Perfluorohexane liquid MRI of mouse lungs in a dual-tuned $^{1}H/^{19}F$ coil

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Target audience – Preclinical researchers initially with a progression to clinical researchers as utility increases.

Purpose – To investigate liquid-based fluorine lung imaging as means of clinically useful lung imaging.

Introduction – Lung MRI is difficult owing to the low proton density in the tissue and, consequently, low signal intensity on conventional ^{1}H MRI. In addition, the large difference in the magnetic susceptibility of the lung tissue and air within the lungs reduces the available signal even further. Hyperpolarization of ^{3}He or ^{129}Xe is a viable, but expensive method of lung MRI. To avoid these problems, we investigated the possibility of imaging of mouse lungs by use of perfluorohexane, a biocompatible liquid at room temperature, and ^{19}F MRI. Perfluorohexane has a very high oxygen solubility (41mL O_2/100g) which makes "fluid-breathing" a possibility. Furthermore, ^{19}F has 83% of the signal of ^{1}H in MRI, which combined with the high ^{19}F concentration in the liquid gives a very high signal. Further, the absence of fluorine in the body results in the lungs appearing bright with no background signal.

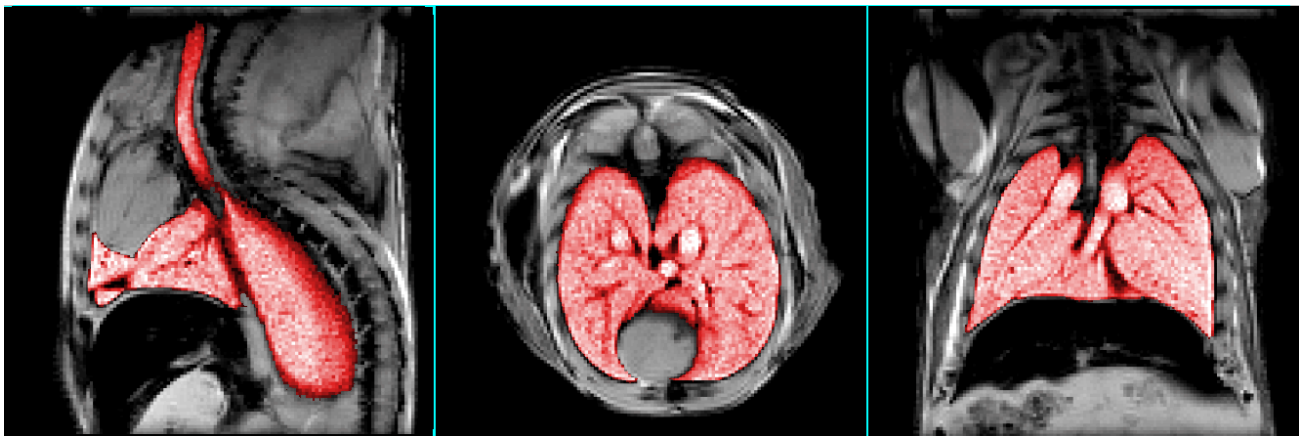

Fig 1. Representative sagittal, axial and coronal sections through a 3D dual nuclei image of a mouse showing region of fluorine sensitivity in red.

Methods – Female BALB/c mice were terminally anaesthetised and tracheotomized, then air in the lungs was replaced with the perfluorohexane. A dual tuned $^{1}H/^{19}F$ 28mm birdcage coil (PulseTeq) was used in a 7T (300MHz ^{1}H, 280MHz ^{19}F) Agilent spectrometer. Images were acquired with standard 2D or 3D spin echo sequences: 2D, matrix=128^2, FOV=25.6x25.6mm, NS=24, Thk=1mm; TR=400ms, TE=4,16ms; Texp=1h; 3D, matrix=128^3, FOV=25.6x25.6x25.6mm; TR=400ms, TE=4,16ms; Texp=1h50min.

Results and discussion – High quality images of the lungs were obtained using ^{19}F MRI (Fig 1 and 2), with typical SNRs of 31 and 17 for 2D and 3D scans, respectively. These SNR values are broadly similar to those obtained from ^{129}Xe hyperpolarization experiments [1]. However, the voxel size in the ^{19}F images (200µm) was considerably smaller than voxels typically used in pre-clinical ^{129}Xe imaging (e.g. 625µm [2]), allowing improved visualization of lung structure. The methodology used is also relatively low cost, in that no special equipment is required as compared to hyperpolarized gas imaging, other than a fluorine-tunable coil, and the perfluorohexane is <3 USD/mouse. Many contrast agents, such as those based upon iron oxide, work by inducing hypointensities in T_2*-weighted images [3]. In this case, the bright and stable image offered by perfluorohexane imaging may be an ideal backdrop for visualization of such hypointensities.

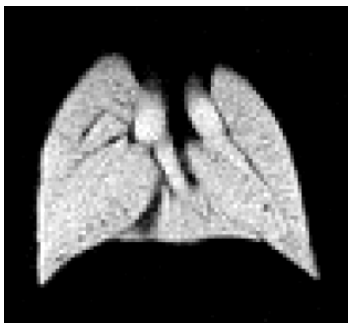

Fig 2. 2D lung slice through a naïve mouse

Conclusion – ^{19}F based perfluorohexane imaging gives bright and detailed lung images which allow visualization of structures not apparent on proton MRI. This approach is more easily and cheaply implemented than hyperpolarized gas setups and is immediately applicable in a range of pre-clinical work.

References – [1] Freeman et al. "Enabling hyperpolarized (129) Xe MR spectroscopy and imaging of pulmonary gas transfer to the red blood cells in transgenic mice expressing human hemoglobin". Magn Reson Med 2013 70(5) 1192-99. **[2]** Iguchi et al. "Direct imaging of hyperpolarized ^{129}Xe alveolar gas uptake in a mouse model of emphysema". Magn Reson Med 2013 70(1) 207-15. **[3]** Serres et al. "Molecular MRI enables early and sensitive detection of brain metastases". Proc Natl Acad Sci USA. 2012; 109(17): 6674-9.

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