Lung Function Decline over 5 Years as Measured by the Hyperpolarized Helium-3 ADC in Smokers

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Introduction: The apparent diffusion coefficient (ADC) of hyperpolarized helium-3 in the lung provides a measure of the degree of restriction imposed by the pulmonary tissues on the displacements of helium atoms within the airspaces. In patients with COPD and in animal models of emphysema, the ADC of helium is increased relative to that for normal lung(*1, 2*), and the elevation in ADC is thought to reflect the degree of emphysematous change within the lung(*3-5*). In clinical trials of treatments for COPD, a frequent outcome measure is the rate of decline in lung function over time. However, when measured using spirometry, the rate of decline is small necessitating long and therefore expensive clinical trials. It has been postulated that the regional information in the helium ADC maps may make it more sensitive than spirometry to small alterations of emphysematous change within the lung. The purpose of this study was to assess the change in the helium ADC over time in a population at risk for smoking-related lung disease, and compare the findings to those of spirometry.

Methods: Six smokers (1 male, 5 female) underwent hyperpolarized helium-3 diffusion MRI and spirometry on two occasions separated in time by a mean of 5.8 yrs (range 5.4 to 6.7 yrs). On both occasions, the subjects inhaled a mixture of approximately 300 ml hyperpolarized helium-3 and 700 ml nitrogen, and held their breath while axial diffusion-weighted slices were acquired using a FLASH-based pulse sequence (TR/TE, 7/2.7 ms; flip angle, 7; b-values, 0 and 1.6 s/cm2; slice thickness, 15 mm and 15 mm gap). The mean ADC from the whole lung was computed for each MR study(*2*). The percent difference between the baseline and repeat mean ADC as well as spirometric indices were computed for each subject.

Results: At the time of the first scan, the mean age of the subjects was 57 yrs (range 53 to 59 yrs), the mean smoking history 33 pack-years (range 28 to 39 pack-yrs), mean ADC 0.27 cm^2/s (range 0.20 to 0.35 cm^2/s), mean FEV_1 %predicted 75% (range 61 to 85%), and mean FEV_1/FVC 73 (range 61 to 84). Under the GOLD criteria for classifying COPD, 3 subjects were Gold stage 0 (at risk) and 3 were Gold stage 1 (mild).

Only one subject attempted to quit smoking during the 5 year interval of the study, however, continued to smoke but at a reduced rate at the time of the follow-up scan. At the follow-up scan, the mean ADC was 0.30 cm^2/s (range 0.22 to 0.45 cm^2/s, p=0.083), mean FEV_1 %predicted 78% (range 59 to 89%, p=0.29) and mean FEV_1/FVC 66 (range 43 to 84, p=0.034). As compared with the first scan, the average percent change in mean ADC, FEV_1 %predicted, FEV_1 (mL) and FEV1/FVC were 10% (range 3 to 29%), 5% (range -13 to 16%), -4 % (range -19 to 6%) and -11% (range 0 to -29%), respectively . The mean rate of decline was 0.031 $cm^2/s/yr$ for the mean ADC, and 23 mL/yr for FEV_1 (mL). There was a strong correlation between the percent change in mean ADC and in FEV_1/FVC, r=-0.91, with one subject experiencing a more pronounced decline in mean ADC and FEV_1/FVC than the other subjects, Figure 1. ADC maps from this subject show an increase in the lung area with elevated ADC values over time (yellow), Figure 2. The subject with least decline in lung function over time had normal ADC and spirometry values at baseline, Figure 3. There was a strong correlation between the mean ADC at baseline and the percent change in ADC, FEV_1, and FEV_1/FVC (r = -0.83, -0.86, and -0.92, respectively), suggesting that elevated baseline mean ADC values are associated with a subsequent more rapid decline in lung function.

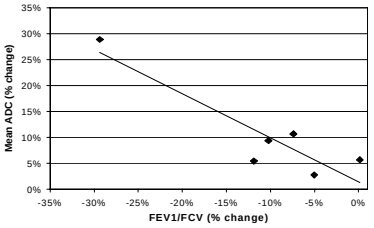
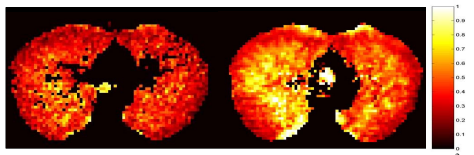


Figure 1. Percent change in mean ADC vs percent change in FEV_1/FVC.

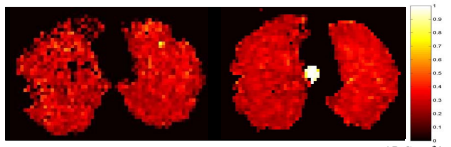


Baseline
FEV_1 68% pred
FEV_1/FVC 61
Mean ADC 0.35 cm^2/s

6 yrs Later
FEV1 59% pred
FEV1/FVC 43
Mean ADC 0.45 cm^2/s

ADC cm^2/s

Figure 2. ADC maps from the subject with the largest decline in lung function.



Baseline
FEV_1 85% pred
FEV_1/FVC 82
Mean ADC 0.23 cm^2/s

5 yrs Later
FEV1 85% pred
FEV1/FVC 78
Mean ADC 0.29 cm^2/s

ADC cm^2/s

Figure 3. ADC maps from the subject with the smallest decline in lung function.

Conclusion: Over a 5 year period, the decline in lung function of a group of 6 smokers at risk for or with mild COPD at baseline was strongly correlated with the baseline mean ADC values suggesting that hyperpolarized helium-3 MRI may be able to detect those smokers at greatest risk for a rapidly declining lung function and for developing clinically significant COPD.

References

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Acknowledgements

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