SB³C2022
Summer Biomechanics, Bioengineering and Biotransport Conference
June 20-23, Eastern Shore, MD, USA

A PHYSICS-BASED MULTI-SCALE MODELING PIPELINE FOR SIMULATION OF VENTILATION IN ADVANCED COVID-19

Shea T. Middleton (1), Elizabeth Dimbath (1), Anup Pant (1), Stephanie M. George, PhD (1), Veeranna Maddipati, MD (2), M. Sean Peach, MD-PhD (3), Kaida Yang, PhD (3), Andrew W. Ju, MD (3), Ali Vahdati, PhD (1)

(1) Department of Engineering, East Carolina University, Greenville, North Carolina, USA
(2) Department of Pulmonary and Critical Medicine, Brody School of Medicine, East Carolina University, Greenville, North Carolina, USA
(3) Department of Radiation Oncology, Brody School of Medicine, East Carolina University, Greenville, North Carolina, USA

INTRODUCTION

COVID-19 disease, generated by a coronavirus called SARS-CoV-2, has caused a deadly worldwide pandemic. The viral infection can result in extensive tissue and organ damage, particularly in the lungs. Computed tomography (CT) images are valuable for analyzing heterogenous COVID-19 lung injuries such as ground-glass opacities (GGO) and areas of consolidation[1].

Physics-based computer models of the lung offer a virtual hypothesis-testing platform to gain a deeper understanding of pulmonary ventilation dynamics in healthy and disease states [2]. *In silico* modeling of COVID-19-afflicted lung mechanics may provide valuable insights into the multi-scale interactions of heterogenous acinar damage with lobar and whole-lung function.

This research aims to develop a physics-based multi-scale computational modeling pipeline for COVID-19-afflicted lungs by coupling airflow and lung tissue mechanics [3]. To this end, this study develops an *in silico* multi-scale workflow for simulating heterogenous patient-specific lung damage using a meso-scale acinar model coupled to a reduced-order conducting airway model.

METHODS

This study utilized a 4D CT scan obtained during tidal breathing of a male patient hospitalized in Vidant Medical Center (Greenville, North Carolina, USA) with an advanced case of COVID-19. The methodology used in this paper was approved by the East Carolina University and Medical Center Institutional Review Board (UMCIRB) with study ID 20-001447. Informed consent was obtained from the patient.

The geometry of the first several airway generations visible in CT images and the lung lobes were segmented from the end-inspiratory and end-expiratory phase using Mimics 23.0 (Materialise NV, Belgium) and the Chest Imaging Platform in 3D Slicer [4]. A space-filling airway generation algorithm with random heterogeneity was then used to create 16 generations of conducting airways [5]. The model included 30,142 acini, each coupled to a terminal bronchiole. 3D Slicer was also used to segment the aerated, GGO, and consolidated COVID-19 regions using the Hounsfield values in the CT images [6].

The C++ simulation package CHASTE (Cardiac, Heart, and Soft Tissue Environment) was used to establish the multi-scale coupling between the macroscale airflow and the meso-scale acinar mechanics model[7]. The airflow equation was presented as a modified Poiseuille flow with corrections to dynamic resistance [3].

Airflow was driven by changes in acinar volume of each of the approximately 30,000 acini as a function of the fluctuating pleural pressure of the lung. Pleural pressure varied based on Equation 1:

$$P_{pl} = P_{pl\,max} + \frac{\Delta P_{pl}}{2}\left(1 - \cos\left(\frac{2\pi t}{T} + \Phi\right) + \pi\right) + P_g \qquad (1)$$

where P_{pl} is pleural pressure, t is simulation time, T is the inspiration-to-inspiration breathing period (four seconds for this simulation), Φ is a phase shift, and P_g is pressure due to gravity

Acinar mechanics were represented by a sigmoidal transpulmonary pressure-volume relationship, incorporating different levels of tissue damage through increased surface

tension and decreased compliance [8,9]. The coefficients for the sigmoidal acinar model were selected based on patient-specific characteristics, including patient sex, height, and age. A hypothetical healthy lung simulation without any tissue damage and a COVID-19-afflicted lung simulation with heterogeneously-distributed damage were run for 12 seconds (three breathing cycles) on a workstation with 128 GB of RAM and a 14-core Intel Xeon CPU.

RESULTS

Our image analysis based on segmentation of CT images showed that the right middle lobe exhibited the least amount of COVID-19-induced damage (29.6% of the lobe volume was made of GGO and consolidated regions), while the right lower lobe had the highest COVID-19-induced damage presence (78.2% of the lobe volume was made of GGO and consolidation areas). In our simulations, the least damaged lobe (right middle) demonstrated a far more minor change in tidal volume and flow between healthy and diseased simulation scenarios (Figure 1).

Furthermore, the COVID-19 simulation scenario demonstrated a re-distribution of ventilation from the most injured lobes (right upper, right lower, and left lower) to the least injured lobes (right middle and left upper lobes). The pressure distributions in the lung for each simulation are shown in Figure 2. These images show that the diseased case simulation demonstrated more heterogeneity in air pressure distribution throughout the lung with lower pressure magnitude on average.

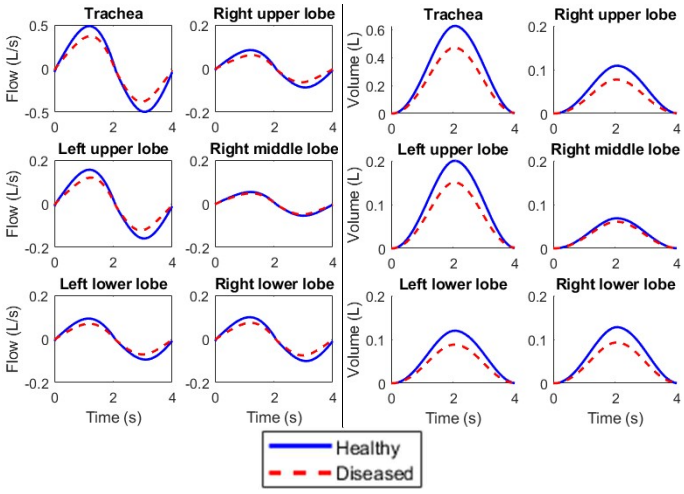

Figure 1: Whole lung and lobar tidal airflows (left) and tidal volumes (right) for the healthy and diseased simulation scenarios.

DISCUSSION

This study presents a multi-scale modeling pipeline to simulate patient-specific heterogeneous COVID-19-induced damage and compares the results to a hypothetical healthy lung simulation scenario.

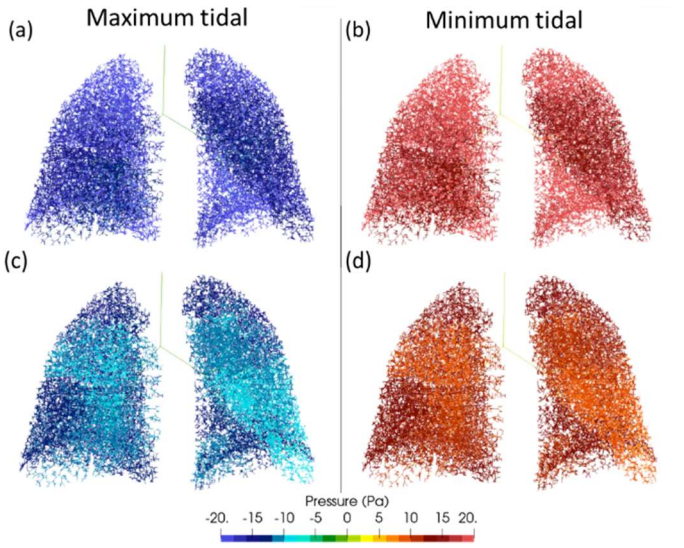

Figure 2: Pressure distribution in coronal view of the healthy (a,b) and diseased (c,d) lung simulation scenarios at maximum inspiration and expiration.

Our simulation results show that as damage manifested in the patient's right upper, right lower, and left lower lobes, ventilation was redistributed to the patient's less damaged lobes (right middle and left upper lobe), which is in agreement with recent clinical observations [10]. Moreover, our multi-scale model reasonably simulated a decrease in overall tidal volume as a consequence of tissue injury and surfactant loss in the meso-scale acinar mechanics model.

The presented *in silico* study is a step towards building digital twins of the human lung incorporating subject-specific heterogenous tissue damage to gain a deeper understanding of pulmonary ventilation and eventually individualized treatment strategies.

ACKNOWLEDGEMENTS

This material is based on the work supported by the National Science Foundation under 9. Special thanks to nurses and respiratory therapists at Vidant Medical Center for their help with this study and to Vidant Radiation Oncology (Greenville, North Carolina, USA) for the use of CT scanner in the facility. Special thanks to Rafel Bordas for insightful email correspondence on lung model generation.

REFERENCES

[1] Barisione, E, *Virichows Arch,* 478:471-485, 2020
[2] Ma, H, *Front. Physiol.*, 11:941, 2020
[3] Bordas, R, et al. *PLoS One*, 10, 2015
[4] Fedorov, A, et al. *Magn. Reason. Imaging*, 30, 2012
[5] Tawhai, M, et al. *J. Appl Physiol*, 97:2310-2321, 2004
[6] Kassin, M, et al. *Sci. Reports,* 11:1-13, 2021
[7] Cooper, F, et al. *J. Open Source Softw.* 5:1848, 2020
[8] Venegas, J, et al. *J. Appl. Physiol.*, 84:389-395, 1998
[9] Fujioka, H, et al. *J. Biomech*, 46:319-328, 2013
[10] Cobes, N, et al. *Eur. J. Nucl. Med. Mol. Imaging 47, 2020.*