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Title: Characterization of the Evolution of Sheep LPS Acute Lung Injury (ALI) by Functional CT Imaging

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Functional CT imaging can characterize the time course and distribution of lung edema, atelectasis, regional aeration and perfusion during the evolution of ALI. **Methods:** 10 anesthetized, mechanically ventilated (Vt 10 ml/kg, f 20/min, 5 PEEP, FiO₂ 1.0) adult sheep had *E.coli* LPS (Sigma L4005) infused at 10mcg/kg/h until Qs/Qt \geq 40% and PaO₂ \leq 200 for 20 minutes. 5 sheep received the LPS infusion prone (P group), 5 supine (S group). Inspiratory and expiratory gated CT images of the entire lung and perfusion images at selected apical and basal slices were acquired at baseline and injury time points (supine), and every hour during the endotoxin infusion (supine/prone). Images were analyzed using PASS and TSIA software (University of Iowa). Total, air and tissue lung volumes were calculated for each image set, along with axial and vertical aeration and perfusion gradients. **Results:** P group animals needed a higher LPS dose to reach injury endpoints. CT imaging showed a progressive reduction in air volume, partially replaced by

tissue volume, in both groups. Apex and non-dependent regions are better aerated in all images. Dependent regions became progressively denser with injury, especially at the base. Apical regions remained better aerated in S group. Blood flow increased in injured regions compared to relatively-spared ones. **Conclusions:** Regional lung CT analysis is useful in defining temporal changes in regional lung aeration, perfusion, and V/Q distribution. In this i.v. LPS ALI model, injury development while prone results in more uniform axial and vertical aeration distributions. Perfusion images demonstrate the loss of hypoxic pulmonary vasoconstriction in injured regions and explain the hypoxemia out of proportion to the loss of ventilated volume.

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