Anatomical Distribution of Hyperpolarized ^{3}He and ^{129}Xe MRI Apparent Diffusion Coefficients in Asthma

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Purpose: The high cost and limited availability of ^{3}He gas worldwide has restricted clinical translation of this structure-function pulmonary imaging method, necessitating a transition to xenon-129 (^{129}Xe) gas for hyperpolarized pulmonary imaging which provides some distinct differences that must be explored. We previously evaluated (1) the anatomical distribution of hyperpolarized ^{3}He MRI apparent diffusion coefficients (ADC) in chronic obstructive pulmonary disease (COPD) with the aim being the development of an understanding of regional gas trapping and emphysema. Here we quantitatively compare ^{3}He and ^{129}Xe MRI ADC in asthma and the relationship of anterior-to-posterior (AP) ADC gradients.

Materials and Methods

Subjects: Seven subjects with asthma provided written informed consent to the study protocol approved by the local research ethics board and Health Canada and underwent spirometry and hyperpolarized ^{3}He and ^{129}Xe MRI. Asthma patients were enrolled between the ages of 18-60 years, with baseline $FEV_1 > 60\%_{pred}$ measured by spirometry. Imaging was performed in the morning before and after inhalation of 400 ug salbutamol and after subjects withheld short-acting bronchodilators overnight. In a subset of subjects (n=5), we compared ^{129}Xe MRI to ^{3}He MRI performed 356±226 days prior.

Image Acquisition and Analysis: 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). For ^{3}He MRI, a polarizer system (HeliSpin™) was used to polarize ^{3}He gas. Hyperpolarized ^{3}He MRI diffusion-weighted images were acquired during breath-hold of a 1L ^{3}He/N_2 mixture obtained using a fast gradient-echo method (FGRE). Two interleaved images (14s total data acquisition, TR/TE/flip angle = 7.6 ms/3.7 ms/8°, FOV = 40 x 40 cm, matrix 128 x 128, 7 slices, 30 mm slice thickness), with and without additional diffusion sensitization (G = 1.94 G/cm, rise and fall time = 0.5 ms, gradient duration = 0.46 ms, Δ = 1.46 ms, b = 1.6 s/cm^2), were acquired. For ^{129}Xe MRI a commercial turn-key polarizer model XeBox-E10 (Xemed LLC, New Hampshire, USA) was used. Hyperpolarized ^{129}Xe diffusion-weighted images were acquired during breath-hold of a 1L ^{129}Xe/^{4}He mixture obtained using a FGRE pulse sequence. Two interleaved images (16s total data acquisition, TR/TE/flip angle = 9.85 ms/11 ms/5°, 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 = 30 s/cm^2 (G = 4.60 G/cm, rise and fall time = 0.5 ms, gradient duration = 2.0 ms, Δ = 5 ms), were acquired. Hyperpolarized ^{3}He and ^{129}Xe ADC maps were generated using in-house software for generation of mean and standard deviation (SD) ADC for each of the four coronal center slices. AP anatomical differences in ADC were generated as: 1) ADC ΔAP, and, 2) measuring the slope of the change in ADC from anterior-to posterior or the AP-gradient as previously described (1). We also evaluated the relationship of ADC measurements to signal-to-noise ratio (SNR) for all slices.

Statistical Analysis: A paired two-tailed t-test was performed for statistical comparison of ^{3}He and ^{129}Xe SNR measurements. Linear regression (r^2) and Pearson correlation coefficients (r) were also used to determine the relationships between spirometry and ^{3}He and ^{129}Xe MRI measurements, as well as to determine the relationship between AP ADC measurements. All statistical analysis was performed using GraphPad Prism version 4.00 (GraphPad Software Inc, San Diego, CA, USA), results were considered significant when the probability of making a Type I error was less than 5% ($p < .05$).

Results: All seven asthma subjects completed ^{129}Xe MRI and five of these completed ^{3}He MRI previously for comparison. For those subjects with both ^{3}He and ^{129}Xe MRI, (44±6 years), ^{129}Xe MRI SNR (16±5) was significantly lower (p=0.005) than ^{3}He MRI (30±20) and there was no significant relationship between SNR and ADC for either gas. There were no significant relationships between ADC and spirometry measurements for either gas. Figure 1 shows ^{3}He and ^{129}Xe ADC maps for a representative asthma subject and Table 1 shows mean ADC for all subjects. The AP difference was statistically significant (p=0.04) for ^{129}Xe ADC. Figure 2 shows ^{3}He and ^{129}Xe ADC AP gradients, the relationship between anatomical location and ^{3}He ADC was strong and statistically significant (r = -0.98, r^2 = 0.95, slope = -0.014, p=0.024).

Conclusions: In this small pilot study we compared ^{3}He and ^{129}Xe ADC anatomical differences from the anterior to posterior slices in five subjects with asthma. For both ^{3}He and ^{129}Xe, the relationship between anatomical location and ADC was statistically significant. Although ^{129}Xe atoms are heavier, have slower diffusion coefficients in air with the potential for less homogeneous mixing, anatomical ADC gradients are similar to ^{3}He MRI which bodes well for translation.

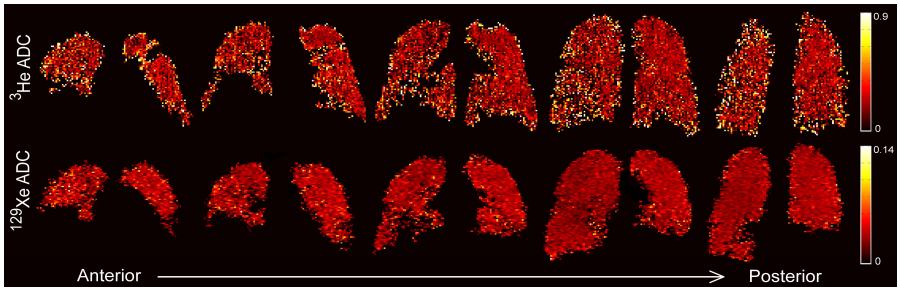

Figure 1. ^{3}He and ^{129}Xe MRI anterior to posterior ADC maps for a representative asthma subject.

Table 1. Mean ^{3}He and ^{129}Xe ADC Measurements

	^{3}He MRI* (N = 5)	^{129}Xe MRI** (N = 5)
Center-slice mean ADC (cm^2/sec)	0.23 ± 0.060	0.035 ± 0.0032
Center-slice SD of ADC (cm^2/sec)	0.11 ± 0.058	0.012 ± 0.0021
ΔAP (cm^2/sec)	0.039 ± 0.033	0.0032 ± 0.0024
AP-gradient (cm^2/sec/cm)	-0.014 ± 0.0022	-0.0010 ± 0.00034

*b=1.6, **b=30

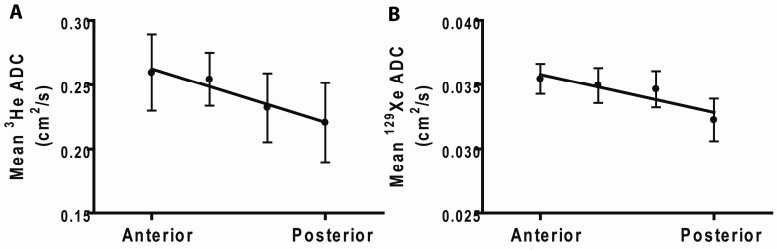

Figure 2. Mean anterior to posterior ADC gradient. A) Mean ^{3}He ADC for five asthma subjects from the anterior to the posterior slices (r = -0.98, r^2 = 0.95, slope = -0.014, p=0.024), B) Mean ^{129}Xe ADC for 5 asthma subjects from the anterior to the posterior slices (r = -0.90, r^2 = 0.81, slope = -0.0010, p=0.10).

References

1. Evans, A. *et al. J Magn Reson Imaging.* (2007)