MRI of Mouse Lung for Quantitative Assessment of Disease Models

M. Scadeng[1], H. Rossiter[2], D. Dubowitz[1], E. Breen[2]

[1]Center for Functional MRI, University of California San Diego, La Jolla, CA, United States, [2]Department of Medicine, University of California, San Diego, La Jolla, CA, United States

Introduction:

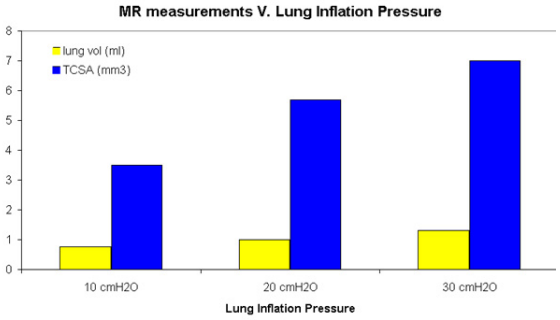
Advances in MR Imaging of lung tissue lags behind that achieved in solid organs for two reasons: Firstly, as the lungs are mostly air filled, there is little tissue, which results in a low spin density of hydrogen nuclei to image. Secondly, lung tissue-air boundaries create inhomogeneity of magnetic field due to susceptibility differences between the tissue and the air. This results in marked signal loss in the images (figure 1a). As a solution to the susceptibility issue we have developed a technique in which we completely replace the air in the lungs with a Perflurocarbons (PFC) emulsion (figure 1b). In this presentation we demonstrate the reliability of this MR technique to detect morphological changes in small lung structures, as well as lung volume, under different experimental conditions.

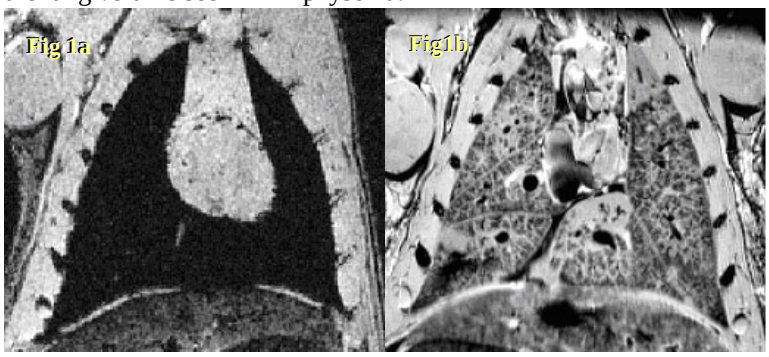
Methods:

All imaging was done ex-vivo in C57BL mice (n=20). Contrast enhancement of the vasculature was accomplished antemortem by injection of gadolinium dimeglumine (Magnevist), I.P. After circulation had ceased, the gas in the lung was aspirated, and replaced with a trachealy instilled mixture of a PBS/perfluorcarbon (PFC). The emulsion was instilled at 3 different airway inflation pressures of 10, 20 or 30 cmH_2O. There were 6 mice per group, and 2 vascular endothelial growth factor (VEGF) deficient mice (emphysema disease model). Lungs were imaged *in situ* using a 2.5 cm custom built volume coil and scanned in a horizontal bore 7T MR scanner (Varian). Data were acquired using a 3D FLASH sequence TR/TE= 28/6.3, FA 25, FOV 20mm, producing datasets at 90 micron isotropic resolution.

Results:

3D rendering of data using Amira software provided quantitative measurements of lung volume and tracheal cross sectional area (TCSA) at the right upper lobe branch. MR measured lung volumes of 0.77 ml, 1.10 and 1.30 ml and TCSA of 3.5 mm^2, 5.7 mm^2 and 7.0 mm^2 were measured at airway inflation pressures of 10, 20 or 30 cmH_2O, respectively (Chart 1). This correlated well with the actual volumes of emulsion instilled. These parameters were also shown to be increased in the 2 VEGF-deficient lungs compared to wild type at comparable pressure, consistent with increased the lung volume seen in Emphysema.





Discussion and conclusion

The combination of aqueous (contrast positive) and perfluorocarbon (negative contrast) substances provided a readily detectable signal along airway surfaces down through the alveolar structures at the same time producing an absence of MR signal throughout PFC filled airspaces (figure2). With this technique we are able to acquire very high resolution quantitative datasets of the pulmonary and vascular microstructure (figures 3a, 3b) which can be used in mouse models of disease such as asthma and emphysema. The MR measured lung volumes correlated well with the actual volumes of emulsion instilled, at each of the inflation pressures. This data is also consistent with air volume measurements (data not shown). These data demonstrate the feasibility of using this technique to measure in situ lung parameters in mouse lung, and provide a new method of imaging transgenic mouse models of lung disease. PFC can also be used for liquid ventilation in-vivo, thus the technique also has in-vivo applications.