Characterization of ^{3}He Diffusion in Lungs using a Stretched Exponential Model

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Target audience: Lung imaging, Diffusion MRI, hyperpolarized agents
Purpose: To assess the suitability of using a stretched-exponential model to describe multi b-value ^{3}He MRI diffusion data from COPD patients.

Introduction

MR diffusion experiments using hyperpolarized gases are sensitive to changes in lung microstructure due to emphysema. The interpretation of the measured ADC is complicated by the complex relationship between the MR diffusion signal behaviour and the geometrical and physical properties of lung microstructure [1] . Furthermore ADC values also depend on experimental conditions such as MR sequence parameters, lung inflation and gas mixture composition. Theoretical models currently used to fit diffusion data [2] are only valid for a limited of range experimental conditions and for idealized geometries which differ significantly from lung microstructure, particularly in emphysematous lungs. In this work, the anomalous diffusion stretched-exponential model is used to describe multi b-value ^{3}He MRI diffusion data from normal volunteers and COPD patients. This model can be used to quantify signals arising from a multiplicity of sources and does not require assumptions about the geometry of the restricting structures, distribution of apparent diffusion rates or the number of compartments present in the voxel [3].

Methods

Seven healthy volunteers (two smokers and five non-smokers) and ten patients with moderate to severe COPD as defined by NICE guidelines (http://guidance.nice.org.uk/CG101) were scanned at 1.5T using hyperpolarised ^{3}He with local ethics approval. A 2D spoiled gradient echo (64x64 matrix, TE: 4.8 ms, TR: 8.0 ms, FOV:35 cm) with bipolar diffusion gradients (rise and fall times 0.3 ms) was used and five slices were acquired consecutively (thickness 15mm and 10mm spacing). Six interleaved acquisitions were obtained for each slice: two acquisitions (first and last) with b = 0 s/cm^2 to obtain flip angle maps for correction of RF depletion effects, and four corresponding to equally spaced b values up to a maximum b = 6.4 s/cm^2. Five healthy volunteers were scanned at two lung inflation levels (FRC+1L and TLC) and a range of diffusion times Δ: 1.4-2.5 ms. The other two healthy volunteers and the COPD patients were scanned at FRC+1L with 1.6 ms diffusion time only. The diffusion weighted images were fitted pixel by pixel to the stretched exponential function [4]: $S(b)/S_0 = \exp[-(b.DDC)^{\alpha}]$; where DDC is the diffusivity and α is the heterogeneity index.

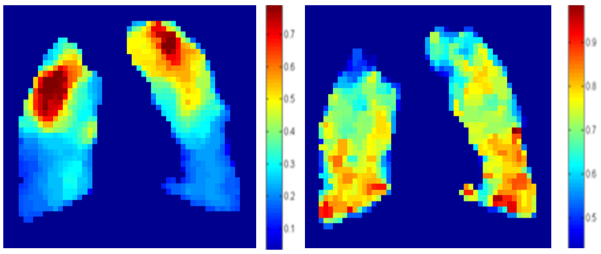

Figure 1. Maps of DDC (left, cm^2/s) and α (right) obtained from a COPD patient.

Results and Discussion

Maps of DDC and α (e.g. Fig. 1) were obtained from the normal and COPD diffusion data. The results (Table 1) demonstrate that while the diffusivity (DDC) varied significantly (standard deviation/mean ~12%) among the healthy volunteers, the heterogeneity index α remained constant (~2% variation), regardless of the diffusion time (in the range 1.6-2.5 ms), lung inflation and subject's size. ADC values also varied between normal subjects (11% variation) and strongly depended on diffusion time and lung inflation level (Table 1). Both, DDC and α were significantly different for the COPD patients (Fig. 2). DDC and α values in healthy smokers deviated slightly from the values obtained in non-smokers (Fig. 2).

These results indicate that α may provide a robust measure of the underlying complexity and patterns of the geometry of the restricting boundaries, which is sensitive to changes in lung structure due to disease, and valid over a range of experimental conditions.

Since the stretched exponential model is not constrained to a specific range of timing parameters, it may be able to reveal information about lung microstructure at different length scales. This information may be sensitive to lung diseases that affect airway morphology at different generations of the lung branching structure.

Subject	FRC+1L			TLC		
	ADC	DDC	α	ADC	DDC	α
1	0.138	0.113	0.877	0.172	0.144	0.87
2	0.155	0.127	0.869	0.185	0.154	0.862
3	0.167	0.142	0.873	0.17	0.146	0.869
4	0.194	0.157	0.837	0.202	0.166	0.842
5	0.187	0.152	0.848	0.212	0.177	0.847

Table 1. Mean (whole lung) ADC, DDC and α values estimated from ^{3}He diffusion images of normal volunteers obtained at two lung inflation levels and Δ= 1.6 ms.

Conclusion

Our results show that the stretched exponential model may provide a robust measure of changes in lung structure due to disease that is valid over a range of experimental conditions. This seems to indicate that the parameter α is insensitive to a range of uncertainties in experimental conditions but sensitive to changes in lung structure due to COPD/emphysema.

Acknowledgements

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References

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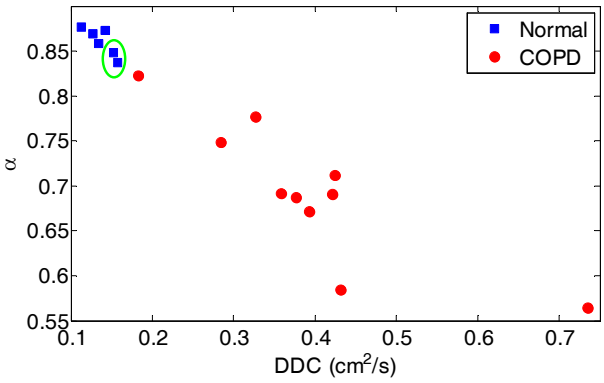

Figure 2. Scatter plot of α vs. DDC obtained from the healthy volunteers (two had identical values α and DDC values) and COPD patients. Note that the values for healthy smokers (circled in green) deviated from the value for non-smokers.

Subject	ADC	DDC	α
1	0.416	0.393	0.671
2	0.444	0.424	0.712
3	0.448	0.421	0.691
4	0.359	0.327	0.777
5	0.615	0.735	0.564
6	0.335	0.284	0.748
7	0.448	0.432	0.584
8	0.388	0.358	0.692
9	0.394	0.377	0.687
10	0.23	0.183	0.823

Table 2. ADC, DDC and α values estimated from COPD patients.