Increased Anisotropy in the Subpleural Lung as Assessed with Hyperpolarized He3 Imaging

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Target audience: Imaging scientists and physicians interested in methods for characterizing the microstructure of the lung.

Rationale & Purpose: The apparent diffusion coefficient (ADC) of inhaled hyperpolarized helium-3 (He3) gas is sensitive to the microstructure of the lung [1]. Histologic studies of the lung have demonstrated that alveolar ducts emanating from terminal bronchioles near the pleural surface show a preferential orientation perpendicular to the pleural surface, in contrast to deeper regions [2]. The goal of the present study was to evaluate the anisotropy of the lung by assessing the dependence of He3 ADC values on the direction of the diffusion-sensitization gradient, and, in particular, to determine whether He3 ADC imaging is sufficiently sensitive to detect subtle microstructural variations such as those near pleural surfaces.

Methods: Hyperpolarized He3 diffusion-weighted MRI of the human lung was performed at 1.5T and 0.43T in 12 healthy volunteers on a clinical whole-body scanner (Avanto, Siemens) using flexible chest transmit/receive He3 RF coils (Clinical MR Solutions, Brookfield, WI). Helium-3 gas was polarized by collisional spin exchange with optically-pumped rubidium/potassium vapor using a custom-built system [3], yielding polarizations between 40 and 60%. Each subject inhaled a gas mixture containing 500 ml of hyperpolarized He3 and medical grade nitrogen for a total volume equal to approximately one-third of the subject's forced vital capacity. After inhaling the He3/nitrogen mixture, the subject then inhaled room air to total lung capacity. All experiments were performed under a Physician's IND for imaging with hyperpolarized He3 using a protocol approved by our institutional review board. Informed consent was obtained in all cases.

A gradient-echo pulse sequence was used with application of a bipolar diffusion-sensitization gradient waveform between the excitation RF pulse and the associated spatial-encoding gradients. During a single breath-hold period, diffusion-weighted data were acquired with diffusion-sensitization along three orthogonal directions (phase-encoding, readout and slice-select) and a b value of 1.6 s/cm^2, yielding ADC maps for three diffusion-sensitization directions per breath-hold. (For a given line of k space, the acquisition order was b = 0, b = 1.6 s/cm^2 [phase, transverse (left-right)], b = 0, b = 1.6 s/cm^2 [readout, craniocaudal], b = 0, b = 1.6 s/cm^2 [slice, anteroposterior]). Other pulse sequence parameters included: TR/TE 9.8/6.4 ms, flip angle 5°, voxel size 3.3 x 6.6 x 25 mm.

Following application of a threshold to suppress background noise, ADC maps for the three diffusion-sensitization directions were calculated from the diffusion-weighted images using the standard equation ADC = $(\ln S_{b=0} - \ln S_{b=1.6})/\Delta b$. In addition, maps of the fractional difference between the ADC corresponding to a particular direction and the ADC mean over all directions (on a pixel-by-pixel basis) were also calculated.

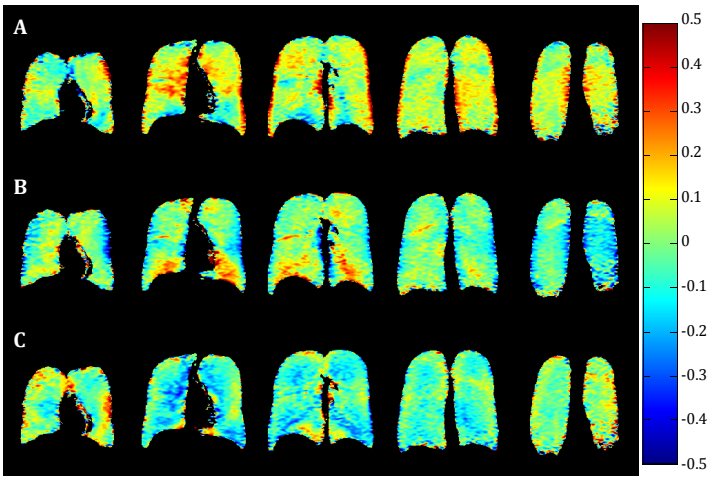

Figure 1. Representative maps showing the difference between the ADC values obtained with the diffusion sensitization gradient applied in the phase (A) readout (B) and slice (C) directions and the mean ADC value, divided by the mean ADC value. The colorbar shown on the right is in units of the fractional difference. Note the relatively increased ADC values along the lateral aspects of the lung when the diffusion sensitization was perpendicular to the lateral chest wall (A) and relatively decreased ADC values along the lateral aspects of the lung when the diffusion sensitization was parallel to the lateral chest wall (B).

Results & Discussion: ADC values were dependent on the direction of the sensitization gradient applied. Compared to the central region of the lung, ADC values were increased at the lateral and medial surface for transverse diffusion sensitization; at the apex, base and along the major fissure for craniocaudal diffusion sensitization; and at the most anterior and posterior lung for anteroposterior diffusion sensitization (**Fig. 1**). This pattern of increased ADC values is consistent with preferential alignment of the alveolar ducts perpendicular to pleural surfaces, since such a preferential alignment would be expected to result in an ADC value higher than that for randomly oriented alveolar ducts when the direction of diffusion sensitization is perpendicular to the surface.

The sensitization direction-dependent pattern of the ADC maps was very similar at field strengths of 1.5 and 0.43T. This finding supports that the observed variations in ADC values are due to microstructural variations rather than being caused by magnetic-susceptibility effects.

Conclusion: These findings suggest that diffusion-weighted hyperpolarized He3 MRI is sensitive enough to detect increased anisotropy in the subpleural lung parenchyma, likely reflecting preferential orientation of the terminal airways/airspaces in the direction perpendicular to the visceral pleura.

References:
1. Yablonskiy DA et al. J Appl Physiol. 2009; 107:1258-1265.
2. Bachofen H at al. J Appl Physiol 1987; 62:1878-1887.
3. Mooney KE et al. ISMRM 2009; 2166.

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