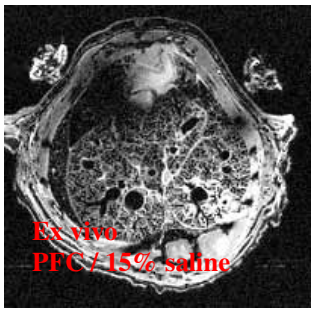
In Vivo MR Imaging of Mouse Lung Structure

M. Scadeng[1], D. J. Dubowitz[1], and E. Breen[2]

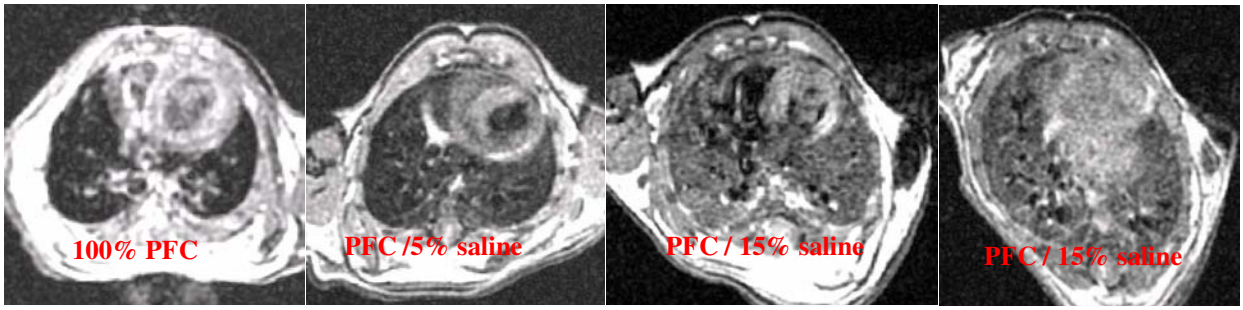
[1]Radiology, UC San Diego, La Jolla, California, United States, [2]Division of Physiology, UC San Diego, La Jolla, California, United States

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 low spin density of hydrogen nuclei to image. Secondly, lung tissue-air boundaries create susceptibility differences between the tissue and the air. This results in marked signal loss in the images. As a solution to the susceptibility issue we developed an ex vivo technique in which we completely replace the air in the lungs with a Perflurocarbons (PFC) emulsion (fig 1). We have demonstrated [1,2] the reliability of this MR technique to detect ex vivo morphological changes in small lung structures, as well as lung volume, under different experimental conditions. PFC's have the ability to carry oxygen and CO2. Here we present a method for PFC imaging in living animals.



Methods: All studies lab studies and imaging was done in vivo using anesthetized (pentobarbitol) C57BL/6J mice. 3 different groups of mice were used (n=13). Mouse Preparation: Gp 1 ventilated mice (n=3) were ventilated with 100% oxygen for 10 minutes through a tracheal cannula, instilled with 20 ul/g of (FC-75) and continued on 100% oxygen ventilation, BR 40, VT 1.0, Insp 40%, TI 0.6, MV 40/44.: Gp 2: spontaneous breathing: mice (n=6) were intubated with 20 ul/g of FC-75. The canula was removed and allowed to spontaneous breath 100% oxygen through a nose cone. Following the MR imaging protocol mice were either sacrificed for blood gas measurements (n=3) or allowed to recover from the anesthesia (n=3). Recovered mice were repeatedly intubated with FC-75, imaged and recovered on at least three subsequent days. Gp 3 spontaneous breathing (n=4) mice were prepped as group 2 but 5-20% of the instilled PFC volume was replaced with saline. Mice were allowed to recover and the procedure repeated on at least one subsequent day.
Imaging: The partially FC-75 ventilated or spontaneously breathing mice were imaged in a 2.5 cm custom built Quadrature volume MR imaging coil, and placed in a horizontal bore 7T MR scanner (GE). Images were acquired using a respiratory gated spin echo sequence TR/TE= 15.38/8 ms. FA 25, FOV 2.2 mm, matrix 128x256, 0.5mm slice. Imaging time 30 minutes. Imaging parameters were limited by respiratory gating.

Results: Blood gases measurements were similar for groups 1&2; PO2 (263 ± 99 mmHg), pCO2 (58 ± 12 mmHg) and pH (7.06 ± 0.03). The images of the lung Images of the animals that were imaged using (FC-75) alone demonstrated the proximal large airways and vessels. More of the lung structure could be seen in the mice who were instilled with additional saline. The combination of aqueous (contrast positive) and perfluorocarbon (negative contrast) substances provided a readily detectable signal along airway surfaces at the same time producing an absence of MR signal throughout PFC filled airspaces as was seen in our ex-vivo studies (PEMRI effect[2]).



Discussion and conclusion: All animals tollerated liquid ventilation (spontaneous or mechanical) with the FC-75 or FC-75/saline, and MR imaging. The blood gasses that were collected were satisfactory and those mice that were allowed to recover did so uneventfully. These preliminary data demonstrate that mice can repeatedly undergo liquid ventilation. The imaging with FC-75 alone would allow for longitudinal studies of lung masses. This is traditionally extremely difficult to do. The addition of small amounts of saline to the instillate accentuated the lung structure, and could provide a new method of imaging transgenic mouse models of destructive lung disease.

1 Scadeng et al. MRI of mouse lung for quantitative assessment of disease models. Proc. Int Soc. Mag. Res. Med. 2005 2 Scadeng et al.High-Resolution Three-Dimensional Magnetic Resonance Imaging of Mouse Lung Investigative Radiology inpress Jan 2007. Supported in part by the National Space Biomedical Research Institute NSBRITD 00701.