REPRODUCIBILITY OF HYPERPOLARIZED XENON-129 MAGNETIC RESONANCE IMAGING OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Purpose: Hyperpolarized helium-3 (^{3}He) magnetic resonance imaging (MRI) has emerged as a highly reproducible research method for the evaluation of structural and functional lung measurements associated with chronic obstructive pulmonary disease (COPD). Unfortunately, the limited access to ^{3}He MRI and the high cost of ^{3}He gas has presented serious roadblocks for clinical translation. Another approach involves the use of hyperpolarized xenon-129 (^{129}Xe) gas and this provides some distinct differences and advantages compared to ^{3}He MRI. However, before ^{129}Xe can be used as an alternative to ^{3}He MRI, the reproducibility of ^{129}Xe measurements over short periods of time must be evaluated. Therefore our objective was to determine the reproducibility of ^{129}Xe functional measurements within the same day (5-min rescan) and after a period of 7 days in subjects with COPD.

Materials and Methods

Subjects: Nine ex-smokers with a clinical diagnosis of COPD between the ages of 50-85 provided written informed consent to a study protocol approved by the local research ethics board and Health Canada. Three of these subjects returned for follow-up imaging 7-days later for evaluation of reproducibility.

Image Acquisition: MRI was performed on a whole body 3.0 Tesla Discovery 750MR (General Electric Health Care, Milwaukee, WI) with broadband imaging capability as previously described[1]. ^{1}H images were acquired prior to ^{129}Xe imaging with subjects scanned during a 1L breath-hold of ^{4}He/N_2 using the whole body RF coil and proton fast spoiled gradient-echo (16s total data acquisition, relaxation time (TR)/echo time (TE)/flip angle = 4.7 ms/1.2 ms/30^o, field-of-view (FOV) = 40 x 40 cm, matrix 256 x 256, 14 slices, 15 mm slice thickness, 0 cm gap). For ^{129}Xe MRI a commercial turn-key polarizer model XeBox-E10 (Xemed LLC, New Hampshire, USA) was used. ^{129}Xe MRI diffusion-weighted images were obtained using a 2D FGRE. Two interleaved images (16s total data acquisition, TR/TE/flip angle = 9.85 ms/11 ms/5^o, bandwidth = 31.25, FOV = 40 x 40 cm, matrix 128 x 128, 7 slices, 30 mm slice thickness), with and without additional diffusion sensitization with b = 12 s/cm^2 (G = 2.90 G/cm, rise and fall time = 0.5 ms, gradient duration = 2.0 ms, Δ = 5 ms) and b = 20 s/cm^2 (G = 3.75 G/cm, rise and fall time = 0.5 ms, gradient duration = 2.0 ms, Δ = 5 ms), were acquired.

Image Analysis: ^{129}Xe non-diffusion-weighted images for b = 12 s/cm^2 and b = 20 s/cm^2 were acquired approximated 5-min apart at the first imaging time-point and again at the 7-day follow-up time-point and were utilized for ventilation analysis. The non-diffusion-weighted images were evaluated by semi-automated segmentation of voxel intensities where cluster 1 (C1) represented regions of signal void or ventilation defect volume (VDV), and cluster 2 to cluster 5 (C2-C5) represented gradations of signal intensity from hypo-intense (C2) to hyper-intense signal (C5)[1] for all 7 slices. ^{129}Xe ventilation defect percent (VDP) was generated as VDV normalized to the thoracic cavity volume. The image signal-to-noise ratio (SNR) for all image slices was calculated as the mean pixel value within a 5x5 voxel region of interest (ROI) for four representative regions within the lung parenchyma divided by the standard deviation of the mean pixel value for noise within four ROI of the same size in the image background.

Statistical Analysis: A repeated measures analysis of variance was performed for statistical comparison of ^{129}Xe ventilation cluster measurements at scan and 5-min rescan for all COPD subjects as well as at scan, 5-min rescan and 7-day rescan for the three COPD subjects with follow-up imaging using SPSS 16.00.

Results: Table 1 shows the ^{129}Xe MRI measurements for all nine COPD subjects (n=1 Stage I, n=6 Stage II, n=1 Stage III, n=1 Stage IV) at scan and 5-min rescan. For all COPD subjects there was no significant difference for ^{129}Xe ventilation cluster measurements between the scan and 5-min rescan time-points (VDP: p=.80, C2: p=.20), C3: p=.14, C4: p=.14, C5: p=.08). Table 2 shows the ^{129}Xe MRI measurements for the three COPD subjects that received scan, 5-min rescan and 7-day rescan follow-up imaging. Figure 1 shows the center slice image for each of the three subjects that performed the 7-day follow-up imaging. There was no significant difference detected for ^{129}Xe ventilation cluster measurements between the three time-points (VDP: p=.06, C2: p=.10, C3: p=.15, C4: p=.81, C5: p=.18).

Conclusions: In this first evaluation of ^{129}Xe MRI reproducibility in COPD ex-smokers, we observed no significant difference in the gas distribution in the lung over short periods of time when no physiological change was expected to occur. These findings agree with previous reports of high short-term reproducibility for ^{3}He MRI measurements and suggest that ^{129}Xe is a highly reproducible noble gas and may be a feasible alternative to ^{3}He MRI with strong translational potential in COPD studies.

Table 1. ^{129}Xe MRI measurements at scan and 5-min rescan

Parameter	Scan (n=9)	5-min Rescan (n=9)	P-value
VDP % (±SD)	26 (12)	26 (12)	0.80
C2 % (±SD)	17 (5)	16 (5)	0.20
C3 % (±SD)	20 (13)	24 (11)	0.14
C4 % (±SD)	20 (13)	24 (11)	0.14
C5 % (±SD)	12 (6)	11 (5)	0.08

SD=Standard Deviation, VDP=Ventilation Defect Percent, C2=Cluster 2, C3=Cluster 3, C4=Cluster 4, C5=Cluster 5

Table 2. ^{129}Xe MRI measurements at scan, 5-min rescan and 7-day rescan

Parameter	Scan (n=3)	5-min Rescan (n=3)	7-day Rescan (n=3)	P-value
VDP % (±SD)	22 (6)	19 (9)	22 (9)	0.06
C2 % (±SD)	17 (4)	15 (2)	14 (0)	0.10
C3 % (±SD)	26 (13)	31 (6)	29 (8)	0.15
C4 % (±SD)	23 (5)	24 (9)	23 (10)	0.81
C5 % (±SD)	13 (5)	11 (7)	11 (10)	0.18

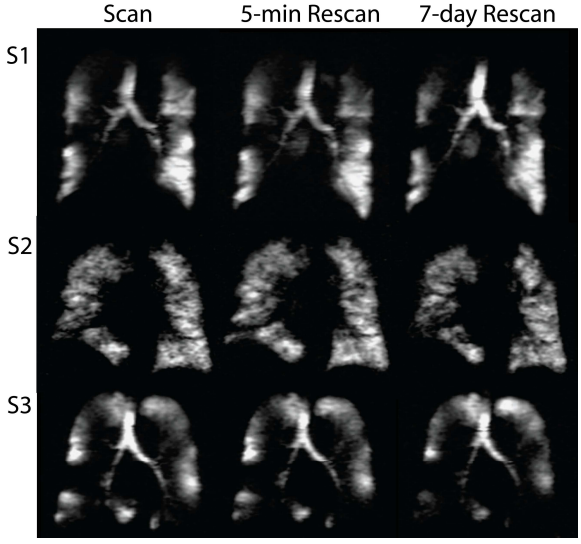

Figure 1. ^{129}Xe MRI at scan, 5-min rescan and 7-day rescan for all three COPD subjects.

References

1. Kirby, M. *et al. Acad Radiol.* (2011).