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Multi-scale modeling of alveolar and airway recruitment/derecruitment dynamics associated with ventilator-induced lung injury: Mechanisms of damage and opportunities for protection

Abstract: The lung consists of many generations of bifurcating airways that terminate with alveoli, the site of gas exchange. Surfactant, a protein-phospholipid mixture, is released from alveolar type-II pneumocytes, and dynamically reduces the surface tension of the lining fluid. Without proper surfactant function the lung is micro-mechanically unstable, leading to airway closure and insufficient gas exchange. Airway reopening can result in large mechanical stresses being exerted onto the airway wall, which can damage airway epithelial cells. This atelectrauma is a component of ventilator-induced lung injury (VILI) and contributes to the high mortality (~40%) of acute respiratory distress syndrome. We asked the question 'is it possible to enhance the surface activity of endogenous surfactant using unsteady flows?' If so, atelectrauma could be reduced through the judicious choice of mechanical ventilation waveforms.

We investigate the fluid-structure and physicochemical interactions that lead to atelectrauma through theoretical and in-vitro experimental investigations of pulmonary airway reopening. We idealize the system as an airway that is lined with epithelial cells, with reopening occurring through the steady and unsteady migration of a finger of air that removes the obstruction. Model studies are conducted using computational simulation and idealized micro-fluid mechanical studies. Biological studies are completed using idealized models with a confluent monolayer of human lung airway adenocarcinoma epithelial cell line NCI H441 (HTB-174, ATCC, Manassas, VA)

We present our observations of cellular damage to epithelial cells as a result of the migration of a bubble progressing along the cell surface and relate the observed damage to stress magnitudes predicted from computational investigations. We explore the capacity of intermittent retrograde flow to lead to surfactant enrichment at the bubble tip that can protect epithelial cells. Benchtop studies demonstrate a reduction of the macroscale pressure drop, and micro-PIV provides the micro-scale velocity field from which Lagrangian methods establish the influence of dynamic surface tension on this system. Cell-based studies demonstrate the capacity of this technique to substantially reduce airway damage in cases of surfactant deficiency within idealized models.

These studies demonstrate the very strong coupling between interfacial flows and atelectrauma. The use of dynamic flow to enhance surfactant function provides an opportunity for 'endogenous surfactant delivery' that may reduce the prevalence or magnitude of VILI.