Comparison of Hyperpolarized Helium MR Imaging of Regional Ventilation with Xenon-enhanced CT in Rodents

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INTRODUCTION: The use of hyperpolarized helium gas to measure regional ventilation in the rodent lung using MR has been suggested recently (1). This approach requires knowledge of the longitudinal relaxation, T_1, of the 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). In diseased animals, where ventilation can be strongly impaired (2), these assumptions are not expected to hold and regional variations in $T_{1,O2}$ in the lung are expected due to variable oxygen uptake by the blood (3). Furthermore, without accurate knowledge of the RF pulse history, the method requires multiple ventilation cycles with air breathing in between in order to completely clear the lung of hyperpolarized helium gas. A more widely-established method for regional ventilation mapping is xenon-enhanced computed tomography (CT) (4), which is independent of relaxation effects and can be performed in a one-shot fashion. In this work, we compare, both theoretically and experimentally, MR helium ventilation imaging with xenon-enhanced CT ventilation mapping in a rat model. The results indicate that regional ventilation measurements obtained by helium MR are comparable to xenon CT without the associated x-ray dose. The effects of $T_{1,O2}$ are discussed and improvements in the MR method are suggested.

THEORY: Following the method of Deninger (1), the MR signal strength following n breaths of helium separated by time τ can be written as:

$$S_n = const\cdot E^{(n-1)(N+n/2)}(1-q)\times\sum_{k=0}^{n-1}\left(E^{n-k-1}q^k\exp\left(\frac{-p_o\tau q^{n-k}}{\xi}\,\frac{1-q^k}{1-q}\right)\right);\ \text{where}\ E=\exp\left(-\frac{\tau}{T_{1,ext}}\right) \qquad [1]$$

where q is the fraction of gas remaining following a breath of fresh gas of fraction r (q + r =1), N is the number of air breaths in between helium breaths, p_0 is the initial oxygen partial pressure and ξ is the inverse relaxivity of helium due to oxygen (= 2.6 bar s) (1). In the xenon-enhanced CT experiment, the Deninger model can be modified to exclude relaxation effects, with the xenon signal enhancement given by:

$$\Delta C_n = \left[\Delta C_{new}\cdot(1-q)\right]\sum_{k=0}^{n-1}q^k \qquad [2]$$

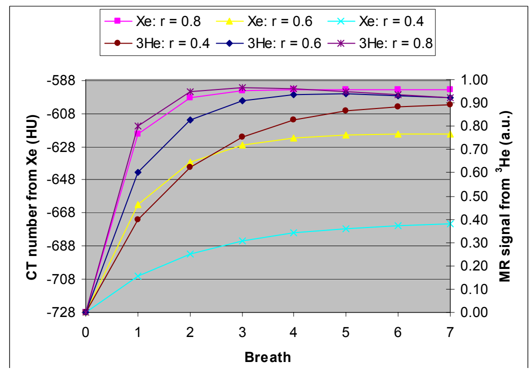

Fig.1: Theoretical comparison of xenon-enhanced CT and helium MR ventilation for varying values of r.

where ΔC_{new} is the difference in CT# between air and fresh xenon in a voxel. The effect of clearance of xenon from the alveoli by the blood has been ignored in Eqn. [2] (as justified below). Figure 1 shows a theoretical comparison of the helium MR and xenon CT methods. In Fig. 1, the curves have been normalized and $T_{1,ext}$=1800 s, p_0=0.135 bar, ΔC_{new}=214 HU, N=20 and τ = 1 s.

METHODS: Helium MR imaging was performed on Wistar rats (200-250 g) at 3T (GEHC) using pure hyperpolarized helium (35%) provided by a turn-key spin-exchange polarizing system (Helispin®, GEHC). 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 gradient-echo method (TE=1.2 ms, TR=4 ms, 128 x 128) triggered by the ventilator following successively increasing numbers of helium breaths (tidal volume ~ 1-2 ml, τ=1 s) separated by intervals of 20 air breaths to generate curves as in Fig. 1. Xenon-enhanced CT imaging was performed on the same rats using a dedicated rodent CT scanner (Locus Ultra, GEHC) at 80 kVp and 70 mA during an 8 s scan using the same ventilator and protocol as above, except with the substitution of stable xenon gas mixed with oxygen (80/20) in the reservoir instead of helium. Ventilation parameters (r, q) were extracted from regions of interest fitted by Eqns. [1] and [2].

RESULTS: Figures 2 and 3 show representative MR and CT images obtained after 10 breaths of helium and xenon respectively. The measured ventilation (r) values obtained by MR and CT, using Eqns.[1] and [2] respectively, in similar regions-of-interest compared favourably (eg. r ~ 0.4 in lower right lobe) and are in the range expected in normal peripheral rat lung (1). The $T_{1,ex}$ and p_0 values significantly affect the ventilation values estimated with the MR method.

DISCUSSION: The helium MR method offers an accurate measure of regional ventilation with no associated dose, provided that $T_{1,ex}$ and p_0 are known. The former is readily measured, but the latter may well change in vivo due to regional differences in ventilation and perfusion, especially in diseased animals. Regional T_1 mapping of the lung may help. The use of variable flip angle (VFA) approaches (5) may also aid the MR measurements by removing the need for air breaths, as the effect of RF pulses is removed with the VFA technique. The effect of xenon clearance by the blood is minimal with the CT method as determined by the agreement between the CT number measured after several xenon breaths and the value calculated based on the lung tissue density and gas mixture (~ -670 HU). One potential limitation of this work is the comparison of ventilation measurements using two different gas types (helium and xenon) which have different densities and diffusion coefficients. In future, we plan to compare our CT results with hyperpolarized xenon gas MR studies.

REFERENCES: 1.Deninger, et al. MRM 2002;48:223-32. 2. Spector, et al. MRM 2005;53:1341-46. 3. Moller, et al. MRM 2001;45:421-30. 4. Marcucci, et al. J. Appl. Physio. 2001;90:421-30. 5. Zhao, et al. J. Magn. Reson. B 1996;113:179-183.

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Fig.2: Representative MR image obtained after 10 breaths of helium.

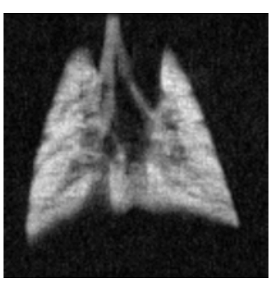

Fig.3: Representative CT image obtained after 10 breaths of xenon.