Comparing Pulmonary MRI using Inert Fluorinated Gases and Hyperpolarized ^{3}He: Is ^{19}F MRI Good Enough?

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Introduction: Fluorine-19 (^{19}F) magnetic resonance imaging (MRI) of the lungs using inhaled inert fluorinated gases is a technique currently under development that can potentially provide images of the distribution of pulmonary ventilation, similar to hyperpolarized (HP) noble gas MRI. Inert fluorinated gases, such as sulfur hexafluoride (SF_6) and perfluoropropane (C_3F_8 or PFP), have several potential advantages over HP gases, as they are nontoxic, abundant, and inexpensive. MR Imaging of thermally polarized inert fluorinated gases is made possible due to the high gyromagnetic ratio and high natural abundance of ^{19}F. Furthermore, the short longitudinal relaxation times of inert fluorinated gases allows for multiple averages within a single breath-hold. Therefore, pulmonary ^{19}F MRI is possible without the expensive polarizer and scarce isotopes that are required for HP gas MRI. Inert fluorinated gas MRI of the lungs has been previously demonstrated in a number of animal studies (1, 2), and more recent work has demonstrated imaging in healthy volunteers (3) and patients with lung diseases such as chronic obstructive pulmonary disease (COPD), asthma, and lung transplants (4). The work to date has been performed in stand-alone studies using various techniques to optimize the image quality. As interest in this new pulmonary imaging technique is growing, validation studies and comparisons to existing pulmonary imaging techniques will be required in order to consider all factors that contribute to image features and image quality, including the physical properties of these heavy fluorinated gases. This preliminary study demonstrates for the first time, a direct comparison between inert fluorinated gas and HP ^{3}He MR lung imaging in the same subjects.

Methods: This study protocol was approved by the local ethics review board and by the appropriate governmental agencies. All imaging in this study was performed using a 3T Philips Achieva scanner and two flexible wrap-around quadrature transmit/receive coils tuned to either the ^{3}He or ^{19}F resonant frequencies (Clinical MR Solutions). Five healthy female volunteers (mean age=23±3 years) were enrolled in this study with no previous history of lung disease. ^{1}H 2D multi-slice gradient echo images were initially acquired using a 1L breath-hold of air, and these images were used as reference scans for planning ^{3}He and ^{19}F image acquisitions. ^{3}He MR images were acquired following inhalation of a 1L bag containing 330mL of hyperpolarized ^{3}He balanced to 1L with N_2. ^{3}He images were obtained during a 15s breath-hold using a 2D multi-slice gradient echo method in the coronal plane with the following settings: TR=56ms, TE=1.53ms, matrix=128x64 reconstructed to 256x256, 14 slices, in-plane FOV=450x450mm^2, 15mm thickness, flip angle=7°, and BW=500Hz/pixel. ^{19}F images were obtained during a 25s breath-hold using either a 3D ultrashort echo time (UTE) or 3D gradient echo acquisition that followed several wash-out breaths of a mixture of 79% PFP and 21% O_2. ^{19}F 3D UTE imaging used the following settings: TR=20ms, TE=0.2ms, matrix=64x64, 12 slices, in-plane FOV=450x450mm^2, 15mm thickness, flip angle=70°, 75% radial sampling density, and BW=200Hz/pixel. ^{19}F 3D gradient echo images were acquired with the following settings: TR=16ms, TE=1.08ms, matrix=64x64, 12 slices, in-plane FOV=450x450mm^2, 15mm thickness, flip angle=70°, 5 averages, and BW=200Hz/pixel. The signal-to-noise ratio (SNR) was measured in Matlab, and a semi-automated segmentation algorithm was used to calculate the ventilated volume (VV), ventilation defect volume (VDP), and ventilation defect percent (VDP) (5). The SNR and volume measurements were compared between HP ^{3}He and ^{19}F imaging using GraphPad Prism.

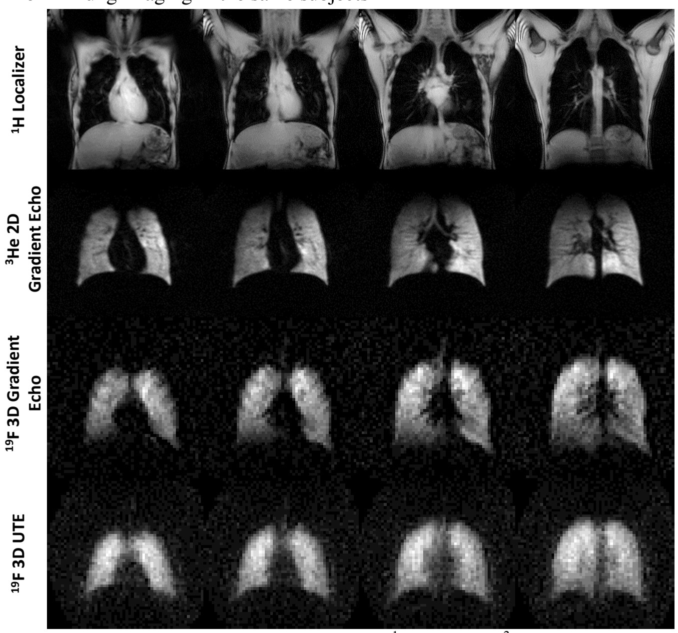

Figure 1: Comparison of representative ^{1}H localizer, ^{3}He 2D gradient echo, ^{19}F 3D gradient echo, and ^{19}F 3D UTE images acquired in the same healthy volunteer.

Results and Discussion: Figure 1 shows a comparison of 4 central coronal slices that were obtained using a ^{1}H localizer, HP ^{3}He gradient echo, ^{19}F gradient echo, and ^{19}F UTE in subject #4. The HP ^{3}He images can easily be reconstructed to a higher resolution than ^{19}F images, such that the major airways and pulmonary vasculature can be seen. On the other hand, the ^{19}F images have a lower SNR, poorer resolution, more poorly defined edges, and T_2^*-induced blurring is apparent in the UTE images. A summary of the measured SNR for all HP ^{3}He and ^{19}F images is shown in Table 1. Note that the type of image acquisition used for ^{19}F MRI is indicated. As expected, the HP ^{3}He SNR was significantly greater than the SNR from inert fluorinated gas imaging ($p=0.01$ from a two-tailed paired t-test). The HP ^{3}He SNR ranged from 39 to 75, while the inert fluorinated gas SNR ranted from 8 to 18. Variability in the HP ^{3}He SNR can be explained by day-to-day variability in polarizer performance, while variability in the inert fluorinated gas SNR can be explained by variations in coil calibration due to body size as well as subject compliance with regard to taking multiple breaths of the fluorinated gas mixture. Although the current image quality from inert fluorinated gas MRI is less than what can be achieved using HP gas MRI, the development of novel and efficient image acquisition techniques is ongoing (6). Table 2 summarizes the volume measurements that were obtained in three subjects. Two of the five subjects in this study were not included in the volume measurements, since a larger slice thickness was used in those cases. Overall, the VV, VDV, and VDP measurements from HP ^{3}He and inert fluorinated gas imaging were statistically indistinguishable ($p>0.05$). More subjects will be required in order to fully validate inert fluorinated gas imaging and to determine if the volume measurements yield meaningful results. It is interesting to note that the VV measurements were similar for both techniques in most cases, as imaging was performed at approximately functional residual capacity (FRC)+1L. In most cases, the VDV and VDP were larger for inert fluorinated gas imaging compared to ^{3}He MRI. This result may be explained by a lower SNR and poorly defined edges, or it may be related to the physical properties of the inert fluorinated gas, such as the high density and low diffusivity compared to ^{3}He (7).

Table 1: Comparison of SNR measurements obtained from ^{3}He and ^{19}F MRI in all subjects.

Subject	^{3}He SNR	^{19}F SNR	^{19}F Sequence
1	72 ± 37	18 ± 8	3D UTE
2	99 ± 50	8 ± 3	3D UTE
3	75 ± 36	8 ± 2	3D UTE
4	40 ± 18	16 ± 6	3D Gradient Echo
		15 ± 6	3D UTE
5	39 ± 16	9 ± 4	3D Gradient Echo

Table 2: Comparison of VV, VDV and VDP measurements obtained from ^{3}He and ^{19}F MR imaging in the lungs of three subjects.

	^{3}He			^{19}F		
Subject	VV (L)	VDV (L)	VDP (%)	VV (L)	VDV (L)	VDP (%)
3	3.8	0.11	2.9	3.34	0.55	14.14
4	4.9	0.28	5.35	6.13	0.55	8.3 (GE)
				5.33	0.24	4.29 (UTE)
5	5.33	0.27	4.83	5.05	0.59	10.5

Conclusions: Although the SNR in inert fluorinated gas MR images was less than HP ^{3}He images, the lung volume measurements in this preliminary study were statistically indistinguishable between the two techniques. Therefore, inert fluorinated gas MRI has the potential to yield meaningful functional information that is similar to HP ^{3}He MRI. Future comparison studies in patients with pulmonary diseases will determine if inert fluorinated gas MRI can become a viable clinical imaging modality that can aid in diagnostic decision making.

References: [1] Kuethe et al. (1998) *Magn Reson Med* 39:85-88. [2] Schreiber et al. (2001) *Magn Reson Med* 45:605-613. [3] Couch et al. (2013) *Radiology* 269:903-909. [4] Halaweish et al. (2013) *Chest*, 144:1300-1310. [5] Kirby et al. (2012) *Acad Radiol* 19:141-152. [6] Ouriadov et al. (2014) Magn Reson Med doi:10.1002/mrm.25406. [7] Kirby et al. (2012) Radiology 265:600-610.