Diffusion Tensor Imaging of the Rat Lung using Hyperpolarized 3He

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Introduction

Chronic obstructive pulmonary disease (COPD) is a complicated disorder of the lung characterized by alveolar damage (i.e. emphysema) and airway obstruction due to mucous plugging and changes in airway mechanics. The ability to distinguish alveolar damage from airway obstruction may help stratify disease and may well determine prognosis and therapeutic approach. Hyperpolarized ^{3}He MR imaging has proven to be valuable in the detection of emphysema based on increases in the apparent diffusion coefficient (ADC) [1]. Since the diffusion of ^{3}He is expected to be different in the alveoli (i.e. isotropic) compared to the airways (i.e. anisotropic), it has been suggested that measurement of the directionality of diffusion may permit the differentiation of lung structures on this basis.

Diffusion tensor imaging (DTI) measures the magnitude and directionality of diffusion in tissues in the body. It has been used successfully to image myelin tracts in the brain [2] but, so far, it has not been applied to image the airways using hyperpolarized ^{3}He. This work presents DTI imaging using hyperpolarized ^{3}He gas in both a physical model system (i.e. phantom) consisting of dialysis capillaries as well as in rat lungs.

Methods

The MR signal attenuation, due to the dephasing effects of diffusion in a magnetic gradient field, is given by $A(\vec{b})/A(\vec{0}) = \exp\{-trace(\vec{b}\vec{D})\}$ [3], where A is the amplitude of the MR signal, $\vec{D}$ is the diffusion tensor and $\vec{b}$ is a 3x3 matrix which can be calculated from the magnitude, direction and timing of the diffusion sensitization gradients. The expression above can be used to map the symmetric diffusion tensor using six or more separate diffusion sensitization gradients in the method of [3] and [4].

^{3}He was polarized using a turn-key spin-exchange polarizing system (Helispin®, GEHC). All imaging was performed at 3T (GEHC) using a quadrature birdcage coil (diameter = 15cm) (Morris Instruments, Ottawa, Canada) and a gradient echo sequence with diffusion sensitization. A variable flip angle (VFA) [5] technique was used in order to minimize the effect of RF pulses on the non-recovering magnetization (5). Diffusion sensitization was applied in six different directions [4], using trapezoidal bipolar gradient pulses applied for a total time of 2920 µs with rise (and fall) times of 500 µs, plateau times of 460 µs and a diffusion time of 1460µs, giving a b value in each direction of 1.6s/cm^2. The images were acquired with a 5 cm x 5 cm FOV. Diffusion tensor maps were constructed and the eigenvalues and eigenvectors of the diffusion tensors were calculated. These were used to calculate the diffusion trace image (Fig. 2) and diffusion ellipsoid maps (Fig. 1 and 3).

DTI was performed in a lung phantom as well as in rat lungs. The phantom consisted of a bundle of dialysis capillaries, each with an inner diameter of 0.5mm, all aligned in the same direction. DTI images were acquired in the axial plane (5 cm slice thickness) with a matrix of 96 x 96 (TE = 4.0 ms, TR = 21.5 ms,). DTI was also performed on Sprague Dawley rats (~500 g) using pure hyperpolarized ^{3}He gas (~35%), following an animal care protocol approved by the University of Western Ontario. The gas was administered using a custom ventilator, modified to include a non-magnetic valve assembly for delivery of ^{3}He within the MR imaging environment and with minimal depolarization. Six wash-out breaths followed by a 20 second breath-hold of ^{3}He were applied and imaging was performed during the breath-hold interval. The rat imaging was performed with a matrix of 64 x 64 in the coronal plane (TE = 4.5 ms, TR = 21.5 ms,), four averages (i.e. separate ^{3}He breath-holds) and with no slice selection to maximize SNR.

Results

Figure 1 shows the diffusion ellipsoids in the axial plane from the phantom experiment. As expected, the diffusion anisotropy is predominantly in the z direction, the direction of the orientation of the capillaries. The eigenvalues (averaged over the image) can be used to give the ratio of the RMS displacement in the z direction to that in the x-y plane [6]. This was calculated to be 3.4. This shows rough agreement to the RMS displacement ratio calculated by assuming that the maximum displacement in the x-y plane is equal to the diameter of the capillaries, which is 3.2. Figure 2 show the trace of the diffusion tensor in the rat lungs. The magnitude of the diffusion is highest in the upper airways where there is less restriction than in the smaller airways and alveoli of the rest of the lung. Figure 3 shows diffusion ellipsoids in the rat lungs. In the trachea, the diffusion anisotropy is predominantly along the axis of the trachea as expected.

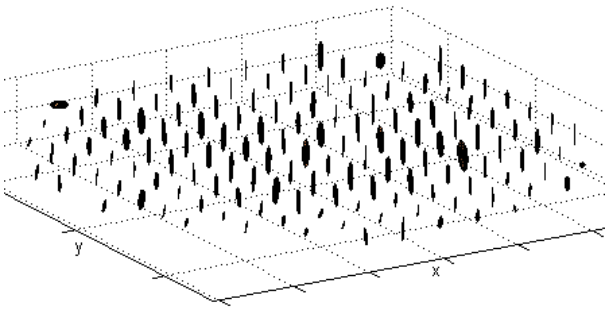

fig. 1: Ellipsoid plot of phantom in axial plane

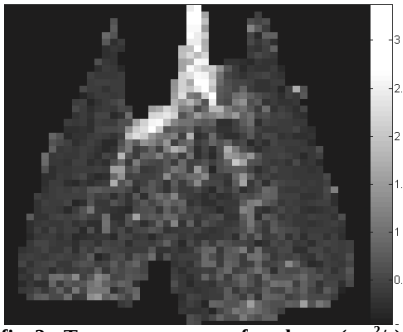

fig. 2: Tensor trace map of rat lungs (cm^2/s)

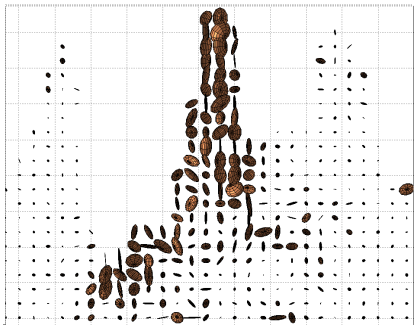

fig. 3: Ellipsoid plot rat upper lungs

Discussion

It was found that DTI can be used to map the full diffusion tensor of hyperpolarized ^{3}He in a phantom and in vivo in rat lungs. The tensors can be used to give full information of the directionality and magnitude of the diffusion.

In this work, six diffusion sensitization directions were used. Increasing the number of sensitization directions can improve DTI quality [3], especially if multiple ^{3}He breath-holds can be performed. The DTI results are also expected to depend strongly on diffusion time (τ_e). Varying τ_e will likely sensitize DTI to different length scales permitting further differentiation of airway structures from parenchyma. The use of lower field strengths will likely permit the use of longer diffusion time due to the shorter echo times. The use of hyperpolarized ^{129}Xe, as a contrast agent, is likely to give greater sensitivity to shorter length scales due to its lower diffusion coefficient. This work suggests the possibility of using DTI to better diagnose lung disease in future.

References

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