

Relationship between Lung Function and Lung Structure in Smokers as Measured by Hyperpolarized Helium-3 MRI

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Introduction: Smoking is considered the most important risk factor for developing chronic obstructive pulmonary disease (COPD). Using hyperpolarized helium-3 diffusion MR the displacement of the helium-3 atoms in the airspaces of the lung can be measured and is denoted as the Apparent Diffusion Coefficient (ADC) [1-3]. Alveolar enlargement in the lungs of patients with emphysema reduces the restriction of the helium atoms and thereby causes an increase in the helium ADC [1-3]. Diffusion capacity of the lung for carbon monoxide (DLCO), exercise stress test and pulmonary function tests (PFTs) are used clinically to evaluate COPD [4]. However, the relationship between the helium ADC and these tests are unclear. In this study, hyperpolarized helium-3 diffusion MRI, DLCO, exercise stress tests and pulmonary function tests were performed in smokers and nonsmokers to investigate the relationship between measures of lung structure and lung function.

Methods: We studied 2 groups of similar aged subjects (Age: 59 ± 8 years, Gender: 4 M, 5F): 5 active or prior smokers and 3 control subjects who had never smoked and had only occasional exposure to secondhand smoke. After helium-3 was polarized to ~30% by the collisional spin-exchange technique using a commercial system (Model 9600, MITI), medical grade N₂ was mixed with 300 – 400 ml helium-3 to a total volume of the subject's FVC. Co-registered short-time-scale (STS) and long-time-scale (LTS) ADC maps were measured at the corresponding diffusion times 1 ms and 1.50 s using a 1.5 T commercial MR scanner (Sonata, Siemens) during a single breath hold following inhaling the gas mixture. The pulse sequence was described in ref. 2. And the STS and LTS b-values were 1.6 s/cm² and 60 s/cm². DLCO, exercise stress test and PFTs were performed in all subjects. Linear regression was performed to study the relation between ADC and DLCO, exercise stress test and PFTs.

Results: The mean helium-3 STS ADC was poorly correlated with %DLCO ($r = 0.20$, $P = 0.633$, Fig 1a), moderately correlated with %_{pred}FEV₁ ($r = 0.54$, $P = 0.171$, Fig 1b), and poorly correlated with peak VO₂ (highest rate of oxygen consumption attainable during maximal or exhaustive exercise) ($r = 0.25$, $P = 0.554$). The LTS ADC was moderately correlated with %DLCO ($r = 0.67$, $P = 0.068$, Fig 1c), moderately correlated with %_{pred}FEV₁ ($r = 0.58$, $P = 0.130$, Fig 1d), but there was poor correlation with peak VO₂ ($r = 0.30$, $P = 0.48$). The LTS ADC did not correlate well with the STS ADC ($r = 0.44$, $P = 0.28$).

Discussion and Conclusion: Both the STS ADC and LTS ADC reflect lung structure with sensitivity to alveolar size but the LTS ADC is expected to have an increased sensitivity to the connectivity of the airspaces. DLCO measures the gas transfer of CO within the lung, a measure of global lung function. Clinically the DLCO is considered as a more sensitive test for early emphysema than spirometry which only measures the dynamics of gas flow at the mouth during forced expiration. LTS ADC correlated with %DLCO while STS ADC did not, which suggests that LTS ADC is more sensitive than STS ADC in detecting early pulmonary injury. Also, both STS and LTS ADC did not correlate with exercise stress testing possibly because many non-respiratory factors contribute to exercise capacity. Our findings support an association between lung microstructural alterations caused by cigarette smoking and functional changes in FEV1 and %DLCO.

Reference:

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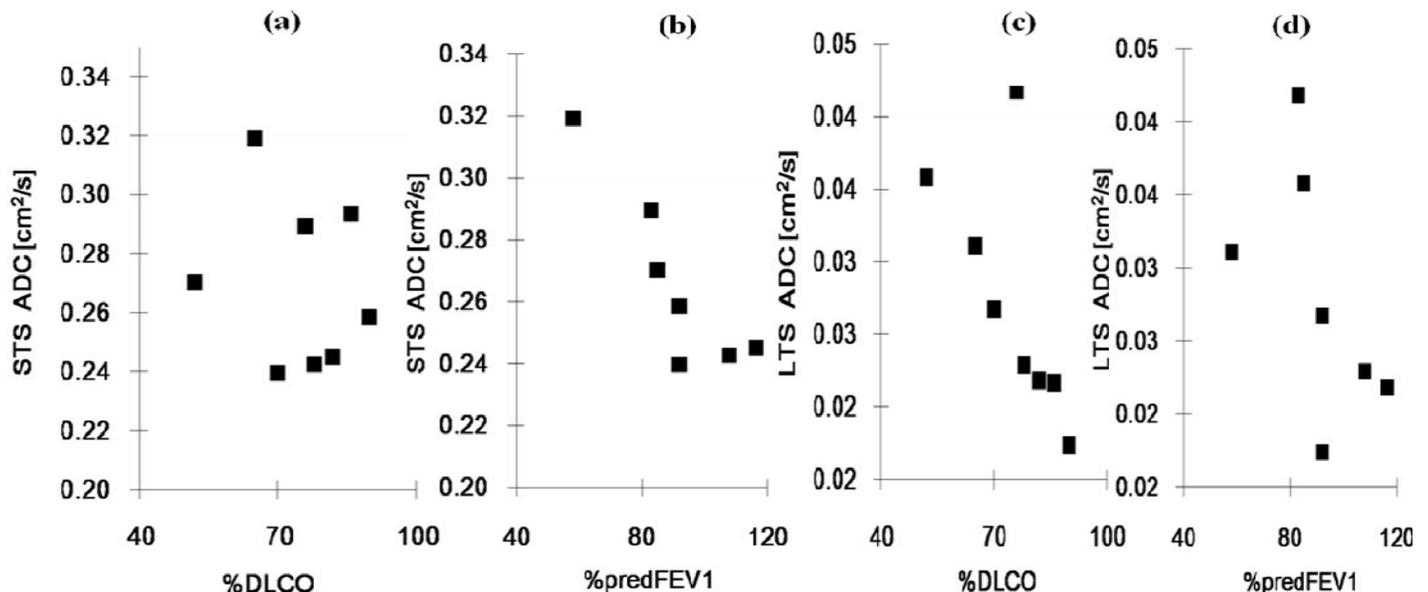


Figure 1. (a). Plot of STS ADC vs %DLCO ($r = 0.20$, $P = 0.633$); (b). Plot of STS ADC vs %_{pred}FEV₁ ($r = 0.54$, $P = 0.171$); (c). Plot of LTS ADC vs %DLCO ($r = 0.67$, $P = 0.068$); (d). Plot of LTS ADC vs %_{pred}FEV₁ ($r = 0.58$, $P = 0.130$).