Microporous lung phantoms for ^{19}F MRI of inhaled imaging agents with physiologically representative relaxation times

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Introduction: ^{19}F-MRI of pulmonary ventilation utilises an inhaled imaging agent such as a 79%:21% perfluoropropane/oxygen gas mixture (PFP/O_2).[1,2] The inhomogeneous magnetic environment proximal to the alveolar walls reduces the PFP T_2^* from 12ms in a magnetically homogeneous environment to T_2^* = 2.2ms in the human lung.[3] A lung-representative phantom that reflects the magnetic environment of human alveoli would permit directly translatable acquisition development without necessitating human subjects. The purpose of this study was to develop stable microporous foams of known pore size, magnetic susceptibility gradients, and gas/liquid ratio, that exhibit a PFP T_2^* close to that measured in the human lung. Two novel foam fabrication methods are presented, yielding monodisperse (uniform bubble diameter) and polydisperse (heterogeneous bubble diameter) phantoms.

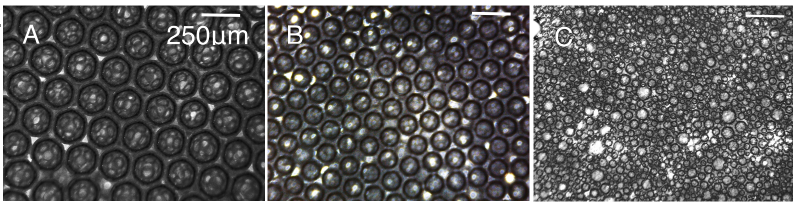
Methods: Monodisperse foams were produced by mixing an aqueous detergent solution with PFP/O_2 gas mixture in a 200µm diameter T-junction microfluidic chip (Dolomite, UK). The detergent solution comprised 2wt% PEG-40 stearate and 1wt% low melting point agarose in water. The resultant foam was collected in a chilled vial to allow agarose gelling, providing structural stability.

Polydisperse foams were produced by mixing an aqueous solution of ovalbumin, citric acid and triethyl citrate (Dr Oetker egg white powder) in a 1:4 ratio with PFP/O_2 gas, and repeatedly passing the mixture through a ~1mm diameter tube to form a homogeneous foam.

Physical and magnetic properties of both foam types were assessed. Foam bubble diameter was measured by photomicrography from 100 bubbles per sample, and intra- and inter-sample variability determined. The magnetic susceptibility of the liquid and gas components of the foams were measured on a susceptibility balance (Sherwood Scientific, UK). Perfluoropropane $–CF_3$ T_2^* was measured using a 2.5cm diameter ^{19}F solenoid coil interfaced to a Philips 3.0T scanner.

Results: The liquid components of both foam types were found to have a magnetic susceptibility equal to that of water. Figure 1 shows photomicrographs of monodisperse foam with two distinct bubble sizes (Figures 1A and 1B, mean diameters = 246±20µm and 138±22µm respectively), and a photomicrograph of polydisperse foam (Figure 1C, mean diameter = 29±12µm). No significant change in bubble size was measured in any of the samples after one hour. The water content of the three foams was 30%, 58% and 20% respectively, and the corresponding perfluoropropane $–CF_3$ T_2^* was 3.3±0.5ms, 2.0±0.1ms and 4.0±0.2ms respectively.

Fig 1.



Discussion: Two lung-representative phantom fabrication techniques were described. Both reflect physical characteristics of human pulmonary alveoli and provide novel tools for the development of quantitative MR imaging of pulmonary ventilation. Although only tested with PFP, it is expected that these phantoms will be equally valuable for protocol development on other perfluorinated imaging agents and thermally polarised ^{129}Xe.

References: 1: Halaweish, A.F., et al. (2014) *Journal of Magnetic Resonance Imaging*, 39(3), pp. 735- 741. **2:** Gutberlet, M., et al. (2017) *Radiology*, 0(0) pp. 1-12. **3:** Couch, M.J., et al. (2013) *Radiology*, 269(3), pp. 903-909.