8th. World Congress on Computational Mechanics (WCCM8)
5th. European Congress on Computational Methods in Applied Sciences and Engineering (ECCOMAS 2008)
June 30 – July 5, 2008
Venice, Italy

# FLUID-STRUCTURE MODELING OF EPITHELIAL CELL DEFORMATION DURING MICROBUBBLE FLOWS

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**Key Words:** *Cell Mechanics, Cell Rheology, Lung Injury, Free-surface flows.*

## ABSTRACT

The deformation response of biological cells exposed to different flow conditions is a problem with important clinical implications. For example, during acute lung injury (AcLI), small pulmonary airways become occluded with a fluid that severely hinders gas-exchange. Although mechanical ventilators can be used to clear the fluid-occlusion, the microbubble flows generated during ventilation exacerbate the existing lung injury. As a result, the mortality rate for AcLI is very high (30-40%). As shown in Fig. 1, microbubble flows in pulmonary airways impart a complex combination of normal and shear stress to the epithelial cells (EpC) which line airway walls. Depending on the EpC's biophysical properties, these hydrodynamic stresses may result in cell deformation and cell death. Although previous studies[1,2] indicate that the large spatial gradient in normal stress generated near the bubble tip is responsible for cell death, it is very difficult to eliminate these microbubble-induced forces in a clinical setting. Instead of preventing the mechanical stimuli responsible for injury, we seek to develop novel cell-based treatments that decrease the EpC's susceptibility to injury during microbubble flows. The goal of this study is to use computational fluid-structure models of cell deformation during microbubble flows to investigate how changes in rheological properties influence cell injury.

Geometrically accurate, imaged-based finite element (FE) models of cell deformation during microbubble flows were developed by first obtaining laser-scanning confocal microscopy (LSCM) images of cultured human alveolar epithelial cells (A549). An image analysis algorithm was used to convert LSCM images into 3D finite element (FE) models of the cells (Figure 2).

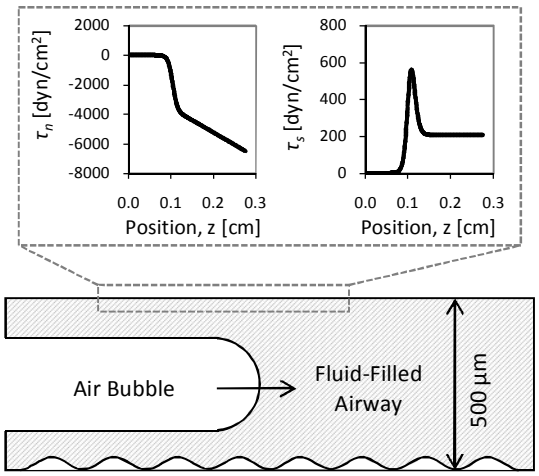


**Figure 1. Microbubble-induced normal ($\tau_n$) and shear ($\tau_s$) stress on EpC that line the airway wall. Stress values are from boundary element solutions at Ca=2E-2. Cells not drawn to scale.**

A large-displacement, linear viscoelastic formulation was used to model cell mechanics.

$$\sigma_{ij}(t) = 2G(0)\varepsilon_{ij}(t) + 2\int_0^t \varepsilon_{ij}(t-\tau)\frac{dG(\tau)}{d\tau}d\tau \text{ where } G(t) = G_\infty + \sum_{i=1}^{N} G_i \exp(-\beta_i t) \qquad (1)$$

Here $\sigma_{ij}$ is the stress tensor, G(t) is the shear modulus, $\varepsilon_{ij}$ is the strain tensor, $G_\infty$ is the long time shear modulus and $G_i$ and $\beta_i$ are the Prony series parameters. Initially, $G_\infty$, $G_1$ and $\beta_1$ were selected based on a Maxwell fluid model. We also followed a model proposed by Balland et. al[3] in which several Prony series terms are used to capture the power-law or soft-glassy rheology of EpC. The transient hydrodynamic loads generated by the microbubble (see Fig. 1) were calculated using a well-established boundary element (BE) technique[4]. These stresses were then applied to the apical cell surface and the maximum effective strain in the membrane during microbubble flows ($\varepsilon_{eff,max}$) was used to quantify the risk of cell death. This hybrid BE-FE approach was used to quantify microbubble induced deformations for a range of bubble speeds or Capillary number, Ca.

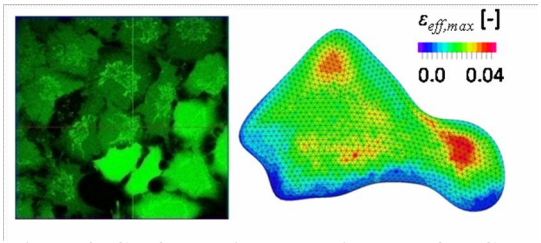


**Figure 2. Confocal microscopy images of EpC (left), 3D finite element models with membrane strain magnitude (right).**

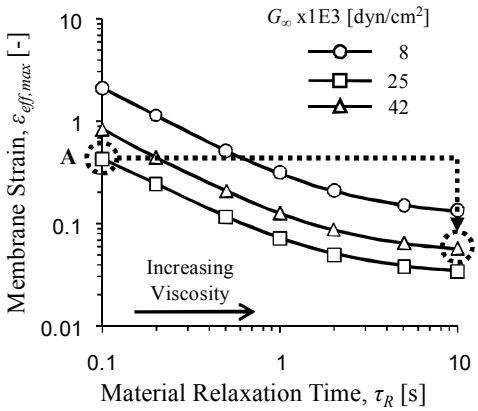


**Figure 3. Increasing viscous damping (higher $\tau_R$ in the Maxwell model) decreases membrane strain.**

As shown in Fig. 3 decreasing cell stiffness (i.e. $G_\infty$) results in larger $\varepsilon_{eff,max}$. In addition, as the relaxation time, $\tau_R=1/\beta_1$, increases, the cell is able to dissipate a majority of the rapidly applied hydrodynamic forces and as a result experiences less deformation. Similar results were obtained with the power-law rheology models. Interestingly, Fig. 3 indicates that a cell with decreased stiffness could have less strain if its relaxation time also increases (move from A to B). Recent experiments in our lab, in which cells with a reduced $G_\infty$ and increase $\tau_R$ exhibit less cell death during microbubble flows, support this conclusion. These computational and experimental results indicate that altering cell rheology may be a clinically relevant way to reduce microbubble induced cell injury during mechanical ventilation.

## REFERENCES


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Supported by the NSF, American Heart Association and Parker B. Francis Foundation.