Demonstration of an Alveolar-Size Gradient in the Healthy Human Lung: A Study of the Reproducibility of Hyperpolarized ^{3}He Diffusion MRI

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Introduction

Although the apparent diffusion coefficient (ADC) of ^{3}He has been measured in the human lung [1,2,3], no studies have determined the reproducibility of ADC values. Since the ADC is dependent on the size of the alveoli, ADC values are expected to fluctuate depending on the degree of inflation of the subject's lungs. This hypothesis is supported by results from Chen et al. [4] that demonstrated a difference in the measured ADC between rats imaged during a tidal breath hold and at end expiratory volume. Furthermore, due to the well-known gravity-dependent effect, there should be a gradient in the ADC values from posterior to anterior. The aims of this study were to: (1) ascertain the reproducibility of ADC values between studies, and (2) determine if a gravity-dependent gradient in the ADC value can be detected.

Methods

Hyperpolarized ^{3}He MRI scans were performed in three healthy volunteers. Each volunteer was imaged on two separate occasions. For two of the volunteers, two sets of diffusion-weighted images were acquired during one imaging session without moving the subject. During each experiment, three coronal slices of the lung were obtained during suspended respiration. The data was collected in 18 seconds after the subject inhaled a mixture of 350ml of 20-30% polarized ^{3}He (Model 9600 Helium Polarizer, Nycomed-Amersham Imaging, Durham, NC) diluted to 1.0L with ^{4}He. Imaging was performed using a 1.5T whole-body imager (Magnetom Vision, Siemens Medical Systems, Iselin, NJ). A gradient-echo (FLASH) pulse sequence (TR/TE 16/6ms, FA 6^o, FOV 38x50cm, thickness 10-15mm, matrix 100x256) was used with additional gradients for diffusion weighting in the readout direction to achieve b-values of 0.4, 0.8, 1.2 and 1.6 s/cm^2. ADC maps were calculated by linear least squares fitting of the natural log of the signal versus the b-value. Only voxels whose p-values were <0.20 were included in ADC histograms.

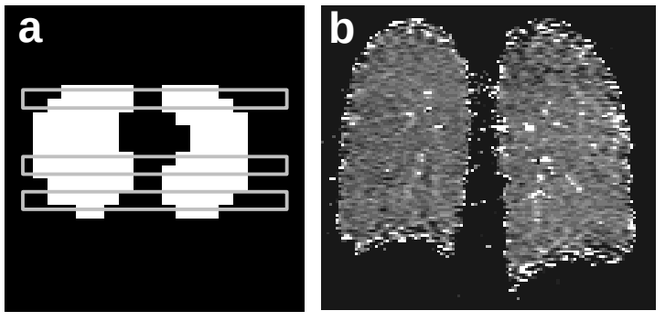

Figure 1: (**a**) Axial ^{3}He scout image showing the slice positions for the diffusion measurements. (**b**) Representative ADC map from one of the healthy volunteers.

Results

An axial scout image showing the approximate slice positions, and a representative ADC map from one of the volunteers, is shown in Figure 1. The mean ADC for all thirty slices that were analyzed was 0.24 ± 0.03 cm^2/s. The corresponding mean width of the ADC histograms (as represented by the standard deviation [SD] of the respective ADC values) was 0.11 ± 0.02 cm^2/s. For each set of three slices, the average standard deviations of the mean ADCs and histogram widths were 0.03 and 0.02 cm^2/s, respectively. For each subject, there was no statistical difference between the means obtained in any two experiments. For any subject, the overall SD in the mean ADC at a given slice position was 0.03 cm^2/s. When the subject was not repositioned between experiments, the SD was 0.01 cm^2/s. Figure 2 shows ADC histograms calculated from the posterior and anterior slices in one of the volunteers. A statistically-significant ($p < 0.02$) posterior-to-anterior gradient in the mean ADC values was seen in all subjects. The average difference in the ADC from posterior to anterior was 0.06 cm^2/s.

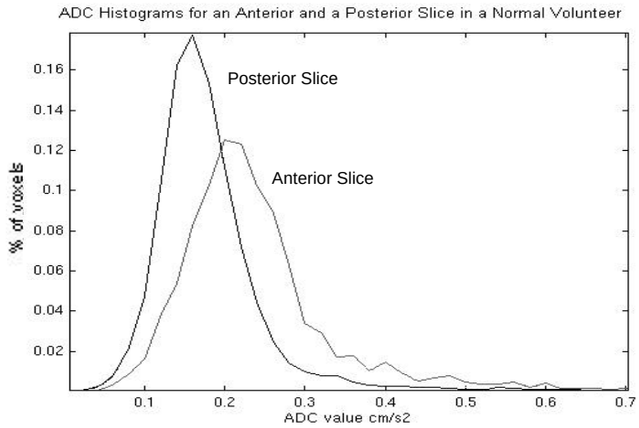

Figure 2: ADC histograms from posterior (mean 0.19 cm^2/s, SD 0.08 cm^2/s) and anterior (mean 0.24 cm^2/s, SD 0.10 cm^2/s) slices demonstrating an inflation-dependent gradient in the ADC values.

Discussion

Despite variations in slice position, polarization, and lung inflation, the mean ADC from a given set of images was reproduced with a SD of 0.03 cm^2/s. This variation is due both to physiological differences in alveolar inflation at different positions in the lung, as well as to experimental noise. For a given slice position, the mean was reproduced between any set of experiments to within 0.03 cm^2/s, while between experiments when the subject was not moved this deviation decreased to 0.01 cm^2/s. In all experiments, the most anterior slice had a mean ADC that was on average of 0.06 cm^2/s higher than that for the posterior slice. This difference correlates with the known gradient in alveolar inflation seen in the upright lung due to gravity, which results in alveoli near the apex being larger than those near the base. This gradient is larger than the variations in the reproducibility of the measured ADC for a given slice, and thus is most likely a result of the gravity-dependent effect.

Conclusion

These results suggest that the mean ADC calculated using hyperpolarized ^{3}He diffusion MRI is reproducible. The detection of the alveolar inflation gradient resulting from the gravity-dependent effect attests to the sensitivity of this technique

References

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