Gravitational Distribution Gradient of Inert Fluorinated Gases in Human Lungs Using ^{19}F Ultra-Short Echo Time MRI

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Introduction: Functional ^{19}F magnetic resonance (MR) imaging using inert fluorinated gases may be a valuable technique for gathering functional and regional information from the lungs. ^{19}F MR imaging has been recently reported in healthy volunteers (1) and subjects with lung diseases (2), and this technique has the potential to provide images that are similar in quality to hyperpolarized (HP) noble gas MRI. Inert fluorinated gases have the advantages of being nontoxic, abundant, and inexpensive. Since ^{19}F has a high gyromagnetic ratio, there is sufficient thermal polarization for imaging, and averaging within a single breath-hold is possible due to short longitudinal relaxation times. It is well-known that pulmonary ventilation exhibits a gravitational gradient due to a gradient in regional compliance. This relationship has been demonstrated with xenon-enhanced CT (3), O_2-enhanced ^{1}H MRI (4), and HP noble gas MRI (5). Inert fluorinated gas MRI is expected to exhibit similar ventilation gradients, especially since they are very dense gases. To our knowledge, a gravitational distribution of pulmonary ventilation has not been quantitatively demonstrated using ^{19}F MRI in humans. In the present study, ^{19}F 3D ultra-short echo time (UTE) imaging was performed in healthy subjects with inert fluorinated gases, and anterior/posterior (A/P) ventilation gradients were measured.

Methods: This study protocol was approved by the local ethics review board and by the appropriate governmental agencies. All subjects provided written informed consent prior to their participation in this study. Imaging was performed using a 3.0 T Philips Achieva scanner and a flexible wrap-around quadrature transmit/receive coil tuned to the ^{19}F resonance frequency of 120.15 MHz (Clinical MR Solutions). Six healthy volunteers (5 female, 1 male) were enrolled in this study with no previous history of lung disease. The mean age of all subjects was 30 ± 13. Subjects were imaged supine during a 15 second breath-hold following inhalation of a gas mixture of 79% perfluoropropane (PFP) and 21% O_2 from a Tedlar bag. For 4 subjects, ^{19}F 3D UTE MR images were acquired in the axial plane following a 1L inhalation of the PFP/O_2 mixture with the following settings: TR = 20 ms, TE = 0.2 ms, matrix = 64 x 64, 8 slices, 22 mm thickness, in-plane FOV = 450 x 450 mm^2, flip angle = 70°, and bandwidth = 140 Hz/pixel. For 2 subjects, ^{19}F 3D UTE MR images were acquired following continuous breathing from a 5 L bag of the PFP/O_2 mixture, followed by a 1 L inhalation of the same mixture from a separate bag and 15 s breath-hold. For these 2 subjects only, 12 slices were acquired with a 15 mm thickness. A threshold was manually set to separate the lungs from the surrounding background and all slices were combined to create a single projection image of the entire lung. The mean normalized signal intensity was plotted as a function of distance from the most posterior edge of the lung, and the slope of a linear regression yielded the ventilation gradient.

Table 1: Summary of measured ventilation gradients, coefficients of determination (R^2), and percent changes in ventilation along the vertical direction for all six healthy volunteers. The first four volunteers inhaled the PFP/O_2 mixture as a 1 L bolus, and the last two volunteers inhaled the PFP/O_2 mixture using the continuous breathing method.

Subject #	Ventilation Gradient [cm^{-1}]	R^2	Percent Change [%]
1	-0.03058±0.00006	0.742	-75.4
2	-0.04107±0.00006	0.747	-81.2
3	-0.03315±0.00004	0.635	-80.4
4	-0.02259±0.00004	0.548	-66.6
5	-0.03759±0.00005	0.808	-76.6
6	-0.03325±0.00003	0.928	-84.2

Results and Discussion: Table 1 shows a summary of the measured ventilation gradients from all six healthy volunteers, along with the coefficients of determination (R^2), and percent changes in ventilation along the vertical direction. Qualitatively, there was no apparent difference between the ventilation gradients calculated for subjects that inhaled the PFP/O_2 mixture as a 1 L bolus (subjects 1-4) and subjects that inhaled the PFP/O_2 mixture using continuous breathing from a 5 L bag followed by a 1 L bolus inhalation and breath-hold (subjects 5 and 6). Figure 1 shows a whole lung axial projection image that was obtained from a representative ^{19}F 3D UTE image that was acquired in the axial plane in subject #6. Figure 2 shows the normalized signal intensity from the image shown in Figure 1 plotted as a function of vertical distance from the dorsal surface of the lung. The solid line represents the calculated ventilation gradient, which has a slope of -0.033 cm^{-1}, which represents an 84% change in signal intensity from the anterior to posterior edges of the lung.

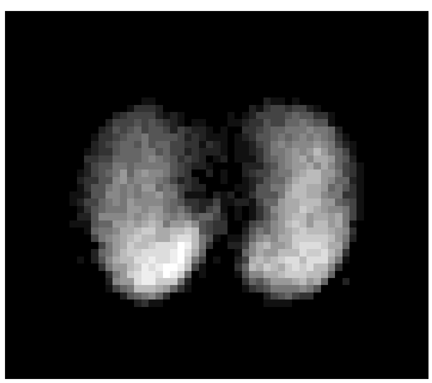

Figure 1: Whole lung axial projection image acquired in a representative healthy volunteer during a 15 second breath-hold of a mixture of 79% PFP and 21% O_2.

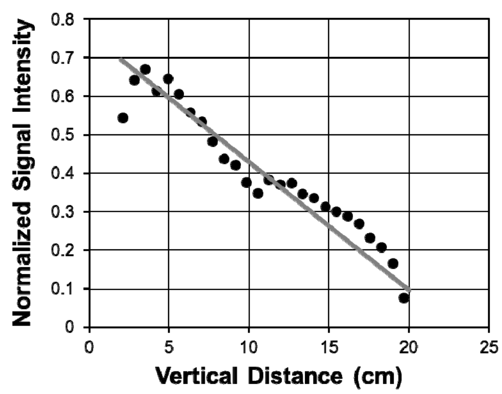

Figure 2: Normalized signal intensity from a representative whole lung axial projection image plotted as a function vertical distance. The solid line represents the calculated ventilation gradient.

Conclusion: This preliminary study demonstrates a clear gravitational distribution gradient of inert fluorinated gases in human lungs using ^{19}F 3D UTE MRI, and there is a potential for this technique to provide functional and regional information regarding lung physiology.

References: [1] Couch MJ et al, (2013) *Radiology*, doi:10.1148/radiol.13130609. [2] Halaweish AF et al, (2013) *Chest*, 144(4):1300-1310. [3] Lam WW et al, (2007) *J Appl Physiol* 103:1848-1856. [4] Sá RC et al, (2010) *J Appl Physiol* 109:1950-1959. [5] Månsson S et al, (2005) J Appl Physiol 98:2259-2267.