Assessment of Lung Volumes using Hyperpolarized ^{3}He MR Imaging in Rodents: Comparison with Xenon-enhanced X-ray CT

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INTRODUCTION: Chronic obstructive pulmonary disease is a leading cause of mortality worldwide, and is predicted to rise from fourth to third in terms of morbidity within three decades [(1)]. Quantitative assessment of lung volumes through imaging has been shown to be effective in providing fundamental insight into specific diseases mechanisms allowing for earlier detection and improved treatment of chronic obstructive diseases such as emphysema [(2)]. Hyperpolarized ^{3}He Magnetic Resonance (MR) imaging is a modality that directly visualizes the inhaled gas mixture, allowing imaging of ventilated lung volumes. Due to the absence of ionizing radiation, ^{3}He MR imaging may be the modality of choice for monitoring the progression and regression of chronic lung disease in longitudinal studies. In addition, quantitative lung imaging may play an important role in basic research using rodent models of disease. In this study, we compared ^{3}He MR measurements of ventilated lung volumes in rats to volumes measured from xenon-enhanced Computed Tomography (CT), under the same ventilation conditions. We propose that ^{3}He MR imaging will provide volume estimates comparable to xenon-enhanced CT without the associated dose of ionizing radiation.

METHODS: Wistar rats (n=3) were anaesthetized, and ventilated at a rate of 60 breaths per minute. Helium MR imaging was performed at 3T (Signa, GEHC) using hyperpolarized ^{3}He gas provided by a spin-exchange polarizing system (Helispin, GEHC). Multislice coronal images were obtained using a fast gradient echo sequence (TE=1.2 ms, TR=4 ms, 128 x 128, FOV=4 cm, slice thickness=4 mm) following 5 'wash-out' breaths of pure helium at peak inspiratory pressure of 8 cm H_2O provided by a custom ventilator (Malmo, GEHC) [(3)].

Xenon CT imaging was performed on the same rats using a pre-clinical micro CT scanner (Locus Ultra, GEHC) at 80 kVp and 60 mA during continuous 1-sec volumetric scans (synchronized with the breathing rate). Rats were ventilated first with air only, and subsequently with xenon gas mixed with oxygen (80/20), using a SAR-830/AP ventilator (CWE, Ardmore PA), with peak inspiratory pressure of 8 cm H_2O. Axial images were acquired during the inhalation of gas with in-plane resolution of 0.152 mm and slice thickness of 0.456 mm [(4)]. In order to assure proper build up of xenon gas in lungs, images acquired after 10 breaths of xenon gas mixture were selected for image analyses. MR and CT experiments were repeated 3 times on each animal to determine measurement precision.

MR Signal voxels were segmented from background noise using a seeded region-growing algorithm (MicroView, GEHC). The volume of the lung was calculated from the volume of connected voxels with intensities above a threshold. The threshold was selected to maximize the between-class variance in the image histogram, thus segmenting signal voxels from background [(5)]. For CT, xenon-enhanced images were subtracted from the air-only image, and similarly, a seeded region-growing algorithm was used to separate 3D lung volumes from surrounding tissue. Therefore, only connected voxels with Hounsfield Unit (HU) intensities within the interval of the xenon gas mean HU value (measured in the trachea) ± 3 times the standard deviation of background voxels were included in the analyses.

RESULTS: Figures 1 and 2 show representative MR and CT images obtained after 5 breaths of helium and 10 breaths of xenon mixture respectively in the same animal. Figure 3 illustrates a xenon-enhanced image obtained from xenon/air subtracted images. Measured ventilated volumes from helium MR and xenon-enhanced CT methods, as well as air-only lung volumes (ventilated plus non-ventilated) are presented in Table 1.

Fig.1: Representative MR image obtained after 5 breaths of pure ^{3}He.

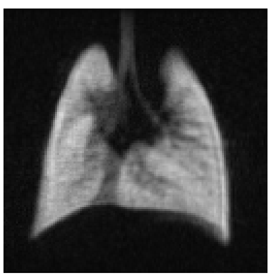


Fig.2: Representative CT image obtained after 10 breaths of Xe/O_2 mixture.

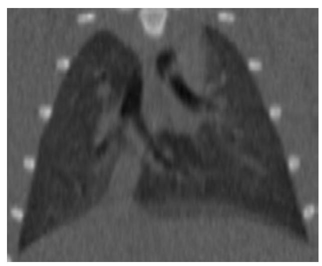
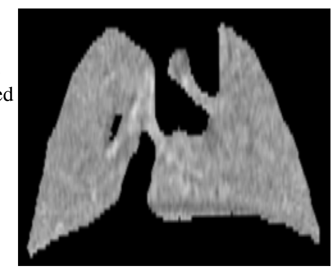


Fig.3: Representative xenon-enhanced image after subtraction.



Rat No.	^{3}He-MR Volume (cc)	Xenon Subtraction-CT Volume (cc)	Air-only CT Volume (cc)
1	**6.61 ± 0.48**	**6.17 ± 0.41**	**6.19 ± 0.38**
2	**6.63 ± 0.18**	**6.37 ± 0.23**	**6.56 ± 0.18**
3	**5.42 ± 0.43**	**5.07 ± 0.06**	**5.09 ± 0.04**

Table 1: Volumes of normal rat lungs measured by MR and CT represented as mean ± standard deviation.

Volumes determined with ^{3}He MR and xenon-enhanced CT were not significantly different ($p = 0.25$). Mean difference between the two technique was approximately 6%, with xenon subtraction CT as the gold standard. Reproducibility of MR and CT experiments, assessed by coefficient of variation, were approximately 6% and 4%, respectively.

DISCUSSION: Our results show that the ^{3}He MR method provides accurate and precise measures of lung volumes as confirmed with xenon-enhanced CT method. Good agreement between subtracted xenon CT volumes and the volumes measured from non-enhanced (air-only) images (Table 1) confirms full ventilation of the lung, as expected in normal animals. This validation technique can be extended to diseased models of animals, since both He-MR and Xe-CT methods are capable of excluding non-ventilated regions of lung (caused by ventilation defects such as gas trapping) from volume calculations. Our calculation of volume included the anatomical dead space (i.e. main airways); however, this did not affect the accuracy of volume estimation because major airways were included in both MR and CT image analyses. Helium MR and xenon CT volumes shown in Table 1 represent an upper limit estimate of ventilated volumes as they don't account for partial volumes in voxels at gas/ tissue interfaces of lung. Measurement of absolute ventilated volume requires an estimate of regional lung density which can be obtained from CT data, but has to be modeled for MR. The systematically-higher volumes measured by MR compared to CT may be due to the stronger partial volume effect of the larger MR voxels. Accuracy of volume estimation can be further improved by acquiring the xenon-enhanced images at breath-hold in order to maintain a steady inspiratory pressure during the image acquisition, and reduce motion artifacts in the subtracted image.

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