Measuring Medium- and Long-Time-Scale Regional ^{3}He Diffusion Using Stimulated Echoes

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Introduction: Hyperpolarized (HP) ^{3}He diffusion MRI of the human lung permits non-invasive characterization of the microstructure of the pulmonary system[1,2,3]. Existing diffusion measurement techniques can access short (~ms) and long (~s) time scales, but cannot measure regional ^{3}He diffusion in the medium time scale, on the order of tens or hundreds of milliseconds. Thus, the characteristics of ^{3}He diffusion in the human lung in this medium-time-scale regime remain unknown. To address this issue, we developed a new STEAM-based MRI pulse sequence that can be used to explore regional ^{3}He diffusion at a selected diffusion time that is longer than 25ms. Phantom studies and preliminary clinical studies were performed to validate this technique.

Methods: The timing scheme for our pulse sequence is illustrated in Fig 1. Between a pair of adiabatic 90° RF pulses, a diffusion-sensitization gradient is applied in the slice-select direction to create longitudinal magnetization that is modulated with a sinusoidal amplitude variation. Following a pause time, a second pair of adiabatic 90° RF pulses with the same diffusion-sensitization gradient is applied. This portion of the sequence is very similar to that proposed by Bourgeois et al. for encoding motion[4]. Prior to diffusion sensitization, two reference images are collected to calibrate for the effects of T1 decay and the imaging RF pulses, and to estimate the signal level before the first pair of adiabatic RF pulses. From the reference images and the 3rd (diffusion-weighted) image, ADC values corresponding to the selected diffusion time (≥ 25ms) can be calculated on a basis of pixel-by-pixel. Compared to the method proposed by Wang et al.[3], the diffusion-encoding time is only limited by two adiabatic pulses and the spoiler gradients, not by the duration of the imaging sequence, so that a much shorter diffusion-encoding time can be achieved.

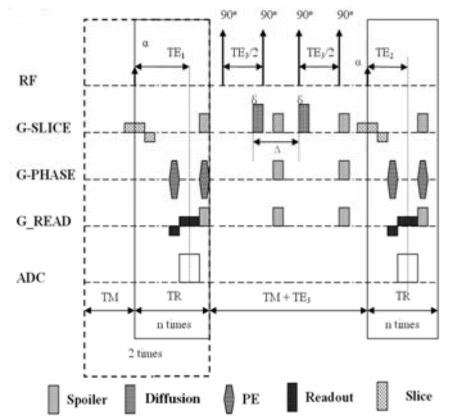

Fig 1. Schematic timing diagram of the pulse sequence used for acquisition of ADC maps.

^{3}He diffusion MRI was performed in 3 healthy volunteers and a 1-liter gas phantom using a 1.5T commercial scanner (Sonata, Siemens) modified by the addition of the multi-nuclear imaging 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, Durham, NC). The 1-liter gas phantom contained 100 ml ^{3}He and 900 ml N_2. The diffusion time was set to 40 ms or 160 ms. For volunteer imaging, 200-300 ml of ^{3}He was used for projection imaging and 400-500 ml of ^{3}He was used for acquisition of multi-slice ADC maps. The diffusion time was set to 50 ms, 200 ms and 1.5 s.

Results: Measured ADC values for the gas phantom were 0.81 ± 0.08 cm^2/s at a diffusion time of 40 ms and 0.80 ± 0.07 cm^2/s at a diffusion time of 160 ms, which are slightly less than, but in good agreement with, the reported ADC values (0.83–0.88 cm^2/s) for the free diffusion of dilute ^{3}He in air or N_2.

All human subjects were able to inhale the HP ^{3}He, perform the required breath-hold maneuvers and tolerate the MR scans. Figure 2 shows example reference images (Fig. 2a, b) and the diffusion-weighted image (Fig. 2c) from subject #2, as well as the ADC maps for diffusion times of 50 ms (Fig. 2d), 200 ms (Fig. 2e) and 1.5 s (Fig. 2f). The regional ADC values were quite homogenous throughout the whole lung with means ± standard deviation of 0.068 ± 0.058 cm^2/s at the diffusion time of 50 ms, 0.026 ± 0.013 cm^2/s at the diffusion time of 200 ms, and 0.0134 ± 0.007 cm^2/s at the diffusion time of 1.5s for this subject. In the healthy subjects, the measured ADC values decreased by 2-3 times when the diffusion time was increased from several milliseconds to 50ms, continued to decrease another 2-3 times when the diffusion time was increased to 200ms, and kept decreasing with further increases in diffusion time.

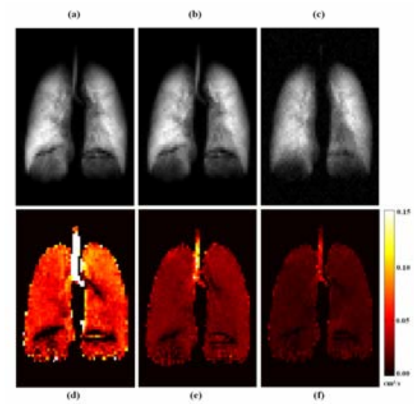

Fig. 2. ^{3}He images and ADC maps from subject 2. (a)-(c) ^{3}He images for a diffusion time (t_d) of 50 ms (a) Reference image 1. (b) Reference image 2. (c) Diffusion-weighted image. (d)-(f) Calculated ADC maps for t_d = 50ms (d), t_d = 200ms (e) and t_d = 1.5s (f).

Conclusion: A stimulated-echo-based technique was developed for measuring the medium- or long-time-scale ADC of HP ^{3}He in the human lung during a single breath-hold acquisition. A gas phantom study verified the proposed method. In 3 healthy subjects, the mean ADC values decreased monotonically with increasing diffusion time and the measured ADC maps at each diffusion time were homogenous. The measured ADC values were in a small range for healthy subjects when measured with the same parameters.

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References:
1. Saam B, et al. Magn Reson Med 2000; 44:174-179.
2. Woods JC, et al. Magn Reson Med 2004; 51: 1002-1008.
3. Wang C, et al. Magn Reson Med 2006; 56:296-309.
4. Bourgeois D, et al. J Magn Reson 1991; 94:20-33.