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Ph.D. DISSERTATION DEFENSE

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Title:	Determinants of oxygenation in acute lung injury
Chairperson:	Dr. Carrie E. Perlman, Charles V. Schaefer, Jr. School of Engineering and Science / Department of Biomedical Engineering
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ABSTRACT

In the acute respiratory distress syndrome (ARDS), a form of acute lung injury, inflammation increases the permeability of pulmonary capillaries. As a result, proteinaceous liquid leaks from the capillaries into the smallest pulmonary airspaces, the alveoli. The condition is known as alveolar edema. Additionally, surface tension at the interface of a thin liquid layer that lines the alveoli is elevated. Edema and elevated surface tension impair oxygenation. The current treatment for ARDS is supportive mechanical ventilation, which improves oxygenation but exacerbates the underlying lung injury. Therefore, the mortality in ARDS is over 35%. In an experimental study in a “two-hit” (lipopolysaccharide plus injurious ventilation) acute lung injury model, I test sulforhodamine B (SRB), a surface-tension-lowering dye, as a therapeutic for improving oxygenation. Then I mimic clinical treatment by administering supportive ventilation. The injury model comprises inflammation, elevated permeability, reduced gas exchange surface area, and impaired oxygenation. I find that prophylactic administration of SRB limits inflammation, limits permeability, and improves oxygenation. Rescue administration of SRB also limits permeability and limits the reduction in gas exchange surface area. I complement the experimental study with a computational investigation. I note that liquid distribution in edematous alveoli is often non-uniform. With non-uniform distribution, oxygen flux through the liquid should be greater than with uniform distribution. I model total alveolar oxygen transport, due to both diffusion and advection, in edematous alveoli with the same liquid volumes but different liquid distributions. I confirm that oxygen transport is higher with non-uniform liquid distribution. Thus, I identify a physiologic mechanism that helps to maintain oxygenation in edematous lungs and a potential surface-tension-lowering therapeutic for further enhancing oxygenation.