Quantification of lung microstructure in asthma using a ^{3}He fractional diffusion approach

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Target audience: Lung imaging, Diffusion MRI, hyperpolarized agents

Purpose: To quantify lung microstructure in asthma patients using a stretched-exponential model of ^{3}He MRI diffusion measurements.

Introduction

MR diffusion experiments using hyperpolarized gases are sensitive to acinar airway dimensions. The fractional diffusion stretched-exponential model has been shown to provide a robust quantitative measure of changes in lung microstructure due to emphysema [1]. In this work, this approach is further developed to allow for in-vivo estimation of the distributions of the microscopic length scales of acinar airways from ^{3}He diffusion MRI data. This new technique is used to assess the acinar microstructure in asthma patients and the results are compared with CT densitometry and macroscopic ^{3}He ventilation distributions.

Methods

Thirty-three patients (moderate-severe uncontrolled asthmatics GINA 2-5) were scanned at 1.5T using hyperpolarised ^{3}He with local ethics approval. A 2D spoiled gradient echo imaging sequence (64x48 matrix, TE: 4.8 ms, TR: 9.0 ms, FOV:38.4 cm) with bipolar diffusion gradients (diffusion time Δ= 1.6ms) was used and five slices were acquired consecutively (thickness 15mm and 10mm spacing). Four interleaved acquisitions were obtained for each slice, corresponding to equally spaced diffusion b values: 0, 2.4, 4.8 and 7.2 s/cm^2.

The decay of the diffusion signal S(b) in the images can be described using the stretched exponential function [1]: $S(b)/S_0 = \exp[-(b.DDC)^{\alpha}]$; where DDC is the diffusivity and α is the heterogeneity index. Unlike existing geometrical models this model addresses the non-mono exponential nature of the diffusion MRI signal without any underlying assumptions of airway geometry. Taking into account that the macroscopic voxel signal originates from the superposition of signals from multiple microscopic compartment with different apparent diffusivities D, i.e. $S(b)/S_0 = \int p(D) \exp(-b.D)\, dD$, the probability density function $p(D)$ for each voxel can then be estimated [2] from the stretched exponential parameters. The distribution of length scales L_D (i.e. root mean squared displacements) associated with the D values can then be calculated using the diffusion equation: $L_D = (2D\Delta)^{1/2}$ for each voxel. The $p(L_D)$ distributions are hence a measure of the distribution of microscopic dimensions of the airways contained within a given voxel. A mean length value Lm_D, was calculated for each patient's diffusion imaging data (average over all voxels) and compared with their corresponding CT attenuation values (full expiration), percentage ventilation volumes (Vv%) from the ^{3}He ventilation images [4] and pulmonary function test (PFT) results.

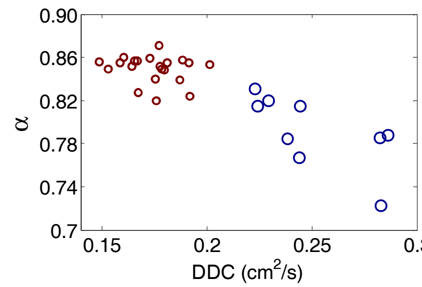

Figure 1. Scatter plot of average DDC and α values in asthma patients. Cluster 1(small circles), cluster 2 (large circles)

Results and Discussion

Experimental results showed a significant variation in the values of the DDC and α parameters among the asthma patients, which were classified into two clusters using a k-means algorithm (Fig.1). Patients in cluster 1 showed values near those found in normal lungs in a previous study [1], while patients in cluster 2 had values of DDC (higher) and α (lower) that deviated from the normal range. This deviation is however lower than that reported in COPD patients [1].

The distributions of airway length scales $p(L_D)$ (Fig. 2) in patients in Cluster 2 were broader and shifted toward higher airway length scales L_D than distributions from patients in Cluster 1. The shape of these distributions are very similar to the distributions of intercept length (Lx) obtained in histological studies [3]. The Lm_D values showed significant correlation with FRC (% predicted): ρ= 0.75, p<0.001 and CT density: ρ= -0.79, p<0.001 (Fig. 3). Unlike average CT density, the Lm_D values are obtained from ^{3}He ventilated regions only (i.e. does not include trapped air). Higher correlation may be achieved if unventilated regions are excluded from the CT average density calculation and we extend to a regional comparison using image registration. Although patients showed a range of ventilation defect sizes affecting different lung regions (Fig. 4) , patients in cluster 1 were generally better ventilated than those with abnormal diffusion parameters (cluster 2). The percent ventilation volume [4] Vv% showed significant correlation with Lm_D (ρ= -0.58, p<0.001), which indicates that patients with the most significant ventilation impairment also presented the largest changes in lung microstructure.

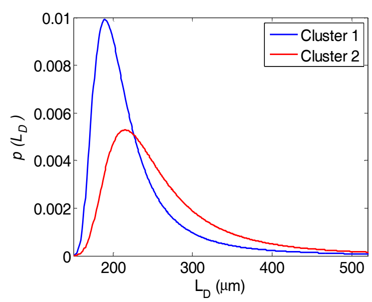

Figure 2. Length scale distributions L_D obtained for representative patients from each cluster.

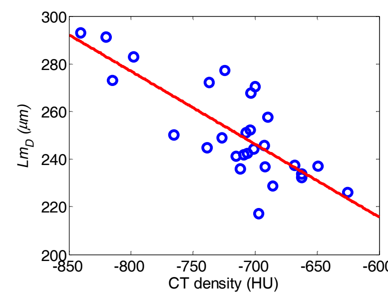

Figure 3. The mean airway length scale Lm_D is linearly correlated to CT density.

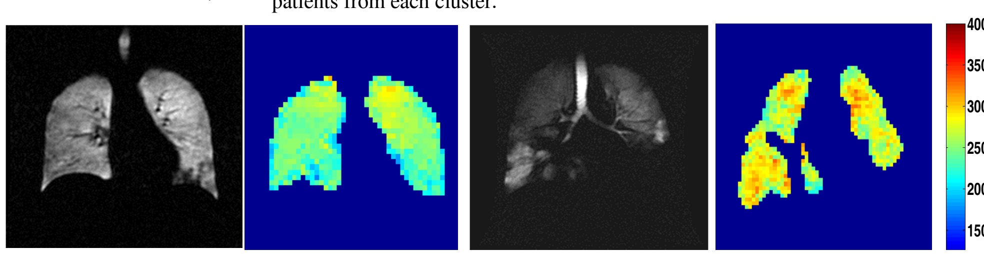

Figure 4. Sample ventilation images (grayscale) and Lm_D (color) maps (in μm) obtained from two patients, representative of clusters 1 (left) and 2 (right).

Conclusion

Our results demonstrate the potential of a fractional exponential model of ^{3}He diffusion MRI for the non-invasive, spatially-resolved analysis of microscopic distributions of length scales of acinar airways. Such information is currently only accessible from histological measurements of tissue samples from discrete biopsy or post mortem. The quantitative parameters estimated with this model (DDC, α and Lm_D) may help to improve the diagnosis and classification of asthma patients.

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References

[1] Proc. ISMRM (2012) 820. [2] Chem. Phys. 315 (2005) 171-182. [3] J. Appl. Physiol. 108 (2010) 412-421. [4] J Magn Reson Imaging 2005 21(4):365-9