Emphysematous changes and normal variation in smokers and COPD patients using diffusion 3-He MRI

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Synopsis: Previously, it has been shown [1-4], that measurement of ^{3}He gas diffusivity in the lung air spaces has potential for identifying changes in lung structure due to emphysema at the alveolar level. This study aims to quantify global and regional changes of lung microstructure, as determined by hyperpolarized 3-Helium MR apparent diffusion coefficient (ADC) measurement, in non-smokers, healthy (symptomatic) smokers, and COPD patients.

Methods All work was done on a 1.5T whole body system, tuned to ^{3}He frequency (Eclipse –Philips Medical Systems). A flexible twin saddle quadrature T-R coil was used (IGC Medical Advances). The MR sequence was based on an interleaved low flip angle gradient echo acquisition with a reference scan (*b=0*) followed by diffusion-weighted acquisition (*b=1.6 scm*$^{-2}$ - bipolar trapezoids of plateau strength 19.5 mTm^{-1} and duration 460 µs with 500µs ramp time –*direction in-slice*). Phase encoding was centric with 112 views, the remaining sequence parameters were: flip angle 7°, 11 coronal slices, 15 mm slice thickness & 5mm gap, FOV =42 cm, TE=2.5 ms, TR=6.7 ms, 128 samples, BW ±16kHz. ^{3}He gas was polarized on site to 30% by optical pumping with rubidium spin exchange apparatus (Amersham Health, Princeton NJ). In-vivo imaging was then performed following breath-hold of a 300 ml ^{3}He/800 ml N_2 mixture from a Tedlar bag. Age matched groups of six healthy non-smokers, five healthy smokers and five patients with moderate COPD were studied with approval from the local Research Ethics Committee. Spirometry was performed on all subjects. Diffusion imaging was performed following hyperpolarized 3-Helium gas inhalation to produce regional ADC maps, which were assessed in random order by an experienced observer who was blinded to all the patient data. Mean and standard deviation of the ADC's were used to compare the subject groups and assess regional variations within individuals.

Results: In the healthy non-smoking group, anterior and superior ADC values were shown to be systematically larger than those obtained for posterior and inferior lung regions, respectively. The mean ADC of the healthy smoking group was larger and the intra-individual standard deviation of ADC was significantly larger than that of the non-smoking group ($P < 0.05$). Compared to the non-smoking group COPD patients had significantly higher mean and standard deviation of ADC ($P < 0.01$). There was a good correlation between percentage predicted FEV1, mean ADC and standard deviation of ADC in the full study group, the small numbers of the groups precluded useful correlations within groups

	Mean ± 1 SD (cm^2/s)	Intra-individual SD of ADC ± 1 SD (cm^2/s)
Non-smoking group n = 6	0.21 ± 0.02	0.01 ± 0.003
Smoking group n = 5	0.23 ± 0.03	0.03 ± 0.02
COPD patients n = 5	0.30 ± 0.06	0.05 ± 0.02

Table 1: Table showing mean and standard deviation of ADC values (above)

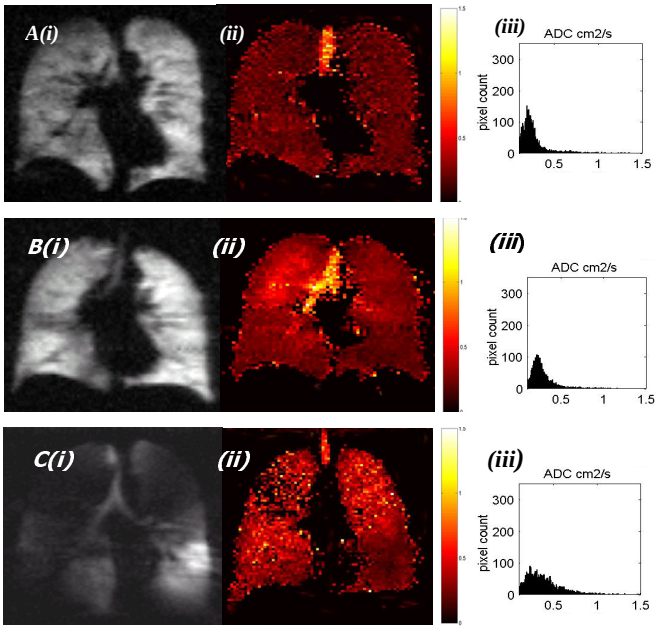

Figure 1. A, shows coronal ventilation (i) and ADC (ii) ^{3}He MR images and the corresponding ADC histogram (iii) in a representative healthy non-smoker . B, shows coronal ventilation (i) and ADC (ii) ^{3}He MR images and the corresponding ADC histogram (iii) in a smoker. C, shows coronal ventilation (i) and ADC (ii) ^{3}He MR images and the corresponding ADC histogram (iii) in a patient with moderate COPD.

Discussion:

Important differences in the regional and global ADC of healthy volunteers have been demonstrated and these results may have implications for the clinical interpretation of ADC changes in relation to lung diseases. These initial results suggest that early smoking related lung damage as well as more severe emphysema can be demonstrated. This could allow longitudinal studies for evaluation of disease progression and effects of novel medical and surgical interventions. It may allow targeting of these therapies to individuals early in the course of the disease, rather than at a stage when the disease is grossly evident and largely irreversible damage has already occurred.

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