Measurement of Regional Alveolar Ventilation in a Normal Mouse Model Using HP 3He MRI

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Introduction

Measuring the regional ventilation of inhaled gas during the respiratory cycle is an interesting yet difficult problem in a mouse due to its very small tidal volume and very high respiratory rate. It is well known that regional ventilation deficiencies are symptomatic of many pulmonary disorders such as asthma. A successful technique to measure regional ventilation will help elucidate the numerous aspects of respiratory physiology associated with many obstructive and restrictive pulmonary diseases. With the advent of hyperpolarized gas MRI, it has become possible to image the regional ventilation with high spatial resolution. However, such measurement in mice with a total tidal volume of 0.20 to 0.25 *ml* is a somewhat arduous task. In this work, we have measured, for the first time, the regional ventilation in mice that results from a build-up of the hyperpolarized ^{3}He gas after an increasing number of inspirations.

Methods

Experiments were conducted under an IACAC approved protocol. Naive 8~12 weeks old BALB/c mice (25 g on average) were induced, canulated via a tracheostomy, and maintained under intraperitoneal (IP) ketamine/xylazine anesthesia. The mice were placed on a surface coil in a supine position. They were then paralyzed with IP pancuronium, attached to a prototype mechanical ventilator (Amersham Health, Durham, North Carolina), and ventilated through the tracheal canula with 100% air at 140 BPM and 0.25 ml tidal volume. Imaging was performed in a 4.7T small bore animal imager (Varian Systems) with a 33%/67% mixture of ^{3}He/N_2 during a breath hold of 3.5 s. The hyperpolarized ^{3}He was generated via the spin-exchange optical pumping method using a commercial polarizer (Amersham Health, Durham, NC). MRI images of the lung were obtained using a 2D fast gradient-echo pulse sequence with the following imaging parameters: T_E = 3.4 ms, T_R = 6.8 ms, FOV of 3x3 cm^2, coronal slice thickness of 4 mm, and matrix size of 128x128 pixels. The small-animal ventilator was programmed to carry out imaging ventilation with ^{3}He breaths delivered as per Deninger [1]. During the experiment, heart rate was monitored with a pulse oximeter, and body temperature was maintained using a steady flow of warm air (37° C) through the bore of the magnet. Image analysis for regional ventilation was performed using a computer program designed at our institution.

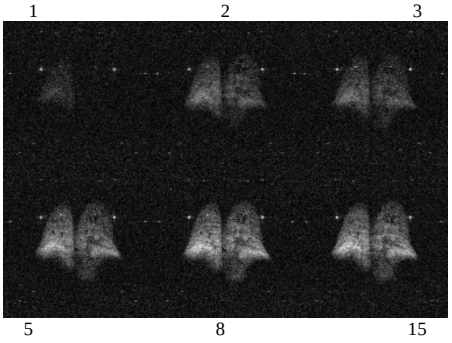

Figure 1. Normal mouse ventilation sequence with corresponding number of polarized breaths

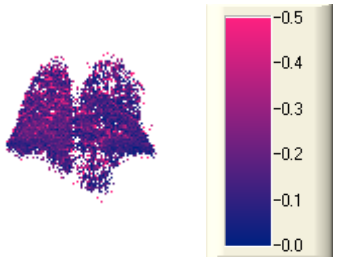

Figure 2. Regional ventilation map of a normal mouse FOV = 3x3 *cm*^{2}

Results and Discussion

Figure 1 shows a representative set of spin density images acquired after 1, 2, 3, 5, 8 & 15 breaths of helium, respectively. A typical value of 8 minutes for the polarization decay time of the ^{3}He reservoir was computed from reference images that were taken at the beginning and at the end of the ventilation measurement. Figure 2 shows the map of the regional ventilation *r* in the mouse. An average regional ventilation of *r* = 0.35 for the pixels located close to the tracheal canula, *r* = 0.2 for the pixels located in the center of the lung, and *r* = 0.1 for the lung parenchyma were obtained in these studies. These values show an almost complete replacement of gas during each breath in the trachea and a small replacement of air in the alveolar air space. Naturally, the fraction of air replaced in the lung parenchyma depends on the diameter of the small airways. Figure 3 shows a typical histogram of the distribution of regional ventilation in the lung of a normal mouse.

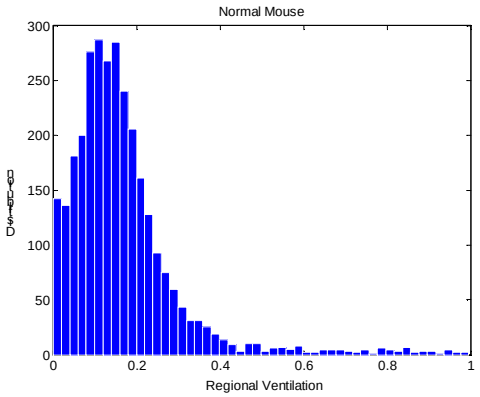

Figure 3. Histogram of the distribution of regional ventilation in a normal mouse

Conclusion

In this work, we have shown for the first time that it is possible to obtain quantitative measurements of the regional pulmonary ventilation of mice, with a high spatial resolution using polarized gas MRI. This work should prove useful in future studies of respiratory physiology and pathophysiology of lung disorders. In particular, this method may play an important role in studying the development of local airway narrowing seen in patients with obstructive lung disorders.

Acknowledgement

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1. Deninger AJ, Mansson S, Petersson JS, Pettersson G, Magnusson P, Svensson J, Fridlund B, Hansson G, Erjefeldt I, Wollmer P, Golman K. Quantitative measurement of regional lung ventilation using ^{3}He MRI. Magn Reson Med 2002;48(2):223-232.