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A Biomechanical approach for *in vivo* Lung Tumor Motion Prediction during External Beam Radiation Therapy

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ABSTRACT

Lung Cancer is the leading cause of cancer death in both men and women. Among various treatment methods currently being used in the clinic, External Beam Radiation Therapy (EBRT) is used widely not only as the primary treatment method, but also in combination with chemotherapy and surgery. However, this method may lack desirable dosimetric accuracy because of respiration induced tumor motion. Recently, biomechanical modeling of the respiratory system has become a popular approach for tumor motion prediction and compensation. This approach requires reasonably accurate data pertaining to thoracic pressure variation, diaphragm position and biomechanical properties of the lung tissue in order to predict the lung tissue deformation and tumor motion. In this paper, we present preliminary results of an *in vivo* study obtained from a Finite Element Model (FEM) of the lung developed to predict tumor motion during respiration.

1. INTRODUCTION

The lung is a mechanically passive organ that inflates mainly due to thoracic pressure variations and forces exerted by the diaphragm to its bottom surface. A biomechanical model of the respiratory system benefits from the physical properties of the lung's soft tissue and its respiration physiology to predict the lung deformation during respiration. Several studies have been conducted to use FEM for biomechanical simulation of the respiratory system. DeCarlo *et al* used a 2D idealized model of the lung to simulate the lung ventilation with FEM. In their model, the interaction between the lung and chest cavity was considered by applying forces which expand the lung model during respiration [1]. A similar concept was utilized by Zhang *et al*, Villard *et al*, Eom *et al* and Werner *et al* where the 3D geometry of the lung was considered instead of the 2D geometry [2,3,4,5]. In these studies, the respiration was modeled by applying negative pressure loading to the lung surface while the lung expansion was restricted by the final volume of the lung or the chest cavity model. Werner *et al* [2] developed a mathematical lung phantom and lung cancer patient models for evaluation purposes. Al-Mayah *et al* performed a number of studies on lung ventilation mechanism simulation. Throughout their modeling procedure, rather than pressure loading, displacement differences between inhale and exhale phases were applied as displacement boundary conditions to the lung model [6,7,8,9]. In this study, as set of 4D Ct images were used to develop a FE model for predicting the motion of a small tumor located in the patient's right lung (Figure 1).

An important novel aspect of the proposed method is that the lung's tissue incompressibility parameter was considered to be variable during respiration. This approach was based on the results presented by a previous study which indicated that, in order to accomplish reliable biomechanical modeling of the respiratory system, variable incompressibility parameter should be used for the lung tissue[10]. The major development in the present study compared to the work described in [10] involves extending the model to accommodate several complexities pertaining to *in vivo* breathing lung. The optimization framework illustrated in Figure 2 is used in this study for determining the lung's tissue incompressibility parameter of Poisson's ratio and thoracic pressure at each phase of respiration.

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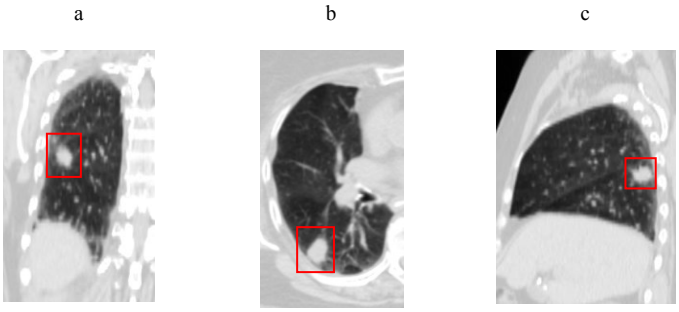

Figure 1.a) Coronal,**b)** Axial and **c)** Sagittal slices of a human lung with a tumor shown within a rectangle.

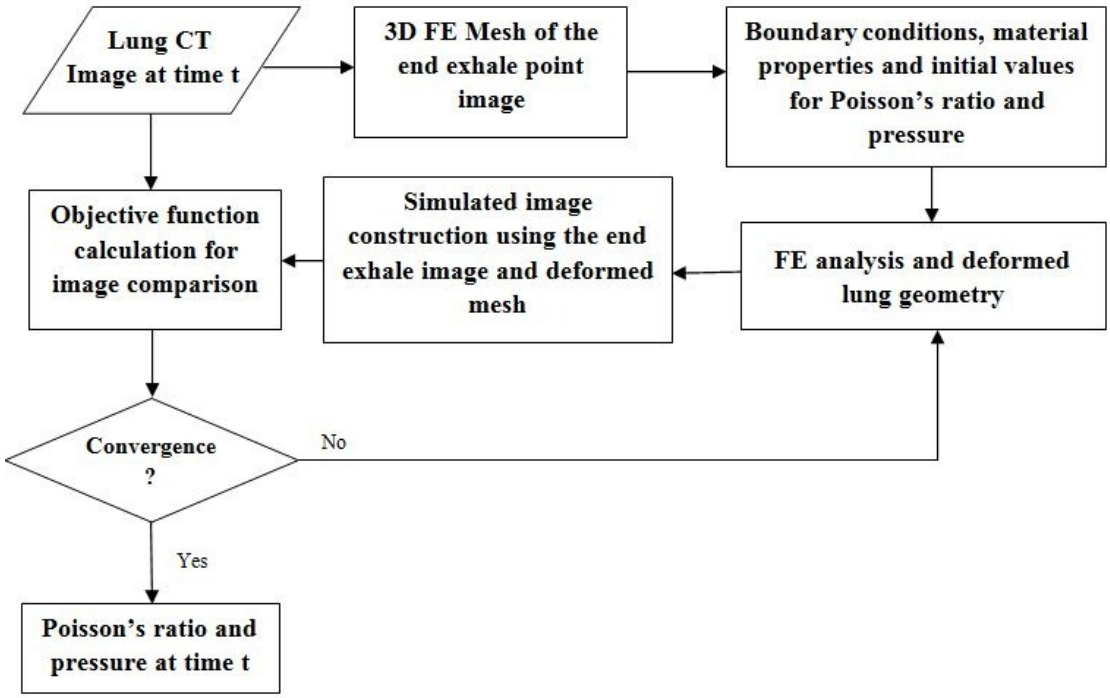

Figure2. Optimization framework for characterising tissue incompressibility and thoracic pressure variations.

For each respiration phase, the optimization algorithm starts with an initial guess for the Poisson's ratio and thoracic pressure and updates them iteratively until the acquired lung image corresponding to the respiration phase matches the one calculated using the lung's FE model.

2- Methods

The purpose of this study is to develop an *in vivo* patient specific lung biomechanical model using the patient's 4D CT images. To achieve high deformation prediction accuracy, the lung tissue incompressibility characterized by Poisson's ratio is treated as a time variable parameter during respiration. The FE model was developed using the end exhalation phase images. As a first order approximation, we assume that the Poisson's ratio and thoracic pressure variations over time during inspiration are symmetrical to those of expiration. As such, to validate the model images of exhalation phases were compared to corresponding images computed using the developed model.

To develop a biomechanical model of a patient's right lung, the lung geometry, tissue mechanical properties, boundary conditions and loading are required. In order to obtain the lung geometry, an automatic region growing based segmentation algorithm was developed to segment the lung in the end exhalation phase of respiration. The segmentation result was input to the model maker module in 3D Slicer software package to create a 3D model of the lung. Next, the IA-FEMesh software was used to create a Finite Element Mesh with hexahedral elements as illustrated in Figure 3. The total number of nodes and elements in the resulting mesh were 2720 and 2160, respectively.

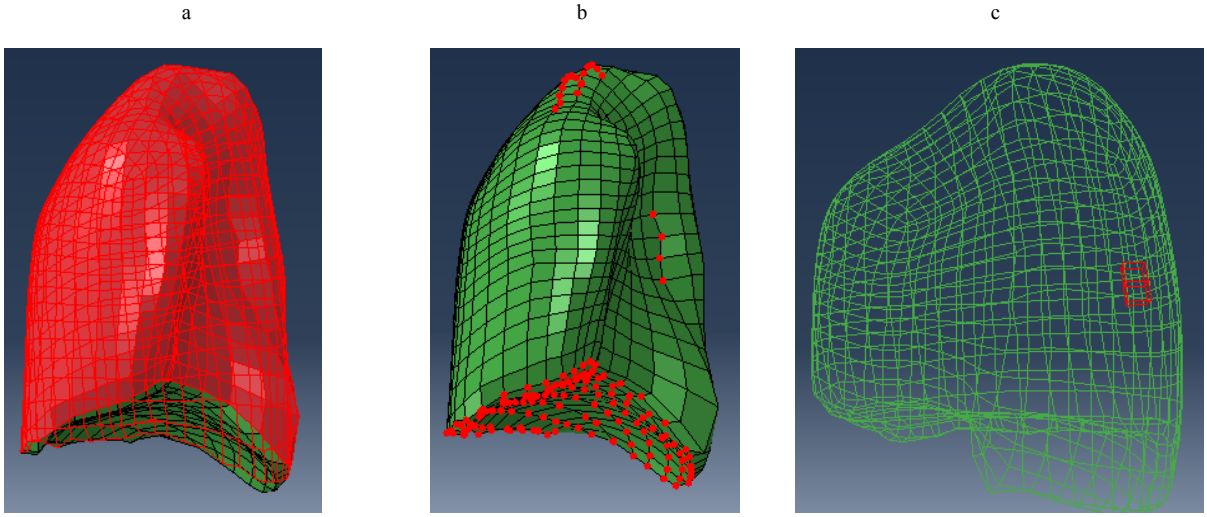

Figure 3. a) The lung surface which undergoes pressure, **b)** The node sets for defining the boundary conditions and, **c)** Tumor elements.

Although the pleural pressure variations play significant role in lung tissue deformation, this is not the case for all the individuals. In fact, as a result of obstructive and restrictive lung disease, parts of the tissue become pathological, leading to alteration in their biomechanical properties. For instance, the acquired 4D CT images used in this study indicated that the tissue deformation occurs mainly as a result of diaphragm motion while no significant motion was observed on the red surface depicted in Figure 3.a. To find the reason, the 4D CT images were assessed by a radiologist. According to the radiologist, this patient suffers from COPD and tissue fibrosis. With these pathologies, the lung pressure-volume curves change significantly such that the lung surface motion is reduced significantly.

To account for this observation, the transpulmonary pressure was considered fixed and very close to zero in the model which was created for this patient. In addition, the motion of the lung's apex was limited by considering fixed boundary conditions at a set of nodal points located at this area. Moreover, as illustrated in Figure 3.b, some of the lung surface nodes that model the trachea's interface with the lung were fixed as no significant deformation was observed in that area. In order to model the lung diaphragm interaction, prescribed displacement boundary conditions were considered for the lung's bottom surface. These boundary conditions were delineated using Free Form Deformation (FFD) non-rigid registration. For this purpose image pairs pertaining to each consecutive phases were registered as such to find the displacements of each node located on the lung's bottom surface throughout the respiration cycle. These displacements were used as prescribed boundary conditions in the FE model as illustrated in Figure 3.b. After defining the boundary conditions, two models were used for lung tissue mechanical behavior. The first is a linear elastic model with a Young's

Modulus of 1 kPa while the second is a Yeoh hyperelastic model with coefficients calculated from the experimental data presented in [11].In both cases, the tumor was modeled as linear elastic with Young's Modulus and Poisson's ratio values set to 1.1kPa and 0.49, respectively. The Tumor's Young's modulus was calculated by measuring its strain values at several points in the tumor using the registered CT images. Next, a comparison was made between tumor strain values and those of the adjacent lung tissue to estimate the tumor's Young's modulus.

Next, for both the linear and nonlinear models, the time variable Poisson's ratio was obtained for the inhalation phase through the optimization framework as was described earlier. The optimized Poisson's ratio values of the inhalation phase are illustrated in Figure 4.

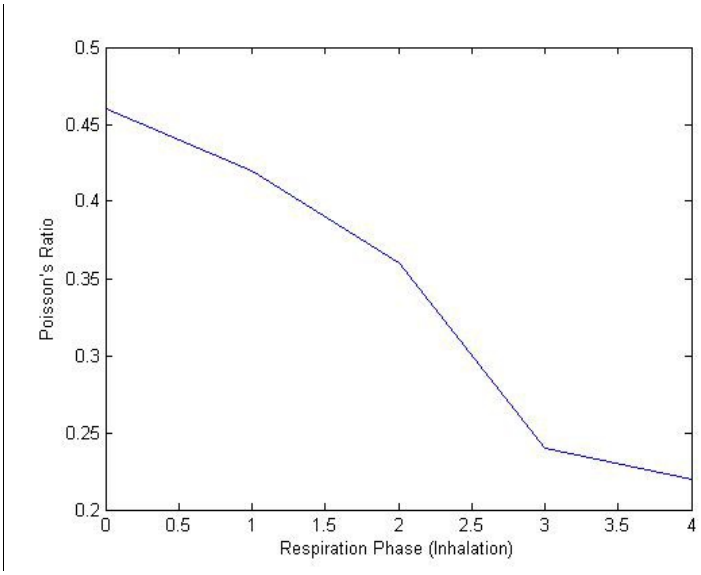

Figure 4. Optimized Poisson's ratio values for inhalation phase versus respiratory phase

As described earlier, assuming that the lung deformation during expiration is symmetrical to that of inspiration, the Poisson's ratio and the diaphragm displacement filed calculated for the inhalation phase were interpolated to obtain those of the exhalation phase. Finally, the results were used in the FE model to predict the tumor motion in the exhalation phase.

3- Results

Figure 5 depicts an example of the predicted and actual positions of the tumor in an exhalation phase where the red colored region corresponds to the predicted tumor location. In order to assess the performance of the model, the tumor was segmented in both of the simulated and acquired CT images for exhalation phase of respiration. The percentage of the overlap between the predicted and actual locations of the tumor is reported in Table 1 for both the linear and hyperelastic models. This table indicates that the amount of this overlap varies from 74% to 92%.

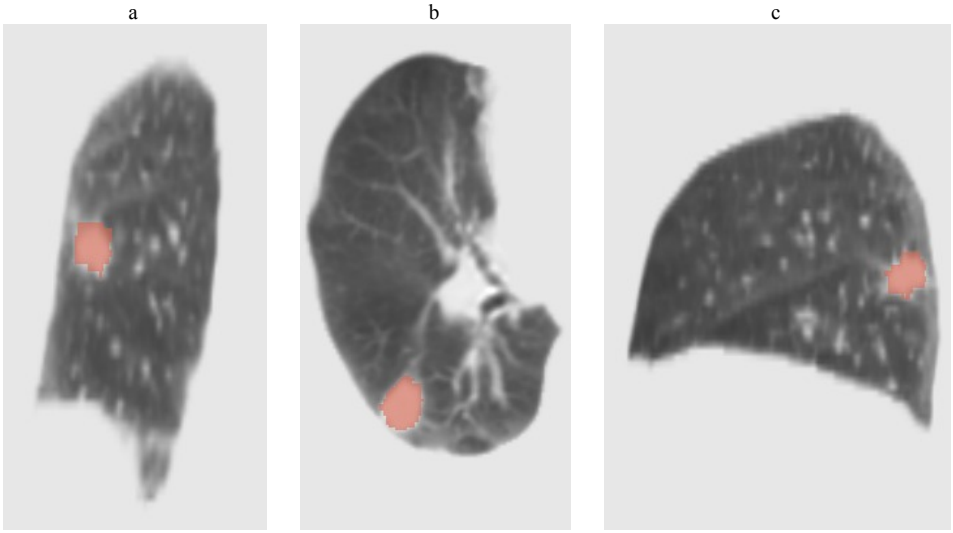

Figure5. An example of the predicted (red labelled area) and actual positions of the tumor in **a)**coronal,**b)** axial and **c)** sagittal slices

Table 1: Tumor motion prediction results

Phase of respiration (Exhalation Phase)	7	8	9	10
Percentage of overlap between the predicted and actual tumor locations (Linear elastic)	%89	%92	%76	%74
Percentage of overlap between the predicted and actual tumor locations (Hyperelastic)	%89	%90	%79	%76

4- Conclusions and future work

An FE model was proposed for the *in vivo* human lung to track the tumor motion during EBRT. The proposed model uses an optimization framework to optimize the transpulmonary pressure and Poisson's ratio values for each phase of respiration. The optimized values obtained from a preoperative 4D CT scan can be used intraoperatively during EBRT to predict the tumor motion. Image registration was used to track the diaphragm's motion and incorporate it in the model. According to our group's radiologist and as indicated by the 4D CT images, the lungs of the cancer patient being studied in this paper were not functioning properly. As such, tissue deformation was negligible except for the lung's base. To account for this observation, the transpulmonary pressure was considered fixed and close to zero during the entire respiratory cycle. The Lung tissue was modeled with both linear elastic and Yeoh hyperelastic models. Preliminary results show that there is at least 74% and 76% tumor volume overlap, respectively between the actual tumor and its predicted model for linear elastic and hyperelastic models, respectively. As expected, the hyperelastic model is slightly more accurate for simulating the lung tissue mechanics compared to the linear elastic model. It is noteworthy that by considering variable incompressibility parameter, the tumor can be tracked reasonably accurately even with using linear elasticity to model the lung tissue. While the results are encouraging, the model should be tested for more cases, especially those in which the tumor has significant motion. Moreover, the respiratory system hysteresis should be considered in the model to obtain more accurate results. These are currently being carried out in our research group.

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