Changes in Pulmonary Vascular Properties in a Human Model of Acute Lung Injury Measured using DCE-MRI

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INTRODUCTION: Of all patients admitted to intensive care unit, about 10% suffer from either acute lung injury (ALI) or acute respiratory distress syndrome [1, 2] with reported mortality rates of 43% [3]. ALI involves a pulmonary immune response that results in increased vascular permeability and accumulation of fluid in the alveoli. Human models of ALI, including lipopolysaccharide (LPS) inhalation, are used to investigate the processes underlying ALI and to develop treatment strategies. To date no studies have applied quantitative measurement of pulmonary vascular properties in ALI or human models of ALI. Our aim was to test dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) as a method to gauge the impact of LPS challenge on lung vascular properties, with potential as a biomarker in development of novel treatment strategies. **METHODS:** Five health volunteers underwent a DCE-MRI scan before ("Scan 1") and at 6-hours after ("Scan 2") inhalation of a nebulised solution of LPS in saline (n=2) or nebulised saline (control, n=3). Pre-contrast T1 measurement and DCE data were acquired on 1.5T Siemens Espree scanner using a 3D gradient echo sequence with free breathing [4] (TR/TE = 3.14/0.91 ms, 128x128x22 matrix over a 350x350x110 mm FOV). T1 mapping employed a variable flip angle approach (flip = 2°, 5°, 10° and 19°). DCE scans employed Dotarem contrast agent at a dose of 0.2 mMol/kg, with 140 dynamics acquired at a temporal resolution of 3.9s/dynamic, with a flip angle of 19°. The arterial input functions were measured from the images orthogonal to pulmonary artery to minimise partial volume effects [5]. Extended Kety model [6] generated parametric maps of the transfer constant describing the diffusive transport of Gd across the capillary endothelium (*K-trans)*, vascular plasma space (*Vp*) and extravascular extracellular plasma space (*Ve)*. A circular ROI that avoided vessels was placed on post-contrast images and later translated to parametric maps to report mean values. Data normality was tested using Shapiro-Wilk test and statistical significance using paired t-test. **RESULTS AND DISCUSSION:** We have successfully implemented DCE-MRI analysis workflow in MATLAB and analysed 5-datasets as part of an ongoing study. Differences in Ktrans, Ve, and Vp were not significantly different ($p>0.05$) between pre and post LPS session (n=5) (FIG 1), although mean K-tr values from LPS group (n=2) showed larger changes than precision errors (33.4%) calculated from control group (n=3) (FIG 2). Naish et al [7] reported an elevated K-tr in smoker lungs than in non-smokers using DCE-MRI. Data acquisition for this study is ongoing and analysis of the complete dataset will allow testing of the hypothesis that LPS-induced changes in vascular permeability and alveolar fluid content can be detected with DCE-MRI. However, if no significant differences are observed the same data will be used to report precision errors of quantitative DCE-MRI parameters in lungs.

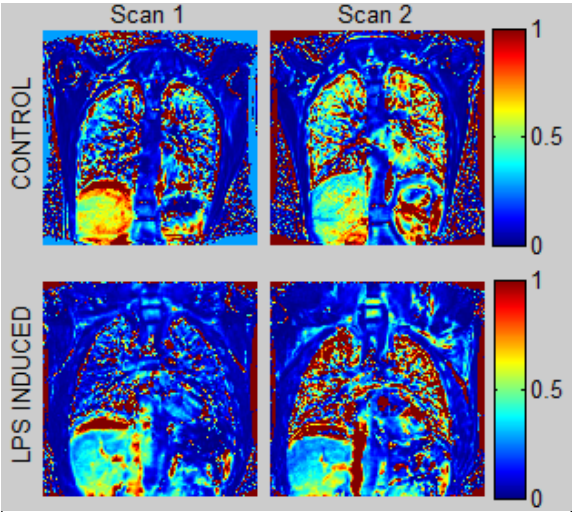

FIGURE 1: K-tr maps of one volunteer from control and LPS group each.

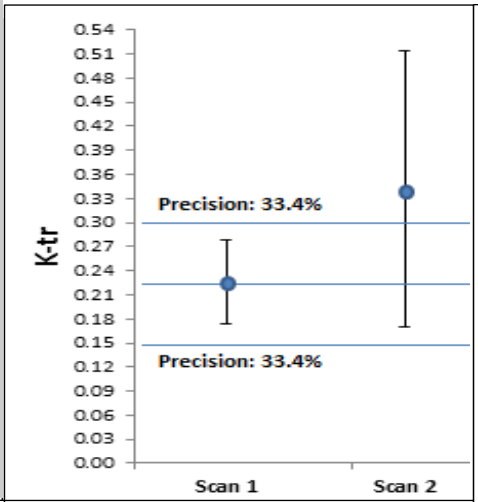

FIGURE 2: Precision lines from control group and bar graph with standard error showing mean K-tr values from two sessions in LPS group.

References: [1] Rubenfed et al. N Engl J Med 353:1685-1693 (2005). [2] Brun-Buisson et al. Intensive Care Med 30:51-61 (2004). [3] Zambon & Vincent. Chest 133:1120-1127 (2008). [4] Ingrisch et al. Invest Radiol. 2014 Jun;49(6):382-9. [5] Kim et al. Radiological Society of North America 2011 Scientific Assembly and Annual Meeting, November 26 - December 2, 2011, Chicago IL. [6] Naish et al. Magnetic Resonance in Medicine 61:1507–1514 (2009). [7] Naish et al. Proc 16th ISMRM p401, 2008.