Functional hyperpolarized Xenon-129 MRI of the ex vivo rodent lung

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Background: Hyperpolarized (hp) ^{129}Xe MRI is an established technique that has permitted imaging of the lung airspaces and has the potential to provide increased functional information over other imaging techniques due to its high solubility in tissue and wide chemical shift range [1]. Physiological parameters such as respiratory dynamics and estimation of lung volumes have previously been studied *in vivo* using hp ^{3}He [2, 3]. The *ex vivo* lung model offers the ability to study parameters that are technically difficult *in vivo,* particularly with the small volumes of hp gas used in rodent lungs, whilst reducing the severity of the procedure to the experimental animal. In addition it is known that *ex vivo* lung tissue responds to bronchoconstricting and relaxant drugs [4] therefore the *ex vivo* model will ultimately allow the rapid investigation of the effects of a variety of pharmalogically active substances.

Purpose: This study was performed to develop the *ex vivo* model to provide a tool for investigation of lung physiology whilst acquiring new informative data on lung mechanics and responses.

Methods: Male Sprague-Dawley rats (175-250 g) and Dunkin Hartley guinea pigs (200-300 g) were terminated by overdose of pentobarbital in accordance with A(SP)A 1986 (Animals for Scientific Procedures Act 1986) with subsequent removal of the heart and lungs *en masse*. The *ex vivo* lungs were suspended in solution in a custom built ventilation chamber and actively inflated by a small degree of suction provided by a ventilation syringe as has been previously demonstrated with hp ^{83}Kr [5] (Figure 1). Bronchoconstriction and subsequent reversal were produced after initial imaging by delivery of methacholine and salbutamol, respectively, via a catheter inserted into the right ventricle or caudal vena cava.

Hp ^{129}Xe was prepared by spin exchange optical pumping with a home-built polarizer in batch mode every 6 minutes using a low pressure mixture of approximately 25% Xe (enriched to > 83% ^{129}Xe) and 75% research grade N_2 (polarization ~35%) and collected into a custom built recompression chamber.

Imaging was conducted at 9.4 T with a Bruker® Avance III microimaging system (Bruker Corporation, Massachusetts, USA) using a modified variable flip angle gradient echo pulse sequence [6] and a home built transmit-receive 25 mm low-pass birdcage coil tuned to the resonance frequency of ^{129}Xe gas in the lung (110.693 MHz). Imaging parameters used- coronal image matrix 128 × 64, TE = 1.4 ms, TR = 200 ms. Subsequent image processing and analysis were conducted offline using IGOR Pro© (Wavemetrics, Oregon, USA).

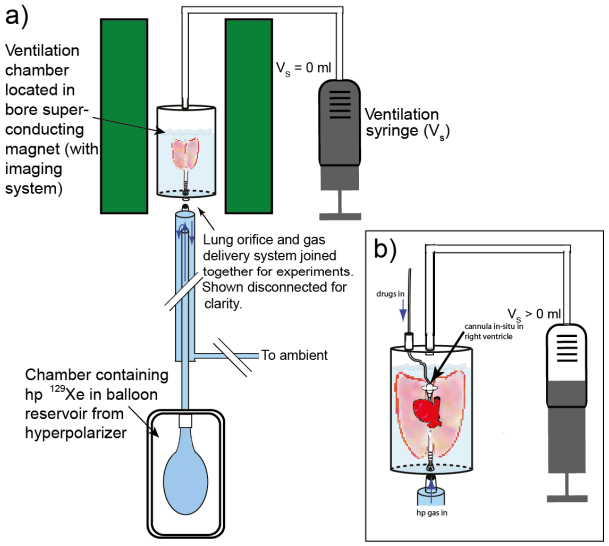

Figure 1- Experimental *ex vivo* setup where prepared hp gas is administered from a reservoir (a) and actively inhaled by negative external pressure applied via a ventilation syringe producing the desired inflation (b). Drugs are injected as required into the pulmonary circulation through a cannula in the right side of the heart.

Results and discussion: Image data illustrating the pattern of hp gas distribution on increasing inhalation volumes and the locations of hp gas inhaled at the start and the end of inhalation will be presented. These images and their analysis potentially provide new insights into respiratory mechanics, challenging established physiological theory as it will be shown that the least dependent regions of the lungs are ventilated first, in this case, the base of the lungs which are inverted in the experimental setup. Striking functional MRI data acquired over several hours showing the pattern of bronchoconstriction in the *ex vivo* guinea pig lung post methacholine challenges and after reversal with salbutamol are shown in Figure 2.

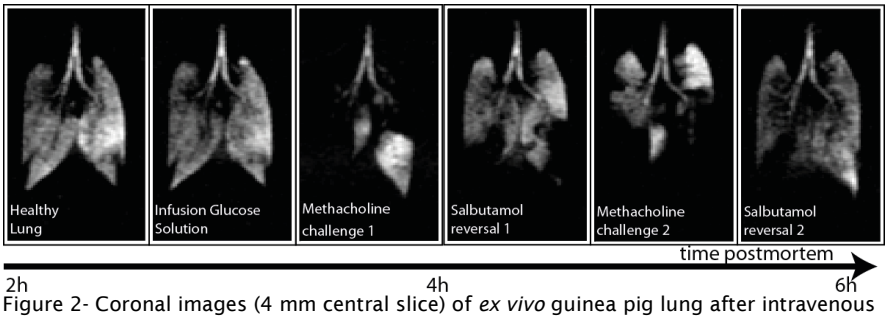

Figure 2- Coronal images (4 mm central slice) of *ex vivo* guinea pig lung after intravenous challenges of methacholine and subsequent reversal with intravenous salbutamol.

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