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Title: Quantifying Mechanical Heterogeneity in Canine Acute Lung Injury (ALI)

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Rationale: ALI is characterized by a heterogeneous pattern of lung injury and, ideally, regional mechanics should dictate how mechanical ventilatory parameters such as rate, tidal volume, and PEEP are optimized. Presently there are no simple bedside techniques that can quantify lung heterogeneity during mechanical ventilation. Previous morphometric modeling studies have demonstrated that respiratory impedance spectra (Z_{rs}), specifically respiratory resistance (R_{rs}) and elastance (E_{rs}) as functions of frequency, may be sensitive indicators of mechanical heterogeneity in the lung (Lutchen and Gillis, *J. Appl. Physiol.* 83:1192-1201, 1997).
Methods: We measured Z_{rs} in anesthetized dogs from 0.078 to 8.9 Hz using broad-band pressure-flow

excitations at baseline and after injury produced by infusion of 0.08 ml/kg oleic acid into the right atrium. Data were obtained at mean airway pressures (MAP) of 5, 10, 15, and 20 cm H_20. The Z_{rs} spectra were then fit by various models of the respiratory system incorporating different distributions of parallel viscoelastic tissue properties. Heterogeneity was quantified using the standard deviation of these tissue property distributions.
Results: Under baseline conditions, moderate increases in MAP decreased mechanical heterogeneity. Following injury, both the level and frequency dependence of R_{rs} and E_{rs} increased, as well as the apparent heterogeneity of tissue properties. The R_{rs} and E_{rs} decreased with increasing MAP up to 15 cm H_2O, but both increased when MAP was increased to 20 cm H_2O. Heterogeneity decreased at moderate MAP, but then increased at the highest MAP.
Conclusions: Our data demonstrate that Z_{rs} can provide specific information regarding mechanical heterogeneity of injured lungs and the impact of MAP. These non-invasive approaches may ultimately allow for the development of ventilation protocols that optimize regional lung mechanics in patients with ALI.

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