Imaging Regional Heterogeneity of Pulmonary Oxygen Tension as a Diagnostic Tool for Obstructive Lung Diseases

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INTRODUCTION: Early detection of chronic obstructive pulmonary disease (COPD) has been thwarted in part by the large inherent variability in pulmonary function test (PFT) results in the presence of small airway disease. MRI of inhaled hyperpolarized ^{3}He gas (HP ^{3}He) has emerged as a promising technique for non-invasive evaluation of the structure and function of the lungs. HP ^{3}He MRI can be used to probe several key aspects of lung function such as regional ventilation and perfusion; in particular, it can be used to assess the homogeneity of oxygen uptake in the alveoli by measuring alveolar partial pressure of oxygen (pO2). Due to additional T_1 relaxation of HP ^{3}He caused by oxygen, the alveolar pO2 can be calculated from the images as reported by [1]. By measuring local pO2 values, HP ^{3}He MRI allows quantification of the structural changes based on heterogeneity of the lungs, and can become a much more sensitive marker of the disease onset compared to the current methodologies. Our hypothesis is that this method can be used to identify early stages of chronic obstructive pulmonary disease (COPD) in humans with a potential to provide a better means for the longitudinal assessment of the disease progression and therapeutic interventions.

METHODS: Seven human subjects were selected between the ages of 40 and 70 years old. Four non-smokers, two healthy smokers, and one subject with early COPD underwent HP ^{3}He MRI imaging and measurements of pulmonary function that were repeated three times within a two-week interval. A physical test was administered to evaluate their eligibility for the study and the pulmonary function was measured in the hospital pulmonary function laboratory according to ATS criteria. During the MRI session, each subject was provided with a mixture of hyperpolarized helium and oxygen gases to inhale (4:1), and 4 sets of HP ^{3}He images with 12 slices per set were acquired. The corresponding pO2 maps of the 12 slices were generated by a pO2 mapping methodology introduced by Hamedani et al. [1].
The standard deviations of pO2 maps were used as a measure of lung heterogeneity. Two such measurements were performed in each session using two batches of gas mixture, resulting in 6 data points over 3 sessions for each subject. Differences in the heterogeneity numbers and pO2 mean values between different groups were determined by a t-test. If the p value for the t-test was less than 0.05, the differences were considered significant.

RESULTS AND DISCUSSION: **Table 1** shows the mean values and standard deviations of all pO2 maps for each subject and demonstrates the high variability within the groups. **Figure 1** shows pO2 maps of a COPD patient's and a healthy subject's lungs. The COPD subject's pO2 map indicates a lower partial pressure of oxygen compared to the healthy counterpart, as illustrated by the darker areas within the image. **Figure 2** represents these maps as histograms where the difference is clearly visible as the COPD subject's histogram shows a markedly wider and lower distribution (95.8±36.7 vs. 102.6±27.4 [mmHg]). **Figure 3** shows analyses of the variances of group mean pO2 values and associated t-test results indicating that the pO2 mean value of each group was not significantly different from the others. **Figure 4** represents analyses of the variances of group heterogeneity and associated t-tests. Notably in this comparison, the heterogeneity number of the non-smoking subject group was significantly different from those of the smoker group and the COPD subject (p=0.00086, p=0.034). However, there was no significant heterogeneity number difference observed between the smoker group and the COPD subject. The healthy smokers exhibited normal pulmonary function, while the subject with COPD had mild pulmonary function abnormalities.

	Test 1	Test 2	Test 3	Test 4	Test 5	Test 6
Healthy #1	117.6±22.8	114.3±19.2	115.2±21.3			
Healthy #2	87.6±26.2	102.6±27.4	97.5±35.3	94.3±32	108.4±30.1	101.7±35.8
Healthy #3	77.1±36.2	83.6±37.8	87.7±30.7	78.9±34.4	93.9±34.3	93.5±42.2
Healthy #4	102.7±22.4	110.8±22.4	109±25	112.8±23.9		
Smoker #1	113.1±71.5	98.2±37.5	100.6±40.6	122.1±38.5	89.5±37.5	
Smoker #2	79.6±48.2	73.4±30.3	75.2±42			
COPD	107.3±36.8	88.8±32.1	95.8±36.7	106±36.6	95.3±35.9	91.9±35.9

Table 1. Mean and Standard Deviation of overall pO2 of all the subjects

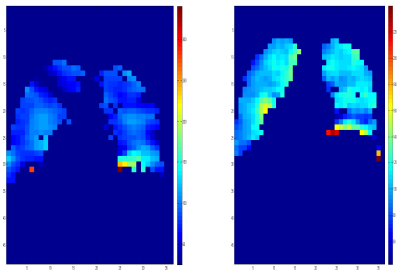

Figure 1. pO2 map of a COPD lung (left) and a healthy lung (right).

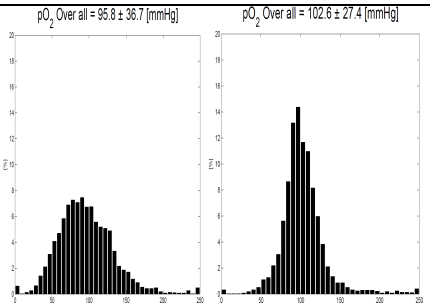

Figure 2. Overall pO2 histogram of a COPD lung (left) and a healthy lung (right).

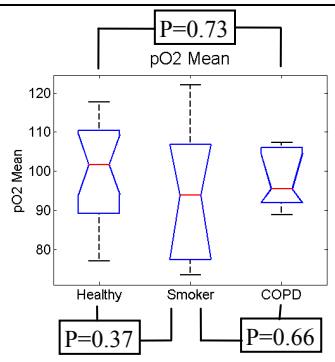

Figure 3. PO2 median values (red lines on box plot) comparison between different groups and t-test results

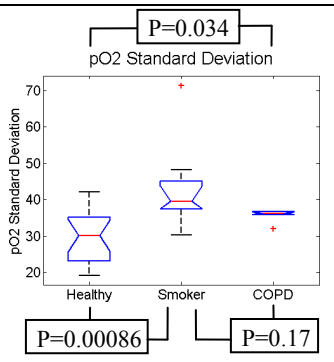

Figure 4. Heterogeneity median values (red lines on box plot) comparison between different groups and t-test results.

CONCLUSION: Based on these results, pO2 mapping utilizing HP ^{3}He MRI is a viable method for the quantification of human lung heterogeneity. In the presence of early disease which begins to alter the lung parenchyma but has not yet reached the detection limit of the current diagnostic methodologies, this technology may prove invaluable to the early diagnosis of COPD. The standard deviation of the pO2 map could potentially be used as a non-invasive metric for not only identifying and diagnosing early lung disease, but could also enable longitudinal tracking of the progression of the disease and monitoring of the therapeutic advances.

REFERENCE: [1] An Improved Scheme for a Robust High Resolution Measurement of Alveolar Oxygen Tension in Human Lungs, H.Hamedani et al., ISMRM 2011