Comparison of Pulmonary Function Testing with Distribution of Alveolar Oxygen Tension and Apparent Diffusion Coefficient in Asymptomatic Smokers Using Hyperpolarized 3He MRI

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INTRODUCTION: Conventional pulmonary function tests (PFT) provide a global measure over the entire lung as a tool for diagnosis and monitoring of a majority of obstructive and interstitial lung diseases. PFT however is considered to have a poor sensitivity for detecting localized, early or small changes in lung function and structure. The use of hyperpolarized (HP) gas MRI has been under investigation for probing both microstructural and functional aspects of lungs on a regional basis and with potentially higher sensitivity. In this study we compared common PFT measurement with distributions of alveolar partial pressure of oxygen (pO2) and apparent diffusion coefficient (ADC) of 3He obtained with oxygen- and diffusion-weighted HP gas MRI respectively. This comparison was performed in two groups of healthy human subjects and asymptomatic smokers to highlight underlying physiological relationships between the two methods. We also attempted to assess the sensitivity of each group of measurements in differentiating the subject groups and to evaluate the potential of MRI metrics as imaging biomarkers in monitoring active smokers...

METHODS: Ten healthy non-smokers (5 F, 36±8 yrs, BMI=27.3±6.6) and twenty asymptomatic smokers (13 M, 53±12 yrs, BMI=25.3±8.4) participated in pO2 and ADC MRI studies. Before MRI session, PFT was performed on all subjects. pO2 imaging was performed over twelve 13-mm coronal slices with 20% interslice gap, using an interleaved oxygen-weighted gradient echo imaging pulse sequence [Hamedani et al. MRM 2011] (spatial resolution 8.3×8.3×15.3mm3, TR/TE=6.73/2.3ms, FOV=30×40cm2, α=5°) and ADC imaging was done using an interleaved diffusion-weighted gradient echo sequence with b-value=0.16 s/cm2 with similar imaging parameters except for spatial resolution (6.25×6.25×15.3mm3). A noroxic mixture of 3He/N2O based on 12% Total Lung Capacity was administered at end-expiration in a single breath and images were acquired during a 12-sec end-inspiratory breath-hold. Imaged whole-lung pO2 and ADC mean (μpO2, μADC), dispersion (σpO2, σADC) and skewness (γpO2, γADC) for each subject were compared to PFT results. Pearson’s coefficient was calculated for each comparison to relate the global values of PFT with MRI. One-tailed ANOVA test was performed on both PFT and MRI results for both groups in order to compare the sensitivity of MRI and PFT parameters in differentiating smokers and non-smokers.

RESULTS & DISCUSSION: Fig.1(a, b) shows a representative coronal slice of pO2 and ADC maps for a representative subject from each group. Fig.1(c-e) summarize pO2 and ADC distributions for both groups. The overall pO2 and ADC values for all subjects were in the range of 102.1±11.9 Torr and 0.22±0.04 cm2/s, respectively. The dispersion of pO2 among all subjects ranged over 33.9±6.1 Torr. No apparent association was observed between ADC and pO2 measurement and their derivatives except for a weak correlation between μADC and γADC (r = −0.37, P = 0.06). As can be seen from Fig.1(c,d), μADC shows a significant variability among all subjects. The global average pO2 does not show any correlation with any of the PFT metrics either. σpO2 on the other hand associates with Maximum Forced Expiratory Flow, FEFmax (r = −0.51, P = 0.004, 95% CI: −0.73, −0.17), suggesting that the heterogeneity of pO2 distribution can be a more sensitive marker to smoking-related changes in the lungs compared to average alveolar oxygen tension. Skewness of the pO2 distribution also shows an interesting trend as it significantly correlates with DL/VA - Diffusion per unit area of Lung Volume (r = −0.57, P = 0.001, 95% CI: 0.27, 0.77). γADC also correlated with Thoracic Gas Volume, Forced Inspiratory Flow and FEV1/FVC as is shown in Fig.2. The mean values of 3He ADC (μADC) showed a significant correlation with DL/VA (r = −0.65, P < 0.01, 95% CI: −0.33, −0.84) and a weaker association with Residual Volume and DLCO. γADC also associated with DLCO (r = 0.52, P = 0.006, 95% CI: 0.15, 0.71). Finally Fig. 3 summarized the results of ANOVA test between the two groups for key PFT metrics, and pO2 dispersion. Among all measurements performed, σpO2 (dispersion of oxygen tension in the lungs) had the smallest overlap and most discrimination power between two groups and its P-value was significantly less than any other PFT measurements as well as ADC values.

CONCLUSION: Regional distributions of oxygen tension and diffusivity in lungs show to have significant correlations with key PFT metrics supporting their physiological relevance. However specific MRI metrics, including pO2 dispersion showed an even more discriminatory power compared to gold standards (e.g. FEV1/FVC). The richer information embedded in regional lung measurements therefore advocates their suitability for further investigation as respiratory biomarkers.