Hyperpolarized ^{3}He MRI at 3.o Telsa: Anatomic Bias of Apparent Diffusion Coefficients in Chronic Obstructive Pulmonary Disease

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INTRODUCTION: The use of hyperpolarized helium-3 magnetic resonance imaging (^{3}He MRI) to measure regional and whole lung apparent diffusion coefficients (ADC) in chronic obstructive pulmonary disease (COPD) has been undertaken by a number of research groups and recently at our center in an assessment of age-matched subjects stratified by disease (1). Studies that exploit ADC measurements to probe the lung microstructure support the understanding that emphysematous destruction of alveoli results in increased ADC measurements as well as the fact that ^{3}He ADC is age- and lung region-dependent (2-4). The variability of same-day scan ADC measures has been established in at least one center (2). One issue that makes interpretation of regional ADC values complex in COPD is ADC variation in specific regions of healthy lung due to gravitational and/or tissue compression. This has been shown in both superior-to-inferior (SI) as well as anterior-to-posterior (AP) directions in normal subjects (4). These 'background' ADC gradients may mask or accentuate changes in ADC measured in subjects with COPD. In this work, we evaluate ADC superior-inferior and anterior-posterior differences in COPD patients and age-matched healthy volunteers. Results indicate that both anterior-posterior and superior-inferior lung ADC gradients differ in healthy and diseased lungs and this has implications for the analysis of regional ADC measurements in COPD.

METHODS: Helium MR imaging was performed at 3.0 Tesla (General Electric Health Care) using hyperpolarized helium (35%) provided by a turn-key spin-exchange polarizing system (Helispin®, GEHC). The gas was administered as previously described (1). Multislice images were obtained in the coronal plane using a fast gradient-recalled echo method (TE=1.2 ms, TR=4 ms, 128 x 128) with (b=1.6 s/cm^2) and without diffusion-weighting (b=0). Same-day reproducibility was assessed in all subjects (N = 25) and twenty three subjects returned within 7+/-2 days for assessment of weekly reproducibility. Spirometry was performed pre and post-MRI. Region-of-interest (ROI) analysis was employed using 3DQuantify (1) and ADC values were computed by a single trained observer as previously described (1). Subjects were stratified to healthy volunteer, mild-moderate COPD and severe COPD subgroups on baseline spirometry values. All subjects provided written informed consent to a study protocol approved by a local ethics board (The University of Western Ontario) and Health Canada.

RESULTS. Figure 1 shows the difference in ADC values in the superior-inferior direction (ΔSI) over 3 lung regions of interest (ROIs) for all subjects stratified by disease group. Figure 2 shows the difference in ADC values in the anterior-posterior direction (ΔAP) for all subjects by subject group as anterior-posterior slice-dependent mean ADC values. Figure 3 shows canonical discriminant analysis results using center-slice mean ADC, anterior-posterior ADC gradient, and center-slice standard deviation of ADC. The results are presented as a 2D plot illustrating the clustering of subjects as separated by the canonical discriminant function.

DISCUSSION: While differences were indicated in ΔSI between all subgroups which is consistent with expected differences in alveolar size from the superior to inferior regions of the lung, these differences were not statistically significant, due to the high inter-subject variability in ΔSI in subjects with mild-moderate and severe COPD. On the other hand, ΔAP differences though smaller than ΔSI differences between subject groups were statistically significant between subjects with severe COPD and those without COPD or mild-moderate disease.

REFERENCES: 1. Parraga et al. J Inv Radiology *Submitted 2006,* 2 Morbach et al. *J Magn Reson Imaging* 2005; 21:765-774 3. Fain et al. *Acad Radiol* 2005; 12:1385-1393 4. Fichele et al *J Magn Reson Imaging* 2004; 20:331-335.

		Healthy Volunteers n = 8		Mild-Moderate COPD n = 7		Severe COPD n = 8	
	Mean ADC* (cm^2/s)	0.25 (0.02)		0.36 (0.11)		0.44 (0.09)	
ROIs	(R...L, 20-25 cm)	0.25 (0.03)	0.27 (0.03)	0.39 (0.15)	0.38 (0.12)	0.49 (0.13)	0.49 (0.13)
		0.25 (0.03)	0.25 (0.02)	0.37 (0.13)	0.37 (0.10)	0.43 (0.09)	0.46 (0.10)
		0.24 (0.02)	0.24 (0.01)	0.33 (0.07)	0.32 (0.06)	0.39 (0.07)	0.40 (0.07)
	ΔSI	0.02 (0.02)	0.03 (0.03)	0.07 (0.09)	0.06 (0.08)	0.10 (0.08)	0.10 (0.10)

Figure 1. ADC Region of Interest (ROI) analysis results where ADC values are in cm^2/s. ΔSI is the change in ADC values in the superior-inferior direction. Bracketed values are standard deviations. ΔSI was not statistically significantly different for healthy volunteers, subjects with mild-moderate COPD and subjects with severe COPD, likely due to high inter-subject variability in the severe and mild-moderate COPD patients.

		Healthy Volunteers n = 8	Mild-Moderate COPD n = 7	Severe COPD** n = 7
	Mean ADC* (cm^2/s)	0.25 (0.02)	0.35 (0.10)	0.44 (0.09)
ROIs		0.28 (0.02)	0.38 (0.09)	0.45 (0.09)
	(R...L, 9.0 cm)	0.26 (0.02)	0.37 (0.08)	0.45 (0.10)
		0.23 (0.02)	0.34 (0.08)	0.44 (0.08)
		0.22 (0.02)	0.32 (0.08)	0.41 (0.08)
	ΔAP	0.06 (0.01)	0.06 (0.02)	0.04 (0.02)

Figure 2. AP analysis of ADC values (cm^2/s). ΔAP is the change in ADC values in the anterior-posterior direction. Bracketed values are standard deviations. ΔAP was statistically significantly different between severe COPD subjects and those with mild-moderate disease or healthy volunteers.
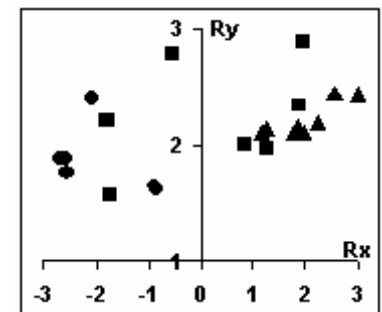
▲ **Healthy Volunteers**
■ **Mild-Moderate COPD**
● **Severe COPD**

Figure 3. Discriminant analysis results using center-slice mean ADC (cm^2/s), anterior-posterior ADC gradient (cm^2/s/cm), and center-slice standard deviation of ADC (cm^2/s) as independent variables. Ry and Rx are unit-less and represent the position of data points on the plane formed by the un-standardized canonical discriminant function coefficients.