Early Detection Of Smoking-Induced Pulmonary Alterations Using Hyperpolarized 3He MRI Derived Alveolar Partial Pressure of Oxygen

Hooman Hamedani1, Stephen J. Kadleccek1, Masani Ishii1, Yi Xin1, Hoora Shaghaghi1, Biao Han1, Sarman Siddiqui1, Sarah Zarrin3, Milton Rossman1, and Rahim R. Rizi2
1University of Pennsylvania, Philadelphia, PA, United States, 2Johns Hopkins University, Merryland, United States, 3University of Pennsylvania, PA, United States

INTRODUCTION: Hyperpolarized gas MRI was introduced over a decade ago to estimate the alveolar partial pressure of oxygen (pO2). However, it has never been systematically investigated for its value as either a diagnostic tool or as a tool for monitoring disease progression and response to new therapies. In this work, the imaged pO2 is compared with the pulmonary function test (PFT), Six Minute Walk Test (6MWT) and St. George Respiratory Questionnaire (SGRQ) results and a logistic regression model is developed to predict the asymptomatic smokers.

METHODS: 43 human subjects, separated in three groups (10 Healthy Nonsmokers; 16 Asymptomatic Smokers and 17 COPD), underwent pO2 imaging followed by a PFT and 6MWT. They were also asked to fill out a SGRQ. A multi-slice, four time-point scheme in [1] was performed across twelve 13-mm coronal slices after a single breath of HP gas. This method used an interleaved acquisition scheme with a gradient echo imaging pulse sequence at a spatial resolution of 8.3 x 8.3 mm (Ts/Ti = 6.7:3.2 ms, FOV = 30 x 40 cm, flip-angle = -5°, Slice-Gap = 20%). A normoxic mixture of 3He:N2O (3:1:1) based on subjects’ total lung capacity was administered with images acquired during a 12-sec end-inspiratory breath-hold. The whole-lung pO2 averages and standard deviations (MpO2±SpO2) were computed. Univariate Pearson correlations were used to analyze the relationship between MRI measures of respiratory function and non-imaging measurements. A stepwise multivariate logistic regression was performed for the prediction of “asymptomatic smoker” status. A p<0.05 was considered for a predictor to retain in the multivariate regressions. A Leave-one-out method was used for cross-validation. An alpha level of 0.05 was considered significant in all analyses.

RESULTS & DISCUSSION: The three cohorts were not significantly different with respect to age and BMI. Figure 1 shows the central coronal 3He MRI static ventilation maps for representative subjects and the corresponding oxygen-weighted maps and histograms. Figure 2 illustrates the correlation between imaging and non-imaging markers. The AS subjects had significantly higher pO2 heterogeneity compared to the HNs (p<0.001) and had significantly lower D3O2 compared to COPD (p<0.001). There were no differences in the global oxygen tension averages (MpO2) between the healthy subjects and smokers (p=0.251). The COPD subjects had elevated MpO2 compared to smokers (p=0.016). A strong negative correlation was observed with FEV/FVC and FEV1 % predicted. A moderate negative correlation was observed with DLCO, which is a measure of gas exchange quality in the lungs. The SGRQ scores significantly associated with the D3O2. Subjects’ 6MWT distance moderately correlated with D3O2. The pack-years smoking directly and strongly related to the oxygen-tension heterogeneity. A stepwise multivariable logistic regression analysis was performed to predict the “asymptomatic smoker” status. The standard PFT parameters of the GOLD criteria (FEV1/FVC, %FEV1) as a measure of obstruction, DLCO as an indication of emphysema, the distance travelled in 6MWT, and the SGRQ overall score, along with imaging markers, were selected to enter the univariate logistic regressions between. Smokers can be distinguished from the healthy nonsmokers by their significantly increased pO2 heterogeneity and slightly lowered FEV1/FVC (p=0.029), which both retained in the final model. MpO2, 6MWTD, and SGRQ score also passed the test to enter the multivariable analysis (p<0.025) but were not retained in the final model. DLCO entered the model as a confounding variable (p=0.092) and significantly improved the model (p=0.035). After scaling of each variable, the odds ratios were calculated. The final estimates and odds for the “asymptomatic smoker” status, together with the statistical results of the logistic regression are presented in Table 1. Figure 3 shows the two-dimensional scatter plots and the 95% confidence intervals. (Green: HN and Red: AS subjects).

CONCLUSION: This study set out to develop a more precise means of detecting, staging, and evaluating early respiratory symptoms of COPD using a functional HP-MRI technique. It is anticipated that using this technique to measure alveolar oxygen tension would help to detect the small, difficult-to-assess functional alterations characteristic of smoking-induced COPD with greater sensitivity than traditional techniques.