High Resolution Measurement of Regional Ventilation in the Mouse Lung by Hyperpolarized 3He MRI

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INTRODUCTION: Pulmonary ventilation is an important marker in lung physiology because it is sensitive to many obstructive and restrictive pulmonary diseases. Hyperpolarized (HP) ^{3}He MRI has emerged as a novel technique with unique capabilities in visualizing ventilated airspaces noninvasively. Several techniques for measuring regional ventilation using this technology have been recently developed using stacked (Deninger, *et al.* [1]) and dynamic (Emami, *et al.* [2]) breaths with advantages and drawbacks specific to each method. With an increasing interest in assessment of pulmonary disease models, and in tests of therapeutic interventions in transgenic murine disease models, it has become necessary to extend functional and structural pulmonary imaging techniques to the mouse lung scale. This extension imposes several technical challenges. In particular, achieving accurate gas mixing and ventilation devices which minimize dead space are required to control the imaging gas volume and to maintain a stable physiological state throughout the course of the study. We demonstrate the implementation of the two previously-developed ventilation measurements schemes in mice and assess the advantages and limitations of each approach.

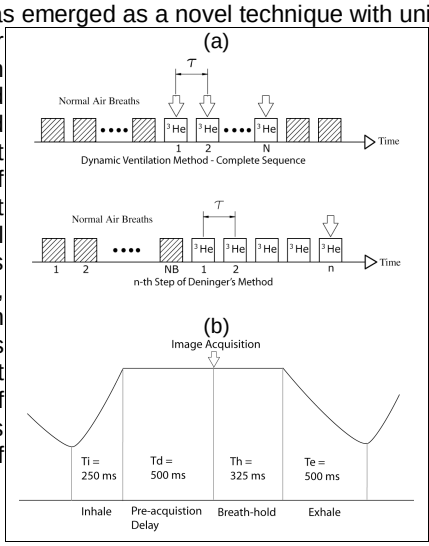

Figure 1. (←) (a) Dynamic ventilation sequence compared to *n*-th step of stacked ventilation sequence; **(b)** Details of the breathing cycle in mice.

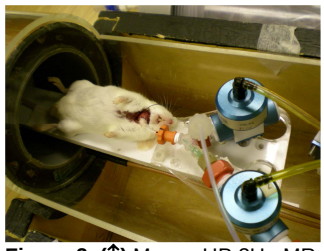

Figure 2. (↑) Mouse HP 3He MR imaging setup.

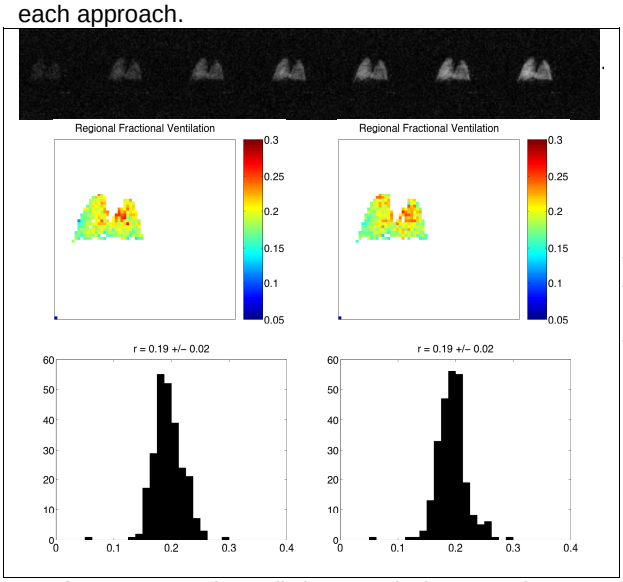

Figure 3. Dynamic ventilation maps in the mouse lung.

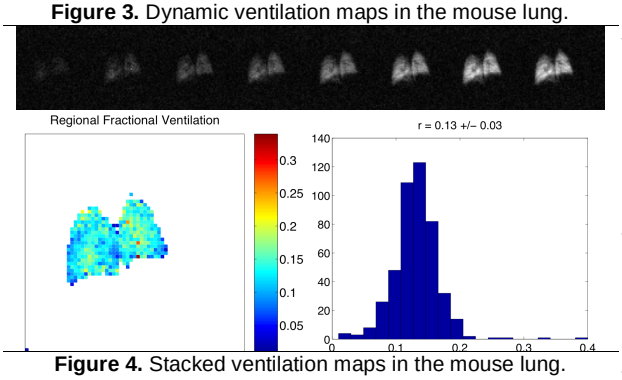

Figure 4. Stacked ventilation maps in the mouse lung.

METHODS: Figure 1.(a) shows the schematic diagram of the two ventilation imaging techniques, namely *Dynamic Ventilation* [2] and *Stacked Ventilation* [1] respectively. Details of each method are described fully in the respective references; briefly, the stacked method utilizes a separate series of breaths, during which no imaging takes place, to prepare each point in the signal buildup curve for a given ROI. This allows using a larger flip angle and therefore a higher SNR, since the signal in each image will be independent from the previous ones. However due to the large number of required HP ^{3}He breaths and necessary intermediate air breaths between each step to washout the polarized gas, the stacked breath technique is practical only in small animal studies. The long acquisition time is also prone to the effects of physiological instability of the animal. In contrast, the dynamic method acquires an image at the end of each HP gas breath, requiring only *n* polarized breaths for the same number of points (approximately a factor of *n*/2 smaller than the stacked sequence). Moreover, the acquisition time in the dynamic technique is at least a factor of *n* smaller than the stacked technique. However, results in the dynamic method depend on RF history requiring a small and well-known flip-angle. Use of a large flip angle is impractical, which can limit the achievable SNR. In our imaging experiments, the mice were ventilated using a custom programmable ventilator (Figure 2) with a ventilation dead-space of 1 mL and a functional dead-space < 100 µL (the fraction of the exhaled gas that may be re-inhaled by the animal). Figure 1.(b) shows the details of the respiratory cycle. Mice were ventilated with a mixture of ^{3}He:O_2 (4:1) at a TV=1.5mL/100g. Images were acquired on a 4.7-T small animal MRI scanner and a 12-leg birdcage coil using a fast gradient echo imaging pulse sequence with the following parameters: FOV=3cm, ST=4mm, RES=64×64, flip angle=5°/30° (dynamic/ stacked), T_E=2.4ms and T_R=4.3ms

RESULTS AND DISCUSSION: Figures 3 and 4 show example MR ventilation images acquired by each method. Also shown are the respective ventilation maps and the corresponding frequency distribution histograms. The two sets of images are acquired from two different animals, hence the different fractional ventilation values. Reproducibility of the dynamic ventilation sequence is demonstrated by comparing two separate acquisitions. For the dynamic ventilation sequence, flip angle maps were acquired (not shown) to correct for the effect of RF-induced relaxation. Both methods deliver comparable planar resolution (470µm) and an excellent SNR demonstrating a reliable measurement of ventilation in mouse lungs.

REFERENCES: [1] Deninger AJ, *et al.* Magn. Reson. Med. 48 (2002), 223-232. **[2]** Emami K, *et al.* A Novel Approach to Measure Regional Lung Ventilation Using Hyperpolarized 3He MRI – Potential in Clinical Studies; ISMRM 16th Scientific Meeting, Berlin, Germany: May 2007.