Hyperpolarized ^{3}He diffusion MRI at two time scales during a single breath hold: Assessment of the lung microstructure in asthmatics with comparison to healthy and COPD subjects

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Introduction: Hyperpolarized ^{3}He (H3He) diffusion MRI at both short- and long-time scales has been used to obtain information about lung microstructure. The short-time-scale diffusion (~1 ms) [1,2] has been commonly measured with a gradient-echo (GRE) based sequence, and several techniques have been developed to measure long-time-scale diffusion (~1 s) [3,4]. Prior studies have found elevations of both the short- and long-time-scale apparent diffusion coefficients (ADC) in emphysema, and there is a suggestion that the long-time-scale ADC may be more sensitive than the short-time-scale ADC to emphysematous change in the lung [3,4]. Currently, little is known about H3He diffusion in asthma. In a prior study, short-time-scale ADC values were found to be similar in asthmatics and normal subjects [5]. The goal of the present work was to measure the short- and long-time-scale H3He diffusion in asthma, and to compare with healthy volunteers and patients with COPD.

Methods: A hybrid MRI pulse sequence was developed to obtain co-registered ADC maps corresponding to two distinct diffusion times during a single breath hold. This hybrid pulse sequence consisted of a stimulated-echo-based long-time-scale diffusion sequence [3] appended to the end of a conventional GRE-based short-time-scale diffusion sequence [1,2]. For the short-time-scale ADC measurement, b values of 0 and 1.6 s/cm^2 and a diffusion time of ~1 ms were used. For the long-time-scale ADC measurement, a b value of 60 s/cm^2 with a tag wavelength of 10 mm and a diffusion time of 1.5 s were used.

The hybrid pulse sequence was used in 14 healthy subjects (6 M and 8 F, age: 46-66 yrs), 14 age-matched patients with asthma (8 M and 6 F, age: 41-74 yrs) and 9 patients with COPD (5 M and 4 F, age: 61-73 yrs) following inhalation of 400-700 ml H3He gas mixed with N_2 to yield a total volume of approximately 1/3 of the subject's FVC. Imaging was performed on a 1.5-T commercial scanner (Sonata, Siemens) using a flexible RF chest coil (CMRS, Brookfield, WI). ^{3}He was polarized to ~30-40% by the collisional spin-exchange technique using a commercial system (Model 9600, MITI). Axial multi-slice MR data was acquired during a breath-hold period lasting no more than 15 seconds, and co-registered ADC maps at both short- and long-time scales were reconstructed from the MR data. The mean ADC and the %ADC-abn (defined as the percentage of pixels whose ADC was greater than a certain threshold) were calculated for each subject. The threshold used here was 2 standard deviations above the mean from all ADC values from all lungs pixels of all healthy subjects. Receiver operating characteristic (ROC) curves were constructed to compare the asthmatic or COPD group with the healthy group, and the areas under the ROC curves were calculated.

Results and Discussion: Representative co-registered ADC maps from a healthy subject, an asthmatic, and a COPD patient are shown in Fig 1. The healthy subject has homogeneous ADC maps at both time scales; the asthmatic has focal ADC elevations that are more conspicuous at the long-time scale; and the COPD patient has severe, diffuse ADC elevation at both time scales. The group-mean ADC for asthmatics was 0.254±0.032 cm^2/s at the short-time scale and 0.0237±0.0055 cm^2/s at the long-time scale, representing an increase of 9% and 27% (p=0.038 and p=0.005), respectively, compared with the healthy group. The group-mean %ADC-abn values were 6.4%±3.7% and 17.5%±14.2%, representing a 107% and 272% (p=0.004 and p=0.006) increase. More marked ADC elevations were found in the patients with COPD, Fig. 2. The mean ADC increase for patients with COPD was 71% (p=0.002) for the short-time scale and 117% (p<0.001) for the long-time scale measurements. Regional ADC elevations were generally more conspicuous on the long-time-scale ADC maps than on the short-time-scale maps. Using a ROC analysis, both ADC metrics (mean and %ADC-abn) at both time scales provided perfect discrimination between COPD and healthy subjects. However, the %ADC-abn provided better discrimination than the mean ADC at both time scales when comparing the asthmatic and healthy subjects, Fig. 3. Thus, asthmatics have changes in the lung microstructure that are detectable on H3He diffusion MRI, and these changes are more conspicuous on a regional basis at the long-time scale.

Conclusion: Patients with asthma were found to have elevated ADC values at both time scales, though less extensive and severe than the patients with COPD. The focal areas of elevation were larger and more conspicuous on the long-time-scale ADC maps but this increase in regional sensitivity did not translate into improved discrimination between the healthy and asthmatic subjects on an ROC analysis using an ADC metric sensitive to focal ADC elevations. Nonetheless, this increased regional sensitivity to changes in the lung microstructure in asthmatics may be important when performing longitudinal studies or evaluating changes with treatment.

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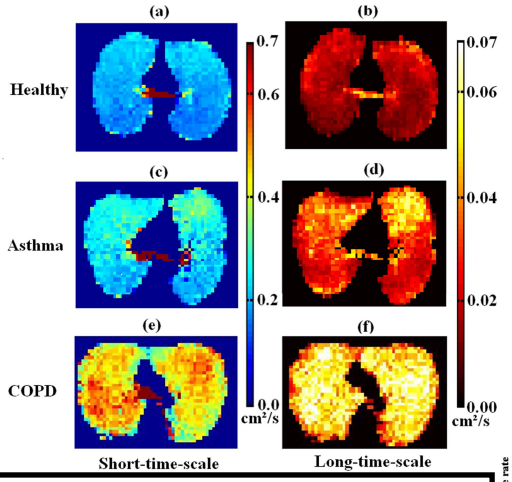

Figure 1. Co-registered axial ADC maps from: a healthy subject at diffusion times of (a) 1 ms and (b) 1.5 s; an asthma subject at diffusion times of (c) 1 ms and (d) 1.5 s; and a COPD subject at diffusion times of (e) 1 ms and (f) 1.5 s.

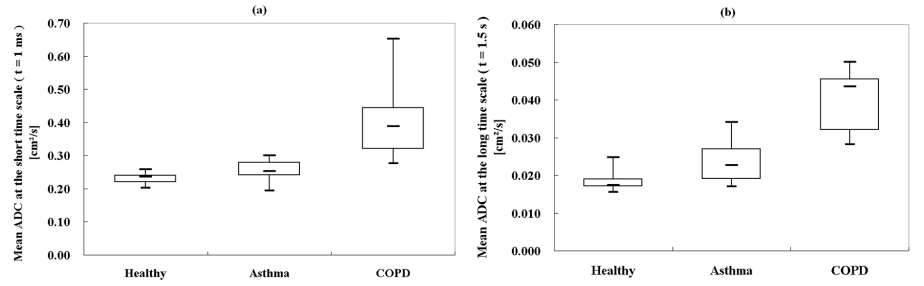

Figure 2. Box plot of mean ADC values from each subject group for (a) the short time scale (t = 1 ms) and (b) the long time scale (t = 1.5 s).

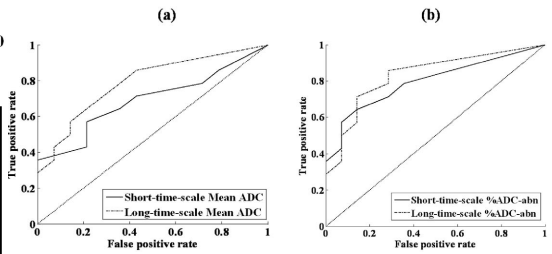

Figure 3. ROC curves of healthy and asthma group at both time scales for the (a) Mean ADC; and (b) %ADC-abn. (The areas under the ROC curves were 0.69 for the short-time-scale mean ADC, and 0.79 for the long-time-scale mean ADC, respectively, and were 0.83 for both short- and long-time -scale %ADC-abn.)