

# INTER-LUNG DIFFERENCES IN <sup>3</sup>HE DIFFUSION MRI IN YOUNG ADULTS WITH CONGENITAL DIAPHRAGMATIC HERNIA: ANALYSIS USING A STRETCHED EXPONENTIAL MODEL

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**Target audience:** Lung imaging, Diffusion MRI

**Purpose:** To assess changes in lung microstructure in young adults with Congenital Diaphragmatic Hernia using a stretched exponential model of <sup>3</sup>He diffusion MR

## Introduction

Lung function abnormalities through different stages of life have been reported in several cross-sectional studies in congenital diaphragmatic hernia (CDH) patients. Neonates with CDH are at risk of developing chronic lung disease due to ventilator induced injury and high concentrations of oxygen. Studies on the morphological substrate for these changes are scarce and it is unknown to what extent normal lung growth occurs after birth. In a recent study [1] we used hyperpolarised <sup>3</sup>He MRI to investigate a cohort of young adult CDH patients. Our results showed ventilation abnormalities and elevated apparent diffusion coefficient (ADC) values in the left lung of the patients. A simple single b-value (i.e. mono-exponential) ADC analysis is insufficient to assess if the elevated ADC values result from lung hyperinflation on the side of the CDH lung or if underlying structural changes are also present. To try to answer this question, in this work we use a stretched exponential model [2, 3] to analyse the non-Gaussian behaviour of the <sup>3</sup>He diffusion signal;

$$S(b)/S_0 = \exp[-(b \cdot DDC)^\alpha] \quad (1)$$

The diffusivity parameter DDC can be thought of as an ADC approximation that is weighted by the continuous distribution of helium diffusivities inside the voxel. The heterogeneity index  $\alpha$  is a measure of the spread of the distribution of diffusion rates inside a voxel [3], and hence an index of non mono-exponentiality of the diffusion signal decay. For <sup>3</sup>He diffusion in human lungs, we have shown [4] that while ADC and DDC are affected by experimental parameters such as lung inflation and gas mixture composition;  $\alpha$  is sensitive to changes in lung microstructure (e.g. in COPD) but is far less sensitive to experimental conditions over a wide parameter range.

## Methods

Nine patients with left-sided CDH born between 1975 and 1993, were scanned with a 1.5T MRI system (Signa HDx, GE, USA) and a <sup>3</sup>He transmit-receive vest coil (CRMS, WI). Diffusion images were acquired at breath hold after inhalation of 300ml hyperpolarised <sup>3</sup>He and 700ml N<sub>2</sub>. A 2D spoiled gradient echo (64x64 matrix, TE: 4.8 ms, TR: 8.0 ms, FOV:35 cm) with bipolar diffusion gradients was used and five slices were acquired consecutively (thickness 15mm and 10mm spacing). Six interleaved acquisitions were obtained for each slice corresponding to b values of: 0, 1.6, 3.2, 4.8, 6.4 and 0 s/cm<sup>2</sup>. The two acquisitions with b = 0 s/cm<sup>2</sup> are used to obtain flip angle maps for correction of RF depletion effects. The diffusion weighted images were fitted pixel by pixel to the stretched exponential function in Eq. (1) [3]; where DDC is the diffusivity and  $\alpha$  is the heterogeneity index. The simple mono-exponential ADC was calculated from the first and second interleaved acquisition (i.e. for b= 1.6 s/cm<sup>2</sup>). The left and right lung regions were manually segmented for each slice, and the mean and standard deviation of ADC, DDC and  $\alpha$  values were calculated.

## Results and Discussion

Similar to seen in the ADC analysis [1], the DDC values were significantly elevated in the left lung of 8 patients and one patient (subject 1) reported similar (normal) values of all parameters in both lungs. In two of the patients (subjects 3 and 4) with elevated ADC and DDC values in the left lung, the  $\alpha$  values were similar in both lungs and similar to those previously reported for normal volunteers [3]. This is similar to what is observed in normal lungs at different inflation levels, DDC at TLC is larger than at FRC+1L, but  $\alpha$  does not change [4]. This result suggest that in the case of these two patients, the elevated ADC and DDC values are due to enlargement of the acinar airways (possibly due to hyperinflation or isotropic enlargement that may be related to stretching from the developmental defect of the diaphragm), but that no changes in the underlying pattern of distribution of the lung micro-structural anatomy have occurred.

In five of the remaining patients (subjects 2, 5, 6, 7 and 9), the  $\alpha$  values in the left lung were lower than the values in the right lung, which showed normal values. These results suggest that in those five patients, not only are the airways in the left lung larger in size, but that changes in the underlying pattern of distribution of micro-structural anatomy have occurred in the left lung. In one patient (subject 8), both lungs showed  $\alpha$  values below the normal range (likely due to CDH structural changes), with the right lung showing the lowest  $\alpha$  value. This suggests that the structural changes of acinar microstructure present in this patient affects both lungs and hence may be due to due to ventilator induced injury and/or high concentrations of oxygen rather than related to the developmental defect of the diaphragm.

Understanding the exact nature of the lung microstructure changes suggested by our results require further research. Although a decrease in  $\alpha$  value indicates a more heterogeneous distribution of diffusivities within a voxel and hence different underlying patterns of geometry of diffusion restricting structures (i.e. acinar airways and alveoli), the relationship between  $\alpha$  and alternative morphological parameters such as surface to volume ratio and airway dimensions are yet unknown and the subject of ongoing research.

## Conclusion

Analysis of <sup>3</sup>He MR diffusion in patients with left lung CDH using a stretched exponential model have shown that although most patients present airway enlargement in the left lung; microstructural changes related to the developmental defect of the diaphragm only occur in some of them.

## References

- [1] Spoel/Marshall et al. ERS 2012; P1694  
[3] Bennet et al, Magn Res Med 56:235-239 (2006)

- [2] Parra-Robles et al. Proc. ISMRM 2010; 2358  
[4] Parra-Robles et al. ERS 2012; P1704

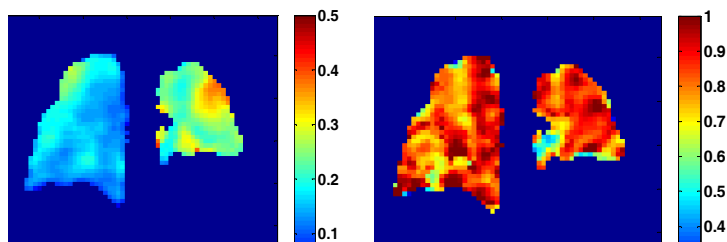


Figure 1. DDC (cm<sup>2</sup>/s) and  $\alpha$  maps obtained from a CDH patient (subject 9).

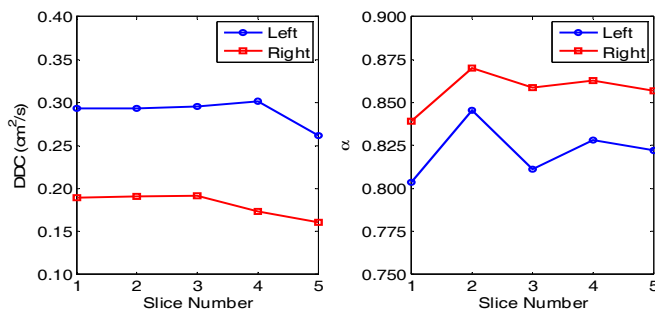


Figure 2. Mean slice DDC and  $\alpha$  obtained from the left and right lungs of subject 9.

Subject	ADC <sub>LEFT</sub> (cm <sup>2</sup> /s)	ADC <sub>RIGHT</sub> (cm <sup>2</sup> /s)	DDC <sub>LEFT</sub> (cm <sup>2</sup> /s)	DDC <sub>RIGHT</sub> (cm <sup>2</sup> /s)	$\alpha_{LEFT}$	$\alpha_{RIGHT}$
1	0.218±0.001	0.225±0.002	0.181±0.001	0.182±0.001	0.852±0.003	0.839±0.004
2	0.209±0.001	0.176±0.001	0.180±0.001	0.149±0.001	0.873±0.003	0.888±0.004
3	0.204±0.001	0.183±0.001	0.174±0.001	0.149±0.001	0.872±0.004	0.879±0.005
4	0.202±0.001	0.184±0.001	0.176±0.001	0.151±0.001	0.872±0.004	0.872±0.004
5	0.218±0.002	0.203±0.001	0.185±0.001	0.171±0.001	0.857±0.004	0.878±0.004
6	0.273±0.002	0.201±0.001	0.241±0.002	0.171±0.001	0.848±0.004	0.876±0.004
7	0.269±0.002	0.213±0.001	0.234±0.002	0.178±0.001	0.838±0.004	0.864±0.003
8	0.252±0.001	0.229±0.001	0.218±0.001	0.185±0.001	0.842±0.002	0.821±0.003
9	0.322±0.002	0.214±0.001	0.288±0.002	0.179±0.001	0.824±0.004	0.858±0.004

Table 1. Mean ADC, DDC and  $\alpha$  values estimated from the left and right lungs of the CDH patients. The errors are the standard deviation of the mean.