How does parenchymal stress change during airway remodeling?

Objective
To develop a multi-scale organ level model of lung mechanics to understand the impact of changes occurring during the diseases of asthma and Chronic Obstructive Pulmonary Disease (COPD).

Motivation
- Asthma and COPD are characterized by airway remodeling, bronchoconstriction and emphysema.
- Whilst the detailed cellular machinery behind remodeling of parenchyma in emphysema is not fully understood, it has been shown that cells take signaling cues from the mechanical stress they experience. Thus, stress may contribute to emphysema progression.
- The distribution of mechanical stress in the lung are known to vary with change of posture due to the influence of gravity.
- It has been hypothesized that the contraction of airways affects the stress distribution in the parenchyma.
- Variability in mechanical stress could lead to significant variability in the progression of emphysema at the organ level.

Computational Modelling
- Models
Two related finite deformation models were constructed at different scales:
  - Lung Scale Model, used to investigate the role of posture changes and gravity on lung stress distribution
  - Airway Scale model, used to investigate the impact of airway remodeling on parenchymal stress
- Lung (Organ) Scale model
The bulk lung modeled using finite deformation theory as an isotropic incompressible hyperelastic material. A strain-energy law due to Fung governs the material properties. Frictionless contact boundary conditions that constrain the lung to slide over the pleural cavity are enforced using a penalty method.

Lung Mesh Generation
A tetrahedral mesh was generated from a segmented CT image of a human right lung at total lung capacity (TLC).

Airway Mesh Generation
Tetrahedral meshes (Fig. 3) of airway walls embedded in a 10 cm radius parenchyma layer were generated using Gmsh. Wall size was specified using lung morphometric data. Wall thickness was increased to represent remodeling. Meshes of both individual and multiple airways were generated.

Airway Simulation Protocol
An outward pleural pressure of 0.49 kPa (5 cmH2O corresponding to FRC) was applied to the parenchymal layer. Active tensions between 0 - 6 kPa (0 - 61 cmH2O) were generated in the airway wall. Resulting Cauchy stresses were calculated from the model.

Results
- Gravity affects stress distribution in the organ scale model with changes in posture.
  The greatest gradient occurs in the upright posture and the maximal stress is found towards the apex (Fig 4).
- Airway wall thickening is predicted to have negligible impact on parenchymal stress.
  Airway thickening alone was seen to not significantly increase parenchymal stress. Peak parenchymal stress was seen in the region bordering the airway wall and stress was seen to drop off sharply moving away from the airway wall (Fig 5).
- Increased active tension in the ASM is predicted to increase subtly radial stress in the surrounding parenchyma.
  Peak parenchymal stress was again seen in the region bordering the airway wall and reduced rapidly moving away from the airway wall (Fig 6).
- Interdependence in parenchymal stress is predicted to occur when large airways are closely spaced.

Conclusions
- We have developed a computational model to predict stress distribution in lung parenchyma at the organ scale and at the scale of the conducting airways.
- The model predicts increased stress in the lung parenchyma towards the apex of the lung and parenchymal stress is predicted to increase close to major airway walls.
- Interdependence in and increased parenchymal stress is predicted when major airways are closely spaced.
- Future work will include integration of airway smooth muscle fibre orientation into the airway model and combining the two models to allow the effect of airway remodeling on parenchymal stress to be assessed at the organ scale.

Acknowledgements
- This study was funded by the AirPROM project, part of the European Union Seventh Framework Programme.
- The CT dataset was collected at Glenfield Hospital, Leicester, UK.
- The lung mesh generated by Materialise NV, Belgium and FluidDA NV, Belgium.

References
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