIR-LAB DATABASE [30], WITH SMALL AND LARGE BREATHING AMPLITUDES.

<table>
<thead>
<tr>
<th>Patients</th>
<th>image dimension</th>
<th>Size of Voxels</th>
<th>Amplitude Diaphragm (mm)</th>
<th>Amplitude Lungs (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>256x256x94</td>
<td>0.97x0.97x2.5</td>
<td>10.1</td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td>256x256x99</td>
<td>1.13x1.13x2.5</td>
<td>20.2</td>
<td>24</td>
</tr>
<tr>
<td>6</td>
<td>512x512x128</td>
<td>0.97x0.97x2.5</td>
<td>24.1</td>
<td>30</td>
</tr>
<tr>
<td>9</td>
<td>512x512x128</td>
<td>0.97x0.97x2.5</td>
<td>12.5</td>
<td>25</td>
</tr>
<tr>
<td>10</td>
<td>512x512x120</td>
<td>0.97x0.97x2.5</td>
<td>22.3</td>
<td>25</td>
</tr>
</tbody>
</table>

Fig. 6. Patient specific compliances for five patients from DirLab database, calculated and identified at each respiratory state directly from 4D CT scan images.

**TABLE III**

A VERAGE SURFACE ERRORS FOR THE DIAPHRAGM AND LUNGS SURFACES AT END INSPIRATION EI BETWEEN FEM SIMULATION SURFACE AND SEGMENTED SURFACES EXTRACTED FROM CT IMAGES FOR FIVE PATIENTS FROM DIRLAB DATABASE [30].

<table>
<thead>
<tr>
<th>Patients</th>
<th>End Inspiration (EI) Diaphragm Mean ± SD (mm)</th>
<th>Lungs Mean ± SD(mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>1.8 ± 1.3</td>
<td>2.0 ± 1.5</td>
</tr>
<tr>
<td>Patient 4</td>
<td>2.0 ± 1.6</td>
<td>2.2 ± 1.7</td>
</tr>
<tr>
<td>Patient 6</td>
<td>1.9 ± 1.6</td>
<td>2.1 ± 1.5</td>
</tr>
<tr>
<td>Patient 9</td>
<td>2.1 ± 1.5</td>
<td>2.3 ± 1.6</td>
</tr>
<tr>
<td>Patient 10</td>
<td>2.2 ± 1.1</td>
<td>2.5 ± 1.8</td>
</tr>
</tbody>
</table>

of a simulated motion with the experimental data provided directly from the 4DCT scan images DirLab database [30]. Fig.6 illustrates the different specific compliances (pressure-volume curve) for each patient, calculated and identified at each state directly from 4D CT scan images. Then, these compliances are used as input in our biomechanical patient specific model to simulate the full breathing cycle. In our FE simulation, we define the simulation time for the inspiration phase is 2 seconds and for the expiration phase is 3 seconds. The mechanical properties and behaviors of the different organs used in our simulations are settled in the Table.I. Fig.7 shows the total deformation and the maximum displacement components of the lungs and diaphragm during breathing. We can observe the maximum displacement of the diaphragm on the right-posterior (RP) and left-posterior (LP) sides. It is also possible to notice a slightly larger (RP) side motion than (LP) side motion, in concordance with the physiological anatomy. For the lungs deformation, the
maximum displacement occurs in the posterior region along the superior-inferior (SI) direction (diaphragm direction).

A. Anatomical landmarks evaluation at end of inhalation (EI) and the end of exhalation (EE)

To measure the precision of our biomechanical simulation, we have evaluated the model accuracy on five selected lung cancer patients, from DIRLab Dataset [30], where the entire thorax was visible and with small and large breathing amplitudes(Table II). We have compared the finite element simulation results on 300 landmarks, at end inspiration (EI), end expiration (EE) states, and 75 landmarks at each intermediate respiratory state, obtained by manual delineations[30]. Table IV illustrates the comparative study between our FE simulation results and the anatomical landmarks displacement vectors for five patients. The average error for anatomical landmarks inside the lung at end inspiration (EI) and end expiration (EE) states for five patients is less than 2.5 ± 1.5 mm. In addition to the need for accuracy, we were also evaluated the % errors distribution on the 300 landmarks for the same five lung cancer patients, and the mean errors for anatomical landmarks in the 2 lobes of the left lung and 3 lobes of the right lung, along the AP (Anterior/Posterior), RL (Right/Left), and SI (Superior/Inferior) directions between EE and EI phases.

B. Anatomical landmarks evaluation at intermediate states between EI and EE

The performance of the proposed biomechanical model has been evaluated by comparing the simulation results with ground truth (CT images) on 75 landmarks at five intermediate states between EI and EE. Table VI shows the

### TABLE IV
Average landmarks lung error (mm) during exhalation at different respiratory states: the first state T00, the end inspiration (T50), the end expiration (T10).

<table>
<thead>
<tr>
<th>Patients</th>
<th>Volume between EE and EI (%)</th>
<th>Mean ± SD (mm)</th>
<th>Mean All states</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>12.8</td>
<td>2.1 ± 1.5, 2.2 ± 1.2</td>
<td>1.1 ± 0.8, 1.8 ± 1.3</td>
</tr>
<tr>
<td>Patient 4</td>
<td>14.6</td>
<td>2.3 ± 1.2, 2.5 ± 1.3</td>
<td>1.5 ± 1.2, 2.0 ± 1.2</td>
</tr>
<tr>
<td>Patient 6</td>
<td>25.4</td>
<td>2.4 ± 1.5, 2.3 ± 1.2</td>
<td>2.0 ± 1.6, 1.9 ± 1.3</td>
</tr>
<tr>
<td>Patient 9</td>
<td>13.4</td>
<td>2.3 ± 1.4, 2.2 ± 1.1</td>
<td>2.1 ± 1.3, 1.8 ± 1.4</td>
</tr>
<tr>
<td>Patient 10</td>
<td>16.7</td>
<td>2.1 ± 1.5, 2.2 ± 1.2</td>
<td>1.1 ± 0.8, 1.8 ± 1.3</td>
</tr>
</tbody>
</table>

### TABLE V
Mean landmark errors in the 2 lobes (inferior (INF), superior (SUP)) of the left lung and 3 lobes (inferior (INF), middle and superior (SUP)) of the right lung, in the AP (Anterior/Posterior), RL (Right/Left), and SI (Superior/Inferior) directions between EE and EI phases.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Lobes</th>
<th>SUP</th>
<th>Middle</th>
<th>INF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Directions</td>
<td>L/R</td>
<td>S/I</td>
<td>A/P</td>
</tr>
<tr>
<td>Landmarks error (right lung)(mm)</td>
<td>1.3</td>
<td>1.3</td>
<td>1.72</td>
<td>1.5</td>
</tr>
<tr>
<td>Landmarks error (left lung)(mm)</td>
<td>1.1</td>
<td>1.1</td>
<td>1.5</td>
<td>-</td>
</tr>
</tbody>
</table>

...
TABLE VI
COMPARISON BETWEEN OUR BIOMECHANICAL PATIENT SPECIFIC MODEL RESULTS AND THE RESULTS FROM FUERST ET AL. [22] AND LI ET AL. [21], ON PATIENT 6, PATIENT 9 AND PATIENT 10 ISSUED FROM DRLab Dataset [30].

<table>
<thead>
<tr>
<th>References</th>
<th>Cycle</th>
<th>Organs Modeled</th>
<th>Boundary conditions</th>
<th>P6 (mm)</th>
<th>P9 (mm)</th>
<th>P10 (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[22]</td>
<td>half</td>
<td>4 pressure zones (sub diaphragm)</td>
<td>No ribs behavior</td>
<td>3.27 ±1.0</td>
<td>2.97 ±1.0</td>
<td>2.83 ±1.0</td>
</tr>
<tr>
<td>[21]</td>
<td>half</td>
<td>Only lungs organ</td>
<td>One CT and uniform pressure</td>
<td>-</td>
<td>3.2±1.4</td>
<td>4.4±2.9</td>
</tr>
</tbody>
</table>

Our model: Full Thorax
Diaphragm
Rib kinematics

personalized pressure-volume curve

Diaphragm
force direction of the muscles

References Cycle Organs Boundary P6 P9 P10

[22] half 4 pressure zones (sub diaphragm) 3.27 ±1.0 2.97 ±1.0 2.83 ±1.0
No ribs behavior 16 pressure zones (thoracic)

[21] half Only lungs organ One CT and uniform pressure - 3.2±1.4 4.4±2.9

Phase EE

T50 ... T70                        T80                         T90

Phase EI

T50                        T40                       T30               ...        T10

Fig. 7. Qualitative analysis of patient specific biomechanical simulation; lungs and diaphragm deformations during the whole cycle of breathing for two patient P1 and P6.

Fig. 8. The histogram of landmark errors distribution for five patients from DRLab database [30] along the AP (Anterior/Posterior), RL (Right/Left), and SI (Superior/Inferior) directions, at end inspiration (EI).

Fig. 9. Evaluate lung tumor motion: rigid registration applied to the segmented lung tumor volume at different respiratory states.
ratio=0.49, is three times larger than the lung landmarks error obtained by Poisson’s ratio=0.33.

C. Tumor tracking and impact of the rib kinematics on lung tumor motion

In order to evaluate the impact of the rib kinematics on lung tumor motion, we have evaluated the tumor motion and 3D trajectory identified in 4D CT scan images on two selected patients (6 and 10) from the same Dataset DIR-Lab [30], where the tumor location is visible. These trajectory are compared and evaluated with the trajectory obtained by FE simulation, during the whole cycle of breathing (10 phases between the EI and EE). To track the lung tumor movement in 4D CT images, we have used the affine registration applied to the segmented lung tumor volume at different respiratory states (Fig.9). Then, the accuracy of the proposed tumor tracking method is evaluated by comparing and calculating the Hausdorff distance between the 3D mesh surface of the segmented tumor and predicted FE lung tumor, including or not the rib kinematics.

Fig. 10. 3D lung tumor trajectory (in mm) issued from 4D CT images compared to the trajectory calculated by biomechanical finite element model including or not the rib kinematics for patients P6 and P10 from DirLab data set [30].

Fig.11 and Fig.10 show the mean errors ± standard deviation of lung tumor position and comparison study between the 3D hysteresis trajectories of the lung tumor during the whole cycle of the breathing without and within the rib kinematics compared to the trajectory calculated directly from 4D CT images. The figures demonstrate that our patient specific biomechanical model for lung tumor position estimation is accurate (less than 3 mm). However, it is important to note that the results for these two patients are slightly better with the rib kinematics but the difference is not significant during the whole cycle (for patient 6 and 10). This is because the respiration for these patients is mainly diaphragmatic. In addition, another investigation conducted to study the impact of rib kinematics on the lung tumor motion prediction. This investigation was conducted by varying the ribs displacement by 10%, 25% and 50% during the whole breathing cycle. Fig.12 illustrates the impact of the rib kinematics on lung tumor trajectory for the patient 6 and patient 10, and the robustness of the proposed approach based on biomechanical patient specific model of the respiratory system.
Fig. 11. Mean errors ± standard deviation of lung tumor position during the whole cycle of breathing (10 phases between the EI and EE) between the trajectory issued from 4D CT images compared to the trajectory calculated by biomechanical finite element simulation coupled with the lung-pressure/diaphragm-force optimization for two patients P6 and P10. The error bars are always higher or same for the without ribs results.

Fig. 12. 3D lung tumor trajectory (in mm) issued from 4D CT images compared to the trajectory calculated by biomechanical finite element model including rib kinematics displacement changed by 10%, 25% and 50% of the rib displacement calculated from CT scan images.

IV. CONCLUSION AND FUTURE WORK

In this paper, a patient specific biomechanical model of the respiratory system was proposed for lung tumor tracking for the whole respiratory cycle. Our results are quite realistic compared to the 4D CT scan images. We can observe that the proposed physically-based FE model is able to predict correctly at high precision the lung tumor displacements including the personalized and physiological lung-pressure/diaphragm-force and boundary conditions of the organs. This could be a potential tool to provide valuable location-specific tumor motion information for medical physicians to reduce the margins between clinical target volume (CTV) and planning target volume (PTV). One of the limitations of our work is the 3D reconstruction organs delineation and treatment of the multiple organs mesh, requiring time consuming, manual operations for each patient. In order to avoid manual contouring and 3D geometry segmentation for different organs, and to reduce the computational costs without lowering the quality, we plan to develop and use a realistic atlas-based 3D shape reconstruction of the respiratory system based on statistical training or machine learning, to get a fast and automatic patient-specific model adaptable taking into account complexities such as geometrical irregularities and organs contacts.

Currently, we are working on real time computation of our patient-specific model. The model should be controlled by external non-invasive surrogates, to predict patient’s lung tumor motion, during treatment. In this context, it is important to investigate the accuracy and reproducibility of RPM versus surface imaging to find an appropriate surrogate for 3D rib motion. In the future, the model should also be validated pre-clinically on a realistic deformable anthropomorphic lung phantom (LuCa). The results of our model can greatly contribute to motion compensation algorithms for diagnosis, beam therapy, dose calculation or online imaging systems.

REFERENCES
