Comparison of diffusion weighted helium-3 MRI in patients with asthma versus those with COPD

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Introduction: Hyperpolarized helium-3 (HP He-3) acts as an inhaled contrast agent allowing measurement of gas diffusion into the airspaces of the lung. The mean apparent diffusion coefficient (ADC) of He-3 measured on MRI has been shown to increase in patients with COPD compared to healthy subjects (1, 2) and in asymptomatic smokers compared to never smokers (3). The role of the ADC measure in obstructive lung diseases such as asthma is less clear. The objective of this work is to evaluate the sensitivity of ADC to changes in pulmonary function associated with asthma.

Methods: Mean ADC in subjects with asthma (Asthma; N = 21, Age = 35 ± 13 yrs) was compared to healthy never-smokers (Healthy Never-Smokers; N = 24, Age = 50 ± 15 yrs), and to active smokers and patients with COPD, analyzed as a single group (COPD+Smokers; N = 16, Age = 53 ± 17 yrs). The combination of smokers and COPD patients was justified based on the similarity of ADC behavior in these subjects (3). All subjects underwent He-3 diffusion MRI in the supine position on a 1.5T whole-body MR scanner (Signa Excite, GE Healthcare, Milwaukee, WI) using a vest-shaped RF coil (In Vivo Research, Milwaukee, WI) tuned to receive at 48 MHz. HP He-3 gas was polarized using spin-exchange optical pumping to polarize He-3 to 30-40% with a commercial polarizer (IGI.9600, GE Healthcare, Princeton, New Jersey). Subjects inhaled a 0.72-1.0 L volume of polarized He-3 (~4.5 mMol concentration of polarized nuclei) equivalent to 15% of total lung capacity from functional residual capacity. The whole lung mean ADC results for each group were compared using analysis of covariance (ANCOVA) and to FEV1 and FEV1/FVC using multiple linear regression. Mean ADC has also been shown to be age-dependent in healthy adult never-smokers (4). Therefore, all ANCOVA and regression analyses included age as a covariate. The diffusion-weighted spoiled gradient echo pulse sequence (SPGR) acquired 10 2D slices at a ±15.63 kHz readout bandwidth, 128 × 80 image matrix, 1.5 cm slice thickness, TR/TE of 8.4 msec/4.5 msec and flip angle of ≈ 7°. Diffusion-sensitization gradients (b = 1.6 s/cm^2, $\Delta = \delta = 1.46$ ms) were added to the slice selection axis (anterior/posterior direction) and phase encoded views were acquired alternately with and without diffusion weighting in an interleaved order. For all studies a FOV within the ranges 32-50 cm x 24-37 cm was used to cover the lung anatomy. An ADC measurement was obtained for each voxel by applying a two point log-linear fit to the non-weighted image, S_0, and weighted image, S_1, for each subject using: $S_1 = S_0 e^{-bADC}$.

Results: There was a statistically significant relationship between mean ADC and FEV1%p in the Asthma subjects ($r_{partial}$ = +0.56, p=0.0095; Fig. 1) but not for mean ADC and FEV1/FVC in Asthma (p=0.46). As expected from prior work, there was a statistically significant relationship between mean ADC and FEV1/FVC in the COPD+Smokers subjects ($r_{partial}$ = –0.70, p=0.0035; Fig. 2) although not for mean ADC and FEV1%p in COPD+Smokers (p=0.28). The mean ADC (± SD) for the Asthma group was **0.201±0.024 cm^2/s**, for the Healthy Never-Smokers was **0.240±0.031 cm^2/s**, and for the COPD+Smokers was **0.266±0.070 cm^2/s**. Although the Asthma group had significantly lower ADC compared to the COPD+Smokers (p=0.007) after age correction, the Asthma group did not differ significantly from the Healthy Never-Smokers group (p=0.38), suggesting the lower ADC in Asthma was, in part, explained by their younger age.

Figure 1

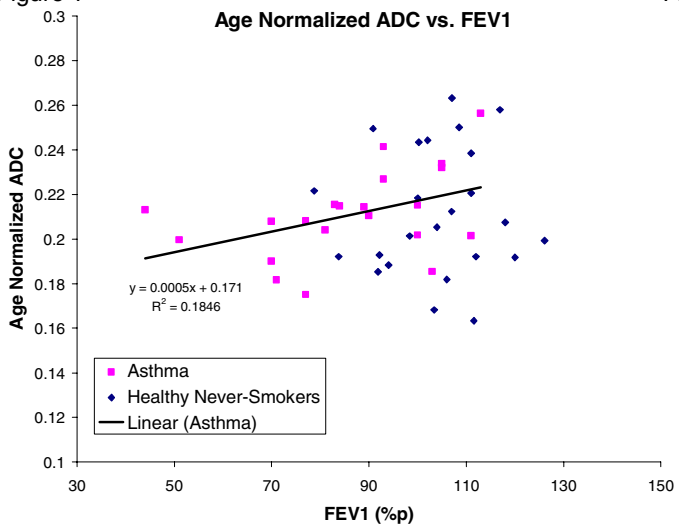
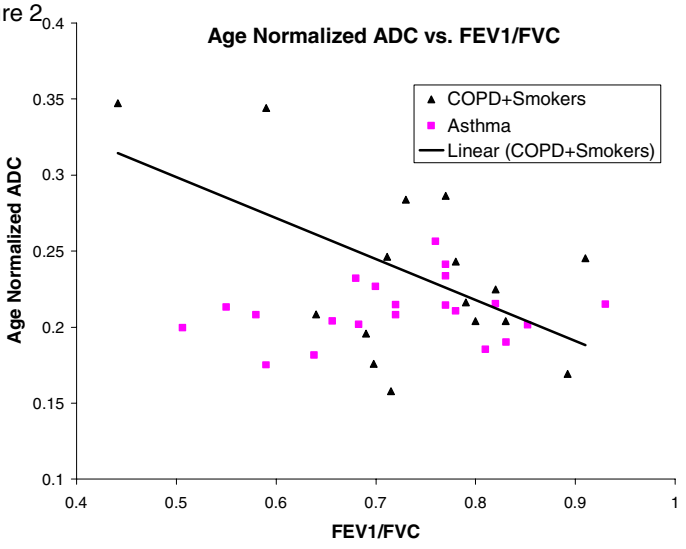


Figure 2



Discussion: In COPD patients, ADC is observed to increase as pulmonary function degrades (1, 2) leading to a negative association between ADC and FEV1/FVC and FEV1%p. The lack of a dependence of ADC on FEV1%p in our data might be explained by the inclusion of asymptomatic smokers as FVC tends to decrease before FEV1%p in early onset of emphysema. Models used to explain these relationships with ADC suggest degradation of alveolar walls (1), and terminal bronchioles at the acinar level (5) that increase the size of airspaces in COPD and in heavy smokers, leading to progressively less restricted diffusion. In contrast to COPD, our results in asthma suggest ADC is positively associated with FEV1%p, but not FEV1/FVC. Asthma is predominantly characterized by airway narrowing and obstruction regionally (6) although the scale of the airways involved is still debated. For the b-value and Δ used in this study, the characteristic diffusion length of 500 μm is well beyond the typical radius of an alveolus of 100-200 μm (1). The results of our study suggest ADC in subjects with asthma may be sensitive to structural changes in the lungs associated with airway remodeling and/or narrowing.

References: 1. Saam B et al., Magn Reson Med 2000; 44:174-179. 2. Salerno M. et al., Radiology 2002; 222:252-260. 3. Fain SB et al., Radiology 2005; (in press). 4. Fain S,B. et al., Academic Radiology 2005; (in press). 5. Yablonskiy D et al., PNAS 2002; 99:3111-3116. 6. Samee S, Altes T, Powers P et al., Journal of Allergy and Clinical Immunology 2003; 111:1205-1211.