Long-range diffusion of hyperpolarized 3He in normal and emphysematous rat lungs

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Introduction: Diffusion weighted imaging and in particular the apparent diffusion coefficient (ADC) are among the main lung gas MRI applications. Since ADC values are related to molecular mobility, they are expected to reflex changes in lung microstructure, and hence be used as a detector for early stage lung diseases. Long-range diffusion can instead provide information about the microstructural sizes and connectivity of the lung airspaces. The main aim of this work was to measure long-range ADC in rats in a single-lobe model of emphysema, at breath-hold and end expiration.

Methods: The left lobe of the lung of 10 Wistar rats were instilled with 25 units of porcine pancreatic elastase dissolved in a volume of 0.1ml/100g animal weight. Five of these animals were measured six weeks after the instillation and another three animals were imaged seven weeks after the instillation. Prior to imaging, animals were anaesthetized with thiopental sodium, intubated and connected to a mechanical ventilator, which ventilated animals at 60bpm with a mixture consisting of 21% O_2 and 79% ^{4}He. The ventilator also applied a bolus of HP-gas to reach a full-inspiration of 25mbar of pressure. A 10s-breath-hold was applied to the animals in the acquisition mode. Animals were imaged during the breath-hold at 25mbar and also at the end of the expiration following the application of a short full-inspiration, they are denoted as BH and EEV, respectively. The gas applied for imaging consisted of 77% HP^{3}He and 23% N_2. This mixture was prepared in order to avoid the effect of having different diffusion coefficients due to having different gases.
The image data were acquired with a Bruker Biospec 70/20 spectrometer operated at 0.5T. A stimulated echo spiral sequence [1] was used to obtain diffusion images with 2 b-values (0 and 7.16 s·cm^{-2}) and diffusion time of 1 second.

Results: Figure 1 shows the ADC mean values obtained from the left (elastase-treated) lobe and from the right (control) lobe of the rat lung measured under the two ventilation conditions, BH of 25 mbar and EEV. One of the EEV datasets was found to be unusable after post-processing. The error bars represent the standard deviation of ADC of the eight and seven animals, respectively. This figure shows significant differences between the two lobes at 25mbar full-inspiration breath-hold ($P < 0.001$) with a remarkable increase in the ADC value for the emphysematous lobe. However, this effect was not seen when animals were imaged at the end of the expiration. At EEV, both the emphysematous and the normal lobe show a relatively high ADC. Figure 2 represents one of the ADC maps obtained at full-inspiration breath-hold. It shows by the scale of colour the different values of ADC.

Discussion: Elastase treated lungs show a larger ADC when measured at breath-hold than healthy lungs. No statistically significant difference was seen when the measurement is performed at EEV. The origin of this difference is unknown, but it could be due to a remodelling of the lung, this is, an increase in collateral ventilation[2]. Why this effect is not seen at EEV cannot yet be explained.

Collateral paths offer a parallel set of routes for long-range diffusivity that avoid the tortuous paths that follow the airways. In emphysema, tissue destruction occurs with an increase of collateral paths[3]. If collateral paths consist of interalveolar pores, then a hypothesis could be that these pores have a greater size at breath-hold, when the pressure of the lung is higher. If this were the case, however, ADC at EEV would be much lower.

An increase in ADC in long-range diffusion in emphysematous lungs has been seen, as well, in studies in dogs[4] and human lungs[5]. In this sense, the ADC increase seen at breath-hold for emphysematous lungs is consistent with those previous studies.

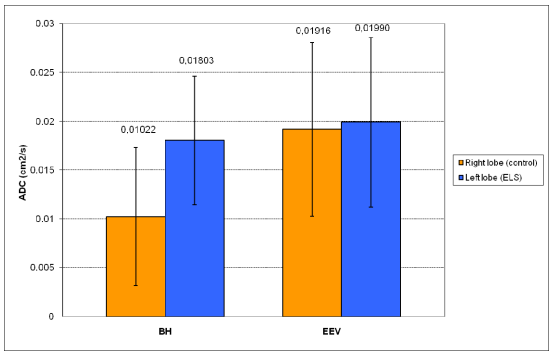

Figure 1: ADC mean values of the control and elastase-treated lobes of the lung of ten animals imaged at full-inspiration breath-hold of 25mbar (BH) and at the end of the expiration (EEV).

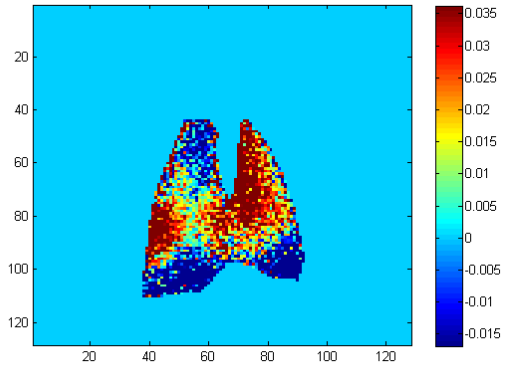

Figure 2: ADC map of one animal obtained in breath-hold. Highest ADC values can be seen in red, whereas the lowest ones (negative values) are seen in blue.

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Acknowledgments: Supported by the EU MRTN-CT-2006-03602, PHeLINet, and Spanish Science Ministry SAF-2008-05412-C02-01.