Imaging Lung Aveolar Fluid Clearance With MRI

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Introduction:

Indirect measurements suggest that the rate of alveolar fluid clearance (AFC) correlates with morbidity and mortality in patients with pulmonary edema (1-3). The development of direct and real time measures of AFC would enhance our ability to understand the mechanisms underlying AFC and to develop new therapies. Currently, fluid clearance is indirectly measured by instilling fluid containing a tracer molecule into the lung. After an hour, the fluid is removed and the tracer concentration change yields the AFC rate. Although an AFC rate estimate is obtained, it is a global estimate, and the relative contributions of different parts of the lung are unknown. In this work we report our initial work on direct measurements of AFC.

Materials and methods:

The right lower lobe was collapsed in 6 anaesthetized piglets (10-15kg) that were inhaling 100% oxygen. Fluid, containing 3 mM Gd-DPTA and a fluorescent gold standard (FITC-dextran) was instilled into the lobe. As fluid is cleared from the lobe, the concentration of these agents will change. All imaging was done on a Signa Excite 1.5 T MR scanner (GE Healthcare, Milwaukee, WI). After fluid instillation, breath held 3D spoiled gradient echo images (3DSPGR) were acquired every 10 minutes. Imaging parameters were: 40 degree flip, TR/TE = 4.2/1.9 ms, 256 by 256 by 42 matrix (interpolated to 512 x 512 x 84), BW was +/- 88 kHz, FOV was 24 cm , parallel imaging was used with a two-fold acceleration factor, slice thickness was 1.5mm and scan time was 23 sec. After an hour, fluid was obtained to measure FITC concentration and estimate the AFC rate. As fluid is cleared from the lung the concentration of Gd will also change. This will change the 3DSPGR signal intensity (4-6). We assumed that the changes in signal intensity were solely due to Gd concentration changes, and that the signal intensity was linear with Gd concentration. To verify the last assumption, ten phantoms were imaged. The signal intensity was measured and plotted against the concentration. Lastly, to ensure that Gd did not affect AFC, sodium ion transport was measured for 0, 3 and 30 mM Gd solutions across distal lung epithelium (DLE) cultures as in (7). Our animal research ethics board approved all experiments.

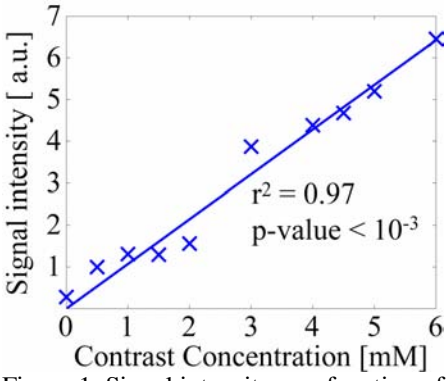

Figure 1. Signal intensity as a function of Gd concentration, the signal intensity has a linear relationship to the contrast concentration. As the contrast concentration doubles, so will the signal intensity.

Results:

The phantom signal vs. Gd concentration is shown in Fig 1. The signal intensity is linear with contrast concentration (p-value < 0.001). Gd did not affect ion-transport across the DLE in our experiments. A lung-fluid clearance map from one of our experiments is shown in Fig 2. The average AFC rate at this slice was 10 % +/- 5 % per hour, which compared well to the FITC measurements of 11 % +/- 0.5 % per hour.

Discussion:

This technique enables us to generate an image of the fluid clearance rate, showing how much fluid is extracted from where. Several studies have shown that lung fluid content is a strongly affected by gravity (3,8). We are currently examining if AFC is similarly affected by gravity. In addition we are improving our technique to ensure that it is robust to motion between scans. We conclude that MRI techniques show promise for direct real-time measurements of AFC. Supported by the Heart and Stroke Foundation, CIHR and ORDCF.

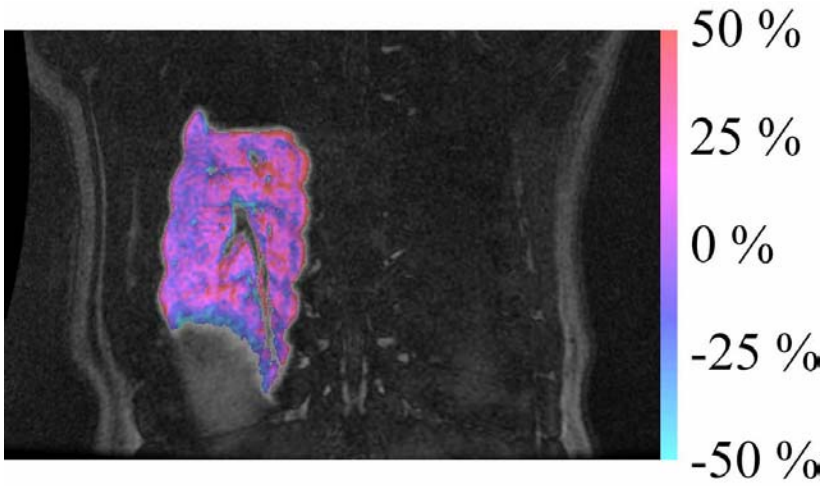

Figure 2. Colorized clearance map showing water clearance rates per hour from the porcine lung. The average clearance rate was 10 % +/- 5 %per hour, which compared well with the tracer measurements of 11 % +/- 0.5 % .

References:

(1) Verghese GM et al. J Appl Physiol 87: 1301-1312, (1999)
(2) Ware LB et al. Am J Respir Crit Care Med 163: 1383, (2001).
(3) Levitzky *Pulmonary Physiol*. McGraw Hill (2003)
(4) Pintaske et al. Inv. Radiology 41(3):213-221 (2006)
(5) Haacke et al. *MRI phys princ…* Wiley & Sons (1999)
(6) Hoffmann U et al. MRM 33:506–514 (1995)
(7) Rafii B et al. J Physiol (Lond) 544: 537-548, 2002.
(8) Bankier AA et al. JMRI 23:115-122 (2006)