Age-dependent Ventilator-Induced Lung Injury

Quintessa Hay[1], Christopher Grubb[2], Rebecca L. Heise[3], Sarah Minucci[1], Michael S. Valentine[3], Jennifer Van Mullekom[2], and Angela M. Reynolds[1]

[1] Department of Mathematics & Applied Mathematics, Virginia Commonwealth University, Richmond, VA, USA.

[2] Department of Statistics, Virginia Polytechnic Institute and State University, Blacksburg, VA, USA.

[3] Department of Biomedical Engineering, Virginia Commonwealth University, Richmond, VA, USA.

Lung insults can lead to a need for mechanical ventilation (MV) in severe cases. While MV is often a life-saving intervention, it can induce further lung damage called Ventilator-Induced Lung Injury (VILI). Experimental data has also indicated an increased risk of VILI in elderly patients. This information along with the increased demand for MV caused by the novel coronavirus SARS-CoV-2 emphasizes the need for further research on the age-dependent aspects of VILI. This paper expands upon a previous ordinary differential equation model for MV (Minucci *et al.*, JTB 2021) by including more biologically realistic dynamics for cell and cytokine diffusion into the alveolar lung space following epithelial damage. Additionally, we utilize *in vivo* mouse data to create plausible parameter estimates associated with both the young and old mice experiments. Parameter sets are then analyzed using various statistical methods, including random forest and other classification methods, to determine the important factors associated with severe or moderate outcomes for both the young and old experimental groups at the end of ventilation. We also identify representative parameter sets that best depict the average transient behavior for each response to MV. Using the representative sets for each group, we simulate an intervention to conceivably improve the response to MV.

Keywords: ventilator-induced lung injury, mechanical ventilation, epithelial damage, parameter estimation, classification