In vivo Lung Morphometry with Hyperpolarized ^{3}He MRI in a Mild COPD Population

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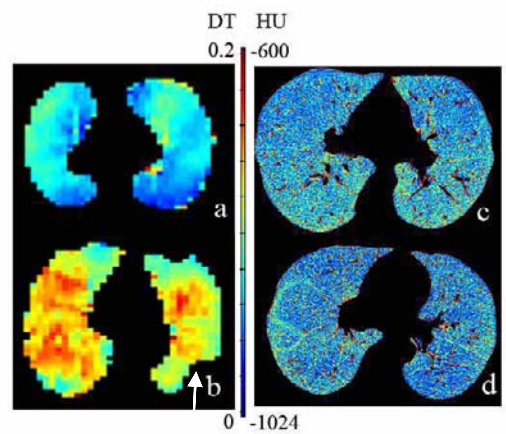
Introduction Hyperpolarized ^{3}He diffusion MRI is increasingly being utilized to non-invasively quantify regional alveolar structure changes in COPD subjects. Regions of increased diffusion have been correlated with pulmonary function testing (PFT) and, in limited cases, CT(1-4). While previous studies have predominately focused on subjects with severe disease, comparatively few (e.g. (1,3)) have examined the early stages of disease where the greatest potential for clinical impact lies through disease detection and intervention. Previous studies almost universally utilize acquisitions at two different b-values to calculate a ^{3}He ADC. Herein we employ in vivo lung morphometry technique that allows decoupling of helium gas ADCs into components oriented along the longitudinal (D_L) and transverse (D_T) axes of the acinar airways (5) providing a powerful tool for characterizing pulmonary pathology in COPD. We correlate pathology determined by this approach with changes found in pulmonary function testing and chest CT. These results provide new insight into early structural changes in the emphysematous lung and suggest which methodology is the most sensitive to the early disease process.

Materials and Methods Thirty "asymptomatic" subjects with significant smoking histories (50 ± 20 pack years, average age 62 ± 3 years) were recruited for hyperpolarized helium-3 MRI from the National Lung Screening Trial (NLST). In the NLST, subjects received a multi-slice axial low-dose chest CT examination on a Siemens Sensation 16 (Siemens Medical Systems, Iselin, NJ) (0.633 x 0.633 x 2 mm resolution) within one year prior to the MRI examination. NLST subjects with coronary artery calcification, lung cancer, or other pulmonary pathologies (besides COPD) were excluded from this MRI study. All procedures were performed with IRB approval and ^{3}He MRI was performed under a ^{3}He IND FDA exemption. A complet*e* pulmonary function test was performed on the day of helium imaging for each subject. Helium diffusion studies were conducted on a 1.5 T Siemens Sonata using a custom-built ^{3}He volume transmit / 8-channel receiver pair (Stark Contrast MRI Coils Research, Erlangen, Germany). Hyperpolarized ^{3}He gas was prepared using spin-exchange optical pumping on either a home-built apparatus or a commercial IGI.9600.He polarizer (General Electric, Fairfield, CT). After practicing breathing maneuvers with room air during proton scout imaging, the subjects exhaled to FRC and inhaled 0.6 liters of hyperpolarized ^{3}He gas mixed with 0.4 liters of nitrogen. Axial 2D multi-slice diffusion-weighted ^{3}He FLASH images were acquired during a nine-second breath-hold (128 x 64; resolution = 7 x 7 x 30 mm; TR/TE = 7.5/4 ms; diffusion time = 1.8 ms; 3 slices; b-values = 0, 2, 4, 6, 8, 10 s/cm^2). The ^{3}He MRI images from each channel of the receiver coil were individually phased and the real data was jointly analyzed using the above microscopically anisotropic macroscopically isotropic model(5) utilizing Bayesian probability theory.



Results and Discussion While significant heterogeneity was observed in PFT and MRI results across subjects, no significant correlations were detected with smoking history in this population, likely due to bias introduced by our selection criteria. PFT findings were generally normal (only five subjects had mildly decreased FEV_1, eleven had increased RV, and fourteen had decreased DLCO). CT images showed lung hyperinflation in a number of subjects and lung volumes across all subjects were correlated between PFT, CT, ^{3}He MRI images, and ^{1}H MRI anatomical images. Helium ADC, D_L, and D_T values averaged across the lung were elevated in thirteen subjects and all three diffusion parameters were correlated with DLCO, FEV_1/FVC, and $FEF_{25\text{-}75\%}$.

An important finding in this study is that there is significant heterogeneity across the lung in D_T maps that was not detected by CT. Images at the right show the D_T maps and corresponding CT images for a representative subject with normal PFTs (a,c) and the subject with most pronounced disease (FEV_1 = 59%) (b,d). While the mean D_T values in (a) are only slightly elevated above normal, there is significant heterogeneity across the lung. The elevated D_T values in image (b) corresponds to a 10% increase in the mean effective airway radius over image (a), with regional changes as high as 45%. The arrow on the left lung in (b) also shows a region that failed to ventilate with helium gas.

Of the techniques studied, hyperpolarized ^{3}He diffusion imaging appears to be the most sensitive to early emphysematous changes in this patient population. While CT detected primarily increased lung volumes in these subjects and pulmonary function testing showed only mild changes, apparent helium diffusion perpendicular to the airway axis (D_T) was able to detect significant, regional changes in pulmonary structure even in patients with normal PFT results. Disease heterogeneity across our population was significant even for subjects with similar smoking histories, suggesting that longitudinal imaging would be required to efficiently study mild COPD subjects for disease progression or treatment efficacy.

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