Patient-Specific Biomechanical Model for the Prediction of Lung Motion from 4D CT Images

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Abstract—This article presents an approach to predict the deformation of the lungs and surrounding organs during respiration. The framework incorporates a computational model of the respiratory system, which comprises an anatomical model extracted from Computed Tomography (CT) images at end-expiration (EE), and a biomechanical model of the respiratory physiology, including the material behavior and interactions between organs. A personalization step is performed to automatically estimate patient-specific thoracic pressure, which drives the biomechanical model. The zone-wise pressure values are obtained by using a trust-region optimizer, where the estimated motion is compared to CT images at end-inspiration (EI). A detailed convergence analysis in terms of mesh resolution, time stepping and number of pressure zones on the surface of the thoracic cavity is carried out. The method is then tested on five public datasets. Results show that the model is able to predict the respiratory motion with an average landmark error of $3.40 \pm 1.0$ mm over the entire respiratory cycle. The estimated 3D lung motion may constitute as an advanced 3D surrogate for more accurate medical image reconstruction and patient respiratory analysis.

Index Terms—Lung, Respiratory Motion, Biomechanical Modeling, Personalization, Motion Prediction

I. INTRODUCTION

A. Clinical Motivation: Thoracic Imaging and Radiotherapy

Thoracic imaging and radiotherapy suffer from complications caused by the complex respiratory motion, which is a source of artifacts in images and makes it difficult to determine critical information for radiotherapy, such as a lung tumor’s shape, size, position and surrounding tissue [1]. Therefore, there is a need for methods to predict the 3D lung deformation during regular and irregular breathing cycles. The accurate estimation of the 3D lung deformation is difficult and currently approximated by one- or multi-dimensional signals from devices such as spirometers, abdominal pressure belts, external markers, or image modalities [2]–[4]. These signals are referred to as surrogates and only part-wise reflect the complexity of lung deformation during a respiratory cycle. For instance, during thoracic image acquisition, a 4D computed tomography (CT) data set is compounded by image segments sorted and combined (binning) either based on the amplitude or the phase-angle of a respiratory surrogate [5]. Because the signal is assumed to be periodic, difficulties arise when the breathing pattern changes [6], resulting in imaging artifacts due to the combination of different breathing states. In a second approach, images are acquired at a specific instance of the respiratory cycle by triggering the imaging modality according to the surrogate signal [7], [8]. This is referred to as gating and is commonly used for nuclear imaging, such as PET [9]. In radiotherapy gating is used to apply the ionizing radiation during pre-defined respiratory states only [1]. Both approaches have drawbacks, such as the increase of radiation dose to achieve oversampling, or increase of treatment or imaging time. Furthermore, for image reconstruction, interpolation due to the lack of information between phases can cause step artifacts. For this purpose, motion models have been proposed to estimate or predict the deformation of lungs, liver or other organs during breathing.

B. Physiology of the Respiratory System

The respiratory motion is complex, as the lungs do not just compress and deform, but also slide along the thoracic cavity thanks to the pleura (see anatomy and explanations in Fig. [1], which is filled with a serous fluid and does not change its volume during respiration. The anatomical properties of the pleura allow nearly friction free sliding of the lungs and diaphragm along the thoracic cavity. The motion is caused by two major groups of muscles: the diaphragm and the intercostal muscles [10], [11]. Their contraction enlarges the thoracic cavity creating a negative pressure causing air to flow into the lungs. Respiratory motion may vary from cycle to cycle, as the contributions of the muscle groups differ. The patient’s orientation and the breathing pattern (shallow, deep, abdominal or thoracic) can have major influence on the lung deformation. Three types of lung motion variations can be identified [12]: 1) intra-cycle variations describe changes within one cycle, and are mostly caused by different paths during inhale and exhale. In [5], [13]–[16], models of intra-cycle
variations have been proposed. However, these approaches cannot deal with ii) inter-cycle variations, which are often caused by changes in breathing patterns. Models, such as those presented in [4] and [17], compensate for such variations, but the authors are interested in reducing artifacts during imaging, rather than in modeling the physiological correct motion. A generative model was not required and their model was based on observations and free-form deformable registration. To deal with iii) inter-patients variations, atlas-based methods have been used to identify motion patterns varying between patients [18]. However, these methods can only describe motion which has been observed and are therefore not generative. By creating a patient-specific biomechanical motion model, our technique attempts to compensate all three motion variations.

C. Image-Based Approaches for Motion Estimation

Image-based models describe the respiratory motion using dense deformation fields. This is achieved by registering the images at different respiratory phases to a phase of reference. Optical flow techniques have been proposed [2], [19], in which the cost function incorporates the temporal difference between the images and the spatial image gradient. However, the regularization process of optical flow techniques is not suited for the sliding motion of the lung, causing wrong deformations close to the thorax/lung interface. To cope with this limitation, new regularization terms have been introduced that distinguish between normal and tangential motion [16].

More sophisticated diffeomorphic image registration approaches have been proposed [20], [21], in particular piecewise-diffeomorphic registration techniques [21], to correctly capture the sliding interface. This approach smooths the deformation field in regions without sliding motion, and allows non-smooth deformation between lung and thorax. Though yielding good results, it is not versatile enough to fully model the sliding of the diaphragm along the rib cage, as the piecewise regularization is only applied on the lung surface, not the boundary between diaphragm and thorax. Therefore, gaps between diaphragm and thorax remain during exhale.

To model inter-patient variations, mean motion models have been presented in [18]. Intuitively, an anatomical atlas is first estimated by averaging the thoracic images acquired at a specified time of the respiratory cycle. Then, for each patient of the database, the respiratory motion is computed using image registration and encoded in terms of deformation fields. These deformation fields are finally transferred to the atlas and averaged to obtain the mean motion model. When a new case needs to be processed, the mean motion model is transferred to its coordinate system and applied for lung motion prediction. However, this approach is not totally generative as it can capture only what is observed in the database. In particular, sudden respiratory changes or disease lung motion are more complex to capture.

D. Biomechanical-Based Methods for Motion Estimation

Image-based approaches cannot fully take into account the variability of the respiratory motion, as they rely on observations and are therefore not generative. To overcome these limitations due to variations in respiratory motion and allow the patient-specific prediction of respiratory motion, biomechanical models have been proposed [13], [14], [22], [23]. Biomechanical models for the lung have been initially presented by West et al. [24], which showed the simulation of a half thorax and the deformation of the lung under its own weight. Current computational models create an anatomical model from patient images and simulate the physiological deformations during respiration cycles [22],[23].

A standard strategy relies on image data, and directly deforms the model by projecting the triangulated surface nodes of the inhale lungs onto the surface of the exhale phase. The deformation is constrained by a fixed boundary condition and is not driven by pressure forces generated by the thorax [22], [25].

Another approach is to define a negative pressure on the lung surfaces and constrain the inflation by lung surfaces extracted from another respiratory phase [26]. Hence, these and similar approaches are still not fully predictive since they
rely on a boundary condition defined by a secondary geometry and do not model the physiology to compute the motion.

A first step towards more accurate biomechanical modeling has been presented in [27], where the authors propose a method to automatically estimate the inhomogeneous material properties in patients. While the hyper-elastic material properties of lung have been identified early [11], [24], [28], it is nowadays not clear whether using non-linear elastic material properties would give significant improvements in terms of motion prediction [22], [25] compared to linear elasticity [23] due to their higher number of parameters to estimate and model complexity.

E. Proposed Solution

To cope with the above-mentioned limitations, we propose in this manuscript a generative biomechanical model of the respiratory system, which, contrary to previous approaches, is driven by patient-specific thoracic and diaphragmatic pressure force fields (Sec. II-B). The motion is not constrained by any fixed boundary condition. The pressure force reflects the muscular forces generated by the thoracic cavity and is transferred to the lung surface through a novel thorax/diaphragm/lung interaction model.

Fig. 2 illustrates the various steps of our method. First, a comprehensive anatomical model of the respiratory system is computed from an image at end-exhale (EE) (Sec. II-A). Using the anatomical model, a biomechanical model is employed to simulate the lung deformation during respiration (Sec. II-B) based on the thoracic and diaphragmatic pressure. These pressure values can not be measured. Therefore, we estimate the values automatically using a trust region optimizer. During this personalization step the pressure values are iteratively improved with respect to the differences between simulated lung and the end-inspiration (EI) image (Sec. II-C). In contrast to our previous work on the estimation of the respiratory motion using a direct parameter estimation [13], this manuscript introduces a novel patch-wise coarse-to-fine optimization strategy during personalization.

In contrast to other approaches, the lung at EI is never used as a boundary condition. The anatomical model at EE, and the personalized thoracic and diaphragmatic pressure are the only components used to predict the respiratory cycle. Varying the amplitude of the personalized pressure can potentially enable the simulation of respiratory motion which was not observed during imaging, which is not possible when using a fixed boundary condition such as in [22], [25], [26].

Furthermore, a convergence analysis in terms of spatial and temporal resolution is presented. The model predictions are evaluated by predicting exhale deformations in five DIR-Lab datasets (Sec. III). We show that modeling the diaphragmatic and thoracic movement decoupled enables the estimation to achieve an average error of 3.40 ± 1.0 mm in predicted landmark positions during a respiratory cycle. Sec. IV concludes the manuscript.

II. Methods

A. Anatomical Model Generation

Our detailed anatomical model of the respiratory system comprises the lungs, thorax, and a sub-diaphragm region grouping abdominal organs including the diaphragm. This allows the individual sliding of lungs and diaphragm along the thorax. The anatomical model is generated from the end of exhale phase of a thoracic 4D CT through three steps herein described: segmentation, mesh generation, and mesh post-processing.

1) Segmentation: 3D CT images are segmented using an automatic multi-organ technique based on a machine learning approach with a level-set optimization [29] (Fig. 3a). While the lung meshes are directly generated from the segmentation, the thorax is based on the skin and lung segmentations. In some patients, the strong diaphragm curvature and deep belly breathing causes a sliding movement of the diaphragm along the rib cage, which can be observed in a 4D CT image set.

To allow this movement, the diaphragm must be segmented independently from the rib cage. The sub-diaphragm area is synthetically generated by casting the lung downwards (Fig. 3b). Due to the non-convex nature of the lung, a simple downward projection of the lung will cause outliers and sub-diaphragm wedges between lung and thorax, as depicted in Fig. 4. To address this difficulty, we first compute the height map of the lower third of the inferior surface (z-axis) of the lung. Then, a modified closing operation is applied: erosion and dilation are only performed on voxels in the height map if more than 60% (set experimentally) of the neighboring voxels have a lower or equal height value. Therefore, anatomically incorrect ridges will be removed in case the height map has a pot-like shape, while preserving the borders and height if diaphragm is represented correctly.

2) Mesh Generation: The volumetric meshes are generated through a 3D-triangulation based on a feature preserving Delaunay refinement. The algorithm explicitly samples corners and edges from the input image, which is a 3D binary volume representing the segmentation and constraining the refinement to preserve these features [20]. After Delaunay refinement, a mesh optimization phase is performed to remove slivers and achieve a good mesh quality, resulting in three tetrahedral meshes for thorax, lung and sub-diaphragm (Fig. 3c showing lung and sub-diaphragm). The Computational Geometry Algorithms Library (CGAL) provides an implementation.

3) Muscular Contact Zones: To capture the heterogeneous muscle forces, thoracic and diaphragmatic pressures are estimated regionally according to pressure zones. For the thorax, the pressure zones are defined automatically by sub-dividing the inner surface in evenly spaced horizontal rings, which are themselves further subdivided into patches based on the relative angular position of each surface triangle (Fig. 3d). The angle is defined to be 0° along the negative x-axis (dexter), and 90° along the negative y-axis (anterior). For the sub-diaphragm, its superior surface (namely the diaphragm interface) is split into zones, based on the relative position

3D-triangulation refers to the partition of a volume into tetrahedra
of each triangle on the antero-posterior \((y)\) and dextro-sinister \((x)\) axis.

\[ \begin{align*}
M^t \ddot{U}^t + C^t \dot{U}^t + K^t U^t &= F^{t=1}_c + F^{d=1}_d \\
M^t \ddot{U}^t + C^t \dot{U}^t + K^t U^t &= F^{t=4}_c + F^{d=4}_d + F^p \\
M^d \ddot{U}^d + C^d \dot{U}^d + K^d U^d &= F^{t=4}_c + F^{d=4}_d + F^p
\end{align*} \tag{1} \]

where the acceleration, velocities and positions of the free nodes of each part are gathered in the vectors \( \dot{U}, \ddot{U}, \) and \( U \). The lumped mass matrix \( M \) is computed according to the mass density \( \rho^t = 1.05 \, \text{g/mL} \) and \( \rho^d = 1.50 \, \text{g/mL} \). The stiffness matrix \( K \) describes the internal elastic forces. The damping matrix \( C \) represents the Rayleigh damping with coefficients of 0.1 for mass and stiffness. The right-hand side terms of (1) represent the forces acting on which the lungs, thorax and sub-diaphragm are subject to. The pressure forces \( F_p \) represent the physiological forces driving the respiratory motion (Sec. 2F3), while the interaction forces \( F_c \) model the sliding interaction between the organs (Sec. 2F4). An implicit Euler scheme is used to integrate Eq. (1) in time since it allows larger time steps.

2) Tissue Model: In this work, the non linear, heterogeneous material properties [26], [27] of lung, thorax and muscles are simplified and represented by a linear elastic model like in [22]. A co-rotational formulation is used to cope with large deformations and rotations [32]. The Young’s modulus \( Y \) and the Poisson’s ratio \( \nu \) define tissue stiffness and compressibility respectively. The sub-diaphragm and thorax tissue is assumed to be equal and fairly stiff with \( Y^{t, d} = 7800 \, \text{Pa} \), while the lung is softer with \( Y^t = 900 \, \text{Pa} \) [23]. The thorax and sub-diaphragm are more incompressible \((\nu^{t, d} = 0.43)\) than the lungs \((\nu = 0.4)\) [22].

3) Respiratory Forces: The lungs are deformed passively by the surrounding thoracic muscles (see [13]). Our model represents this behavior by applying pressures on the automatically pre-defined thoracic pressure zones. For every zone \( v_i \), the pressure \( p^i \) is applied as force \( F^i = p^i n \, dS \), where \( n \) is the unit normal of the surface element \( dS \).

4) Collision and Sliding Interaction: A collision model of pleural behavior is proposed to transfer the thoracic pressure force field to the lungs. The collision model attempts to keep the distance \( d \) between thorax and lung greater than the contact distance \( d_c = 1 \, \text{mm} \), as the typical pleural thickness is reported to be \( 1 - 2 \, \text{mm} \) [33]. When the distance is smaller than the alarm distance \( d_a = 5 \, \text{mm} \), a collision is detected and the contact force \( F_{c,m_1 \rightarrow m_2} \) is applied from mesh \( m_1 \) to mesh \( m_2 \). To avoid decoupling or interpenetration, the force is defined to keep the meshes at an optimal distance \( d_o = \frac{1}{2}(d_a + d_c) \):

\[ \begin{align*}
F_{c,m_1 \rightarrow m_2}(v) &= -n_m k_s (u(v) \cdot n^{m_2}), & \text{if } d_o \leq d \leq d_a \\
F_{c,m_1 \rightarrow m_2}(v) &= +n_m k_s (u(v) \cdot n^{m_2}), & \text{if } d_c \leq d \leq d_a \\
F_{c,m_1 \rightarrow m_2}(v) &= 0, & \text{otherwise}
\end{align*} \]

where \( u \) is the vector between the vertex \( v \), which belongs to the triangle \( T^{m_2} \) on mesh \( m_2 \), and the corresponding collision point on mesh \( m_1 \) (see Fig. 3), and is used to compute the current distance \( d = \| u(v) \| \). Furthermore, \( n^{m_2} \) is the normal of the triangle \( T^{m_2} \) and \( k_s \) is the penalty force stiffness coefficient, set to 0.1 \, \text{N/m} in this study. The interactions \( F_c \) between all three objects are defined in a similar way.

5) Three Stopping Criteria: When forces are applied, the biomechanical model converges towards an equilibrium where
the dynamics equations (Eq. (1)) are balanced (steady state). For the optimization process (see Sec. II-C), the steady state needs to be detected automatically in order to compute the cost function. This is achieved by testing three criteria at every iteration of the computational model. The first criterion is met when the user-defined maximum simulation time (e.g. \( T_{\text{max}} = 1 \) s) is reached, \( T_{\text{max}} \) in normalized time. The second and third criterion are based on the velocities and computed at every time step \( i \). The second criterion is met when the simulation becomes unstable: if the velocity of any node in the lung becomes physiological impossible, the simulation is aborted. The test is performed by comparing each magnitude of the velocity vector to infinity (\( > 10^{10} \) m/s). However, we could not observe speeds beyond 1 m/s in stable cases. The third criterion is met when the sliding average (window size of \( n = 50 \) time steps) of the mean velocity of all nodes in the lung falls below a given threshold \( \epsilon = 2.5 \cdot 10^{-1} \) mm/s (set experimentally) for robustness with respect to potentially slight numerical instabilities. The values in the sliding window are initialized with zeros and the test is enabled after \( i > n \).

C. Model Personalization

The pressure necessary to load the lung from EE to EI is estimated by minimizing a multi-variate cost function using Powell’s NEWUOA algorithm [34], a trust-region method that does not explicitly calculate cost function gradients. Three different cost functions are investigated, defined as

\[
e_1 = d_S, \quad e_2 = d_{LM}, \quad \text{and} \quad e_3 = d_S + d_{LM},
\]

where \( d_S \) is the mean Hausdorff surface-to-surface distance between the deformed EE lung surface at system equilibrium and the segmented lung surface at EI, and \( d_{LM} \) is the average Euclidian distance between internal landmarks at EI and their corresponding EE landmarks moved according to the internal deformation provided by the biomechanical models. Note that during personalization only landmarks at EI are compared to the simulated landmarks, while for the evaluation of the respiratory motion, the landmarks between EI and EE are used. To minimize risks of local minima, the following coarse-to-fine strategy is employed. First, the personalization is performed with each one zone on the sub-diaphragm and the thorax with an initial value of 0. Then, the thorax zones are split horizontally and vertically into four equal zones, the pressure values are set to the previously obtained values, and the personalization is restarted. This is repeated until the desired number of pressure zones is reached.

D. Implementation

The anatomical modeling pipeline is implemented in C++ and includes the automatic segmentation, detection of the anatomical model, and meshing based on CGAL. The biomechanical model and the collision algorithm are implemented within the Simulation Open Framework Architecture (SOFA) framework [35] using CUDA. Finally, the optimization framework, incorporating NEWUOA, calls SOFA as cost function to estimate the pressure distribution.

III. EXPERIMENTS AND RESULTS

A. Patient Data

Our framework was evaluated using 4D CT data sets from DIR-Lab [36], where the entire thorax was visible (cases 6 to 10), image resolution of 0.97 \times 0.97 \times 2.50 \text{mm}, average image dimension of 512 \times 512 \times 128, an average of 414 landmarks was available, but no respiratory trace was provided. For evaluation the lung volume at each phase needs to be computed in order to allow the synchronization of the predicted lung with observations. The segmentation of the lungs and skin was performed automatically for the CT phases 0 to 5 (end-inspiration to end-expiration), and our pre-processing pipeline automatically defined the lung, thorax and sub-diaphragm regions. When applying the modified closing operation, parts of the mediastinum were merged to the thorax instead of connected to the sub-diaphragm, as illustrated on case 6 in Fig. 4.

B. Computation of Landmark and Surface Errors

The landmark error is the euclidean distance between the landmark’s simulated position and the position at the target phase. To compute the simulated position, first the surrounding tetrahedra and the corresponding barycentric coordinates were computed during initialization. The simulated position is then computed with respect to the deformed tetrahedra using barycentric mapping. The surface error is the average distance between two triangle meshes. We use the symmetric Hausdorff distance defined as the average bi-directional point to triangle distance.

C. Numerical Analysis

All convergence analyses were performed using the same patient data (DIR-Lab data set case 6, see II-A) and the cost function \( e_3 \) (Eq. (2)), with, if not otherwise specified, four pressure zones on the diaphragm and 16 pressure zones along the thoracic cavity. Four different mesh configurations were generated with 0.8k, 1.4k, 2.6k and 5.7k tetrahedra elements for the lung (Fig. 3i). The number of elements in the thorax and sub-diaphragm were kept constant with 6.8k and 0.9k respectively.

1) Convergence analysis in terms of spatial resolution: In virtue of the spatial discretization, the accuracy of predicted landmark position and quality of the surface representation may be directly related to the number of tetrahedra elements. However, the number of elements also affects collision accuracy and computation time.

Therefore, we perform the convergence analysis to assess the number of elements necessary to reach the convergence of the system. As metric, we use the landmark distance with respect to the ground truth. As depicted in Fig. 3i and Tab. I, the observed landmark and surface errors do not change significantly once the mesh yields 2.6k or more elements. At this point, the errors are no longer influenced by the resolution, but other components of the method (i.e. temporal resolution or coarse-to-fine personalization strategy). It should be noted that we are interested in finding the number of elements for
which the system converges, which may not be the optimal one in terms of landmark error.

2) Convergence analysis in terms of temporal resolution: Similarly, we analyzed the effect of the time step on the prediction accuracy, as illustrated in Fig. 5(b). Results suggested that time steps lower than 1 ms did not improve the results, while a higher time step significantly worsened the results, mainly because of poor collisions (the time resolution is not sufficient to detect collisions). Therefore, the time step was set to 1 ms for all subsequent experiments as a compromise between accuracy and computational time.

3) Evaluation of the coarse-to-fine personalization strategy: The proposed hierarchical personalization strategy aims at automatically finding the optimal trade-off between number of surface zones, accuracy and computational efficiency. Fig. 6 shows a comparison between a direct strategy and the coarse-to-fine strategy as presented in Sec. II-C. Three configurations of pressure zones were used:

- **Low**: 1 zone on the sub-diaphragm, 1 zone on the thorax.
- **Medium**: 2 zones on the sub-diaphragm, 2 rings and 2 zones per ring on the thorax. The coarse-to-fine strategy used the result of the low optimization as starting point.
- **High**: 4 zones on the sub-diaphragm, 4 rings and 4 zones per ring on the thorax. The coarse-to-fine strategy used the result of the medium optimization as starting point.

As one can see, stability and more accurate solutions were gained when there were 4 zones on the diaphragm and 16 on the thoracic surface. Furthermore, the NEWUOA software converged as fast using the coarse-to-fine strategy (295 iterations in total including low, medium and high), as compared to the direct personalization (high configuration, 292 iterations), while getting more robust and accurate solutions using the coarse-to-fine strategy. Furthermore, estimated pressure fields were more spatially consistent when using the coarse-to-fine strategy, as illustrated in Fig. 6(b). For the following experiments, the optimal profile (high), as well as the coarse-to-fine strategy were employed. To conclude, we used the following settings for the patient experiments:

- 2.6k tetrahedra elements for the lung.
- a time step of 1 ms.
- a coarse-to-fine strategy.
- 4 and 16 pressure zones on the sub-diaphragm and thoracic cavity respectively.

### D. Validation of Motion Prediction on Patient Data

1) Generation of Anatomical Model: Using the patient data described in Sec. III-A, the meshing resulted in an average over all patients of 3.4k, 18.6k and 2.3k tetrahedra for the lung, thorax and sub-diaphragm respectively. In the following sections we present the results for the left lung only. It should be stressed though that our approach is generic and can handle both lungs irrespectively.

2) Biomechanical Model Personalization: For each proposed cost function (Eq. 2), the personalization automatically estimated pressure values per muscular contact zone, which enabled the deformation of the lung from end-expiration (EE) to end-inspiration (EI) (Tab. II blue rows indicate the surface and landmark distances after personalization). Depending on the number of pressure zones, the optimization algorithm converged after an average over all patients of 24, 55, 198 and 277 iterations for low, medium, high and total number of zones respectively while using the coarse-to-fine strategy. Each optimized iteration ran a full simulation of a lung motion based on a set of pressure values, where the average computation time is 2 min. The quality of each personalization was then evaluated by predicting the exhalation (EI to EE), without any image information.

3) Evaluation of Motion Model Prediction: A full cycle was simulated to evaluate the quality of the prediction, based on the three cost functions (Eq. 2). The simulation of inhale was driven by the personalized pressure values, while exhalation was simulated by setting the pressure values to zero. The surface and landmark errors were computed for all corresponding phases during exhalation, where the synchronization was performed by means of the lung volume and therefore represented a real-world scenario (binning and gating is already performed on basis of lung volume). The quality of the exhalation prediction was evaluated by comparing the landmarks for every intermediate phase, which are shown in Fig. 7. As Tab. II and Fig. 8 show, the model based on cost function $c_3$ performed best, and despite simplifications, a mean landmark error over all landmarks and phases of $3.40 \pm 1.00$ mm was obtained.

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2Configuration: single-threaded simulation with CUDA based collision detection, Intel Xeon 3.07GHz, 3.50GB RAM and NVIDIA Quadro 2000
Fig. 5. (a) The landmark and surface errors converge around 2.6k. The goal of a convergence study is to investigate at which point a parameter will no longer influence the entire method. Therefore, not the resolution yielding the smallest error is of interest, but for which resolution the system converges. Note that the computational effort grows exponential. (b) The convergence in terms of temporal resolutions was reached at dt = 1 ms, suggesting that a simulation using temporal resolution of less than 1 ms is indistinguishable from a simulation using 1 ms.

Fig. 6. (a) Evaluating the personalization with respect to different numbers of pressure zones showed that the coarse-to-fine strategy results in lower errors, while converging after the same number of iterations compared to a direct personalization. (b) Furthermore, the coarse-to-fine strategy results in smoother, more-realistic pressure distributions.

Fig. 7. (a) The lung motion is computed during exhale and shown as a solid lung. The ground truth from CT for each phase is overlayed as wireframe. (b) Average landmark error during exhale prediction for three experiments: personalization with 20 pressure zones using $c_1$, $c_2$ and $c_3$ as cost function.

IV. DISCUSSION AND FUTURE WORKS

This manuscript presented a framework to predict respiratory motion in patients based on a personalized biomechanical model. To the best of our knowledge, our pipeline is the first to segment the lungs, generate the anatomical models, personalize the model to reflect the patient-specific physiology, and predict the deformation without being explicitly driven by image forces. The personalized model allowed the generative prediction of the motion, where the obtained results were of the same order of magnitude as state-of-the-art respiratory motion models [22], [23], [37], but in contrast to our method, previous techniques rely on a fixed boundary condition, are not generative, and do not model the physically correct pressure and interactions between lungs and thorax. Furthermore, the method outperformed our previously presented biomechanical models for full cycle prediction [13], [14]. We have only presented results on the left lung, but the extension to both lungs is straightforward, as for the anatomical model, personalization, and prediction of motion, and the lungs can be treated individually for each lung. However, as the real motion of the lungs is coupled, the modeling of constraints defining the coupling should be investigated.

As tissue model linear-elastic material properties were chosen. Previous publications (e.g. [22]) indicate that hyper-elastic
material properties may yield better simulation results. However, a closer look at the experiments in [22] shows that the change of errors between models using linear and hyper-elastic properties is far less significant compared to models that allow nearly friction-free sliding motion. This coincides with our observations that the linear-elastic properties in combination with nearly friction-free sliding are sufficient to simulate the respiratory motion, and the proposed model is still predictive in terms of internal landmark position, as demonstrated in five cases. However, our efforts to improve the model and make it more realistic will include further investigations into the possible benefits and potential difficulties of using hyper-elastic material properties. Note that the tissue properties are especially complex, as the real properties of lung and thorax depend strongly on the patient’s health, age, gender, and physical condition. Therefore, several approaches would need to be combined, such as the hyper-elastic material properties and the automatic estimation of spatially varying tissue properties such as presented in [27]. Currently, the simplifications in terms of linear material properties were partly compensated for by the personalized and spatially varying thoracic pressure values. These pressures, indeed, may not correspond to the actual forces exercised in the patient, but rather a "lump" force to cope with model simplifications. We have observed that the applied pressures directly correspond to the linear-elastic material properties (e.g., higher stiffness leads to increased pressure estimation). Therefore, personalization of pressures partially compensates for the rough approximation of the Young’s modulus of lung, thorax and sub-diaphragm.

In summary, the personalization is based on three different cost functions. We have shown that in most patients the direct surface distance between simulated and observed EE phase is not sufficient to predict the pressure distribution. On the contrary, in this manuscript we have shown that a model which has been personalized based on landmark and surface distance \( c_3 \) yields a better prediction of the internal deformation of the lung during the respiratory cycle. The improved behavior of the model is caused by the personalization considering the sum of surface and landmark errors, instead of relying on one or the other separately. This results in a better approximation of the physiological correct pressure values, which in turn provides an improved model. These findings make it necessary to provide landmarks together with the segmentations. Therefore, automatic detection of landmarks in the lung, such as in [38], [39], would need to be added to the framework. We have not investigated the influence of tumors and have considered these to behave as the surrounding lung. This simplification will be removed in future. While our previous papers [13], [14] relied on a direct estimation of each pressure value, the novel coarse-to-fine personalization strategy during personalization results in a smoother and physically plausible pressure distribution. Due to the lack of a respiratory trace for the patient data, the model and the observations were synchronized based on the lung volume, which was computed from the images through automatic segmentation of all 4D phases. This actually represents a real-world scenario, as the trace during imaging is often not available, or due to inter-cycle variations, hard to acquire. However, once available, a possible extension of the framework would be to introduce time-varying pressure values and improve the personalization process by considering the intermediate respiratory phases as well. While this is an interesting approach, the amount of unknown parameters to estimate would significantly increase. We therefore propose to further investigate the correlation between the 1D trace and the pressure values.

Our anatomical model represents the lung, thorax, and sub-diaphragm area. The separation into these three parts allows the sliding of the diaphragm and lung along the thoracic cavity, which was a major problem in the method presented in previous work [14] and for image based methods, even for most recent methods such as [27]. The mechanical decoupling of thorax and diaphragm is therefore not only a major contribution of this manuscript, but indicates possible extensions to other image based and non-image based methods. Indeed, the real anatomy is more complex than currently represented. Enhancing the model to include further details such as the tethering of the lungs by the airways, or the definition of a spatially varying tissue model to represent inhomogeneity for regions such as bones, muscles, tumors and organs may constitute potential areas for future research. In conclusion,
our method may provide novel, 4D surrogate information for
thoracic image reconstruction and analysis.

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