Measurement of the Diffusion of Hyperpolarized ^{3}He in Human Lungs over Short and Long Time Scales During One Breath Hold

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Introduction: Hyperpolarized (HP) ^{3}He diffusion MRI has been used in numerous studies to investigate the pulmonary microstructural changes that occur in emphysema[1-4]. These studies have included measurements at both short (~1 ms) and long (~1 s) diffusion times. For a short diffusion time, the measured apparent diffusion coefficient (ADC) has been shown to correlate well with histology[2]. For a long diffusion time, the ADC showed improved sensitivity to early emphysematous changes and it was hypothesized to reflect the connectivity of the lung microstructure[3,4]. These results suggest that a more complete description of the disease process may be obtained from acquiring ADC maps at both short and long time scales. To permit direct comparison of such diffusion measurements, a new MR pulse sequence was developed that acquires, in one breath hold, regional maps of the ADC of HP ^{3}He in human lungs at both short and long diffusion times and with identical spatial registration.

Methods: ADC maps can be obtained with the established interleaved-GRE method for short-time-scale (~1 ms) HP ^{3}He diffusion measurements while consuming only a small fraction of HP magnetization. Such a short-time-scale measurement can thus be appended before a stimulated-echo-based, long-time-scale (~0.2-5 s) diffusion pulse sequence[4], which requires a large fraction of the magnetization to yield adequate image quality. In this manner, ADC maps corresponding to two distinct diffusion times, but with the same spatial registration, can be acquired in one breath-hold. A schematic timing diagram for this approach is shown in Figure 1.

Fig. 1. Schematic timing diagram of the pulse sequence for acquisition of co-registered ADC maps at two different diffusion times in one breath hold.

^{3}He diffusion MRI was performed in 15 healthy volunteers (male: 5; female: 10; age range: 45-79 yrs) and a 1-liter gas phantom using a 1.5T commercial scanner (Sonata, Siemens) modified by the addition of the multi-nuclear package and a flexible RF coil (CMRS, Brookfield, WI). ^{3}He was polarized to ~30% by the collisional spin-exchange technique using a commercial system (Model 9600, MITI). The 1-liter gas phantom contained 100 ml ^{3}He and 900 ml N_2. For measurements in humans 400-700 ml of ^{3}He was used, diluted to ~1 liter with N_2. Parameters for the GRE-based technique included: *b* values, 0 and 1.6 s/cm^2; diffusion time (t_d), 1 ms. Parameters for the stimulated-echo-based technique included: *b* value, 60 s/cm^2; tag wavelength, 10 mm; t_d, 1.5 s. Four or five axial ADC maps were acquired at each diffusion time.

Results: Measurements in the gas phantom yielded uniform ADC maps and values consistent with the diffusion coefficient of dilute ^{3}He in nitrogen (~0.8 cm^2/s); the mean ± std was 0.86 ± 0.01 cm^2/s for the short time scale and 0.80 ± 0.11 cm^2/s for the long time scale. High-quality ADC maps with identical spatial registration were obtained at the two diffusion times in all subjects. Figure 2 shows the two sets of ADC maps from a healthy subject. The mean ± std of the ADC values for the healthy group was 0.245 ± 0.042 cm^2/s for the short time scale and 0.0195 ± 0.0037 cm^2/s for the long time scale. These values are in good agreement with the literature. The short-time-scale ADC maps were relatively uniform for all slices. In contrast, the long-time-scale ADC maps were typically uniform except for the most superior 1 or 2 slices. In many cases, regionally elevated ADC values could be clearly observed in superior slices, consistent with the expectation that early lung damage is often first observed in the apices.

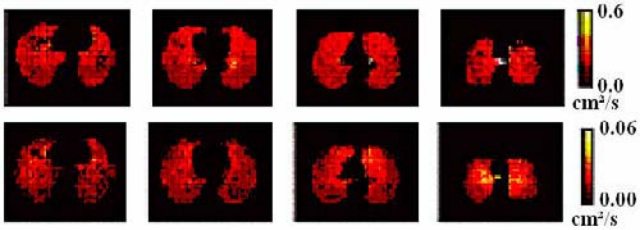

Fig. 2. Co-registered ADC maps from a healthy subject acquired at two different diffusion times in one breath hold. Top row: Short-time-scale, diffusion time = 1 ms; Bottom row: Long-time-scale, diffusion time = 1.5 s.

Conclusion: A new MR pulse sequence was developed for acquiring co-registered ADC maps of HP ^{3}He at two time scales in one breath hold. Studies in a gas phantom validated the proposed pulse sequence. Co-registered ^{3}He ADC maps were acquired in 15 healthy subjects and the measured ADCs were in good agreement with literature values. Regionally elevated long-time-scale ADC values were observed in the apices of the lung. The ability to collected spatially-registered ADC maps at two diffusion times may improve detection and evaluation of pulmonary diseases such as emphysema.

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