Variable Flip Angle MR Imaging of Regional Ventilation using Hyperpolarized Helium in Rodent Lungs

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INTRODUCTION: The use of hyperpolarized helium gas to measure regional ventilation in the rodent lung using MR imaging has been suggested recently (1) and has been compared with xenon-enhanced CT imaging methods (2). This method requires knowledge of the longitudinal relaxation, T_1, of the helium gas in the ventilator system ($T_{1,ext}$) and in the lung ($T_{1,O2}$), the latter requiring knowledge of the alveolar oxygen partial pressure (p_AO_2). Furthermore, without accurate knowledge of the radiofrequency (RF) pulse history, the method requires multiple breathing cycles (*ie.*, pre-breaths) with air breathing in between in order to completely clear the lung of hyperpolarized helium gas which is time-consuming and costly. We propose a variable flip angle (VFA) approach for obtaining regional ventilation in a single set of breathing cycles (*i.e.*, no pre-breaths or wash-outs). The VFA approach can be adjusted to compensate for both RF pulse history and $T_{1,O2}$ and the speed of the technique (<10 s) removes any dependence on $T_{1,ext}$. In this work, we compare experimentally, VFA helium ventilation imaging with conventional (*ie.*, multiple pre-breath) helium ventilation imaging in rats. The results indicate that regional ventilation measurements obtained by the VFA method are comparable to the conventional method without the need for multiple pre-breaths of helium gas.

THEORY: Following the method of Deninger et al. (1), the MR signal strength following each n^{th} breath of helium for N remaining VFA RF pulses (3) at that breath can be written as:

$$S_n = const \cdot \sin(\alpha_N)(1-q)\times\sum_{k=0}^{n-1}\left(q^k\right); \qquad [1]$$

$$\text{where } \alpha_N = \tan^{-1}\left[\exp\left(-(N-1)TR/T_{1,O2}\right)/\sqrt{N-1}\right] \qquad [2]$$

and q is the fraction of gas remaining following a breath of fresh helium gas of fraction r (*i.e.*, $q + r = 1$).

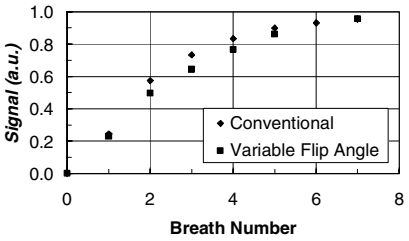

Fig.1: Helium signal from whole lung as a function of breath number using conventional and T_1-compensated methods.

METHODS: ^{3}He MR imaging was performed on Brown Norway rats (200–400 g) at 3T (GEHC) using pure hyperpolarized helium (35%) provided by a turn-key spin-exchange polarizing system (HeliSpin™, GEHC) following an animal care protocol approved by the University of Western Ontario. The gas was administered using a custom ventilator, modified to include a non-magnetic valve assembly for delivery of helium within the MR environment and with minimal depolarization (1,2). Single-slice images were obtained in the coronal plane using a fast VFA gradient-echo method (TE = 1 ms, TR = 3.3 ms, 128 x 128) triggered by the ventilator following each helium breath (7 breaths, 2 s apart). For comparison, ventilation images were also obtained in the conventional way following successively increasing numbers of helium pre-breaths (tidal volume ~ 2.6 ml, PIP = ~ 10 cm H_2O) separated by intervals of 20 air wash-out breaths. The RF pulse trajectory for VFA was calculated using Eqn. [2] for each breath based on measured $T_{1,O2}$ maps (for each breath) and the total remaining number of RF pulses (N). RF pulse tip angle was calibrated by ensuring a uniform VFA signal across all images following a single helium breath-hold. Ventilation parameters (r, q) were estimated on a pixel-by-pixel basis by fitting with Eqn. [1] using Scilab (INRIA ENPC, France) to yield parametric ventilation "r" maps and histograms.

RESULTS: Figure 1 compares ^{3}He signal from the entire lung as a function of breath number for the conventional technique and the VFA method. Note the excellent agreement between the two methods. The average r value obtained from the whole lung with the traditional method was 0.264 and the VFA method was 0.266. The precision of the two methods is reasonably similar (~8%). Figures 2 and 3 show representative histograms of r for both MR methods. Note the relatively high ventilation values (r ~ 0.9) for the major airways compared to the periphery (r ~ 0.1). The measured ventilation values obtained in similar regions-of-interest for the two techniques compared favourably (*e.g.*, r ~ 0.3 in lower right lobe) which is in the range expected in normal rats (1).

DISCUSSION: The VFA method offers an accurate and efficient approach to measurement of regional ventilation using hyperpolarized ^{3}He. The $\sin(\alpha_N)$ term in Eqn. [1] corrects for the increasing flip angle necessary to utilize the available helium polarization due to both the gas remaining from previous breaths as well as incoming fresh gas. This implementation requires measurement of the appropriate $T_{1,O2}$ following each breath a priori to calculate the corresponding VFA flip angles (Eqn. 1) and also assumes that $T_{1,O2}$ is constant throughout the lung which may not be the case for diseased lungs. It can be shown that ignoring $T_{1,O2}$ leads to errors in r of less than ~10%, which is on the order of the expected precision of the technique and therefore may be acceptable if $T_{1,O2}$ maps are not available.

CONCLUSION: The VFA method offers comparable precision and accuracy as the conventional helium ventilation imaging method but with minimal effect due to RF pulses and T_1 in the lung and the ventilator. This approach eliminates the need for multiple pre-breaths of helium resulting in a saving of factor of 5 to 6 of hyperpolarized gas. Furthermore, the elimination of multiple air wash-out breaths with VFA gives a time saving of factor approximately 10 to 20. The elimination of multiple ventilation cycles also should reduce variabilities due to ventilator performance.

REFERENCES: 1. Deninger, et al. MRM 2002;48:223-32. 2. Santyr, et al. ISMRM 1334, 2006, 3. Zhao, et al. J. Magn. Reson. B 1996;113:179-183.

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Fig. 2: ^{3}He ventilation "r" histogram obtained using conventional ventilation imaging method.

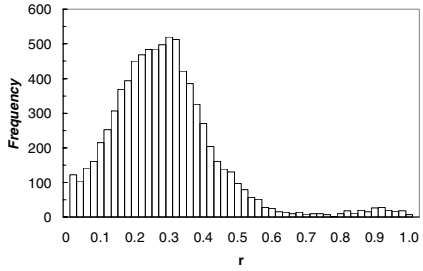

Fig. 3: ^{3}He ventilation "r" histogram obtained using the VFA ventilation imaging method.