Lung Micromechanics of Pulmonary Fibrosis: A Finite Element Analysis

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Introduction

- Human lungs consist of a branching network of airways that start at the trachea and terminate at the alveolus.
- There are ~300 million alveoli, which are microscopic balloon-like sacs found in small clusters (Fig.1); providing a large surface area for gas exchange (>1 m^2/kg per body mass) [2].

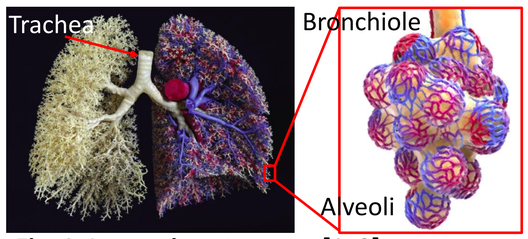

Fig. 1: Lung microstructure [1, 2].

- The alveolar wall contains elastin and collagen fibers, and is coated on the inside with a layer of fluid.
- Tension in the fibrous tissue, in combination with surface tension at the air-fluid interface, maintains the internal lung structure by exerting a deflating force, often referred to as elastic recoil [3].
- Limited tools (MRI & LDCT) are available to understand the effect of changes in lung tissue structure with respect to lunch mechanics and function.
- Finite Element (FE) Modeling can be used to understand the effects of certain lung diseases such as Emphysema and Pulmonary Fibrosis (PF) and to improve treatment.
- We developed a FE model of a single alveolus to determine the effect of pulmonary wall fibrous tissue mechanics and PF on alveolar function.

Methods

Geometry & Mesh

- Alveoli geometry was obtained from an electron micrograph (Fig. 2A) [2].
- A single alveolus has the form of an ellipsoidal shell (major axis:122 ± 6.1 µm, minor axis: 93 ± 3.5 µm, circular opening: 70 ± 3.0 µm, wall thickness: 7 µm; Fig. 2B).
- A 3D mesh was created (~54k hexahedral elements) with a custom-written algorithm.

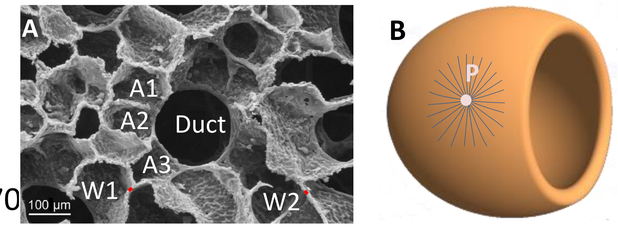

Fig. 2: (A) Electron micrograph of human lung parenchyma [2]. Alveoli (A1-3) and wall thickness (W1-2) used to define model geometry. (B) Alveolus model in FEBio [4] and an arbitrary point (P) with 12 groups of fibers.

Material Coefficient

- ***Collagen fibers*** were described using a tension-only exponential stress-strain energy function (material coefficients: ξ, α, and β) with 12 groups of fibers (15º between adjacent fiber populations; Fig. 2B – blue lines around point 'P').
- ***Ground matrix*** was described as a Neo-Hookean material (parameters of E and ν).
- ***All 5 material coefficients*** were calibrated by comparing the PV response from our simulation with data in the literature (R^2>0.9) [3, 5].
- For parameter identification, we used PV curves of saline filled cat lungs, which eliminates the contribution of surface tension forces during lung recoil.
- To simulate ***pulmonary fibrosis***, the alveolar wall thickness (t) and fiber modulus (ξ) were increased by 30%.

Boundary & Load Conditions

- The alveolus opening was constrained in all directions, and varying pressure was exerted on the inner surface, resulting in cycles of inflation and deflation.
- An internal pressure range from 0 to 8 cmH_2O was applied, where 8 cmH_2O corresponds to the pressure at total lung capacity in the saline-filled lung experiment [5].

Results

- Curve-fitting to experimentally determined PV response resulted in the following material coefficients: E = 1 KPa, ν = 0.45, ξ = 0.03 KPa, α = 0.1, and β = 2.5 (Fig. 3A – black circles (data) vs. black line (model fit); R2 = 0.97).

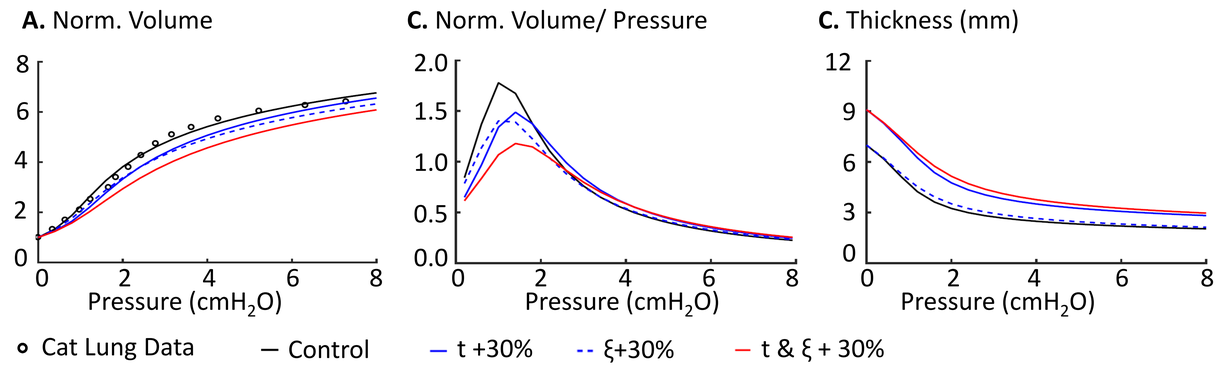

Fig. 3: (A) Volume (normalized by reference configuration volume) for the model of cat lung experiment, and different cases modeling PF vs. Pressure; (B) Volume change per cmH_2O (C) Alveolar wall thickness.

- Alveolar wall thickness decreased steeply at low pressures, reaching a plateau of ~2 µm thickness at higher pressures (Fig. 3C).
- At maximum applied pressure, alveolus inner wall strains were ~200% with an effective stress of 40 kPa. Strain and stress decreased to ~160% and 11kPa, respectively, on the outer wall surface (Figs. 4A & B).

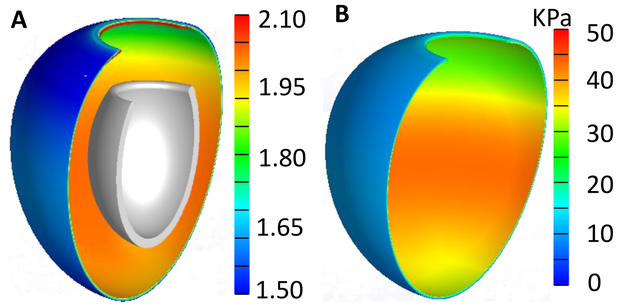

Fig. 4 (A) Cross sectional view of alveolar reference configuration (grey), effective Lagrangian strain and (B) stress distribution at 8 cmH_2O.

- PF decreased alveolar pressure, and the changes in alveolus capacity was more pronounced at lower pressures (2-4 mmH2O; Fig. 3A & B).

Discussion

- We developed a FEM based on human alveoli geometry and calibrated to PV curves reported in the literature. This model is valuable for understanding mechanisms of lung disease, including pulmonary fibrosis.
- An alveolus undergoes expansion and contraction during breathing with stresses being 3.6X greater on the inner walls than the outer wall.
- Symptoms associated with PF, thicker wall and stiffer fibers, both caused the alveoli to become less compliant.
- A combination of the two symptoms led to a drastic decrease in surface area available for gas exchange, which agrees well with clinical observations [6, 7, 8].
- Full model validation for human lung mechanics is limited due to the lack of necessary data in the literature (reported data used cat lung).
- In this model, we assumed equivalence between the PV curve of the whole lung and that of a single alveolus, which is not very well understood.
- Future work will incorporate the effect of surfactants in the fluid lining, which can alter gas exchange and surface tension mechanics.
- ***In conclusion, alveoli wall structure and mechanics play an important role in oxygen gas exchange potential, which is important for understanding how certain lung diseases affect lung function.***

Acknowledgements

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References

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