Simultaneous measurements of Regional Alveolar Oxygen Pressure, Oxygen Depletion Rate and Apparent Diffusion Coefficient by Hyperpolarized 3He MRI

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Introduction: Regional alveolar oxygen partial pressure (P_AO_2), oxygen depletion rate (ODR) and apparent diffusion coefficients (ADC) measured via hyperpolarized ^{3}He MRI have given new insight into a number of physiologic and pathophysiologic conditions. There is considerable interest in measuring these parameters simultaneously, particularly in human trials, since it will allow for the direct correlation of lung function with the lung's microstructure. A simultaneous measurement technique is also important from a practical standpoint, since it reduces study time and gas utilization. During a hyperpolarized ^{3}He MRI experiment, the signal decay of a series of images can be expressed using the following mathematical expression: $S(n) = S_0 \cdot \exp[Nn\ln(\cos\alpha) - \xi(PO_2 \cdot t - 0.5 \cdot ODR \cdot t^2) - b \cdot D]$. This expression relies on the observation that the exponential decay of a ^{3}He's signal intensity in the presence of a bipolar gradient and oxygen depends on the partial pressure of oxygen, the oxygen depletion rate, and the diffusion coefficient. A factor accounting for the RF relaxation due to imaging is also included in the expression.

Method : These four effects can be separated by imaging at least five times and choosing an appropriate group of delays and bipolar gradient factors. The imaging is configured to take advantage of the different decay pattern of each mechanism. Of the three factors, RF and P_AO_2 cause unrecoverable ^{3}He depolarization, while the ADC signal development pattern can be controlled, since we have the freedom to choose the gradient factors. The scan scheme is shown in fig. 1. A nonlinear fitting method is applied after the data is acquired (no difficulty with convergence has been encountered in these studies). The scan scheme shown is not unique, but can be optimized for robust behavior in a noisy environment or patient comfort as desired.

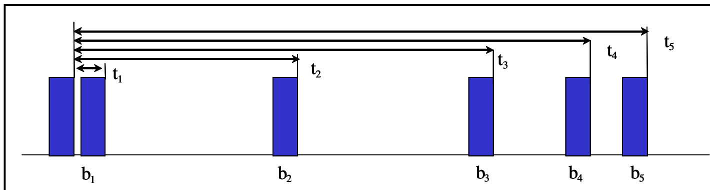

Fig.1. scan scheme for the simultaneous measurements of PO2,ODR&ADC

Result and Discussion: A phantom experiment, using a plastic bag filled with 500ml ^{3}He and 110ml O_2, was performed for the validation of this technique. 6 images were acquired with the timing scheme [0 0.6400 10.6800 20.7200 25.7600 28.8025] (seconds), and the gradient factor group [0 0.4944 0.3287 0.2016 0.0944 0](s/cm^2). A diffusion-sensitization gradient echo (GRE) sequence was used, with the scan parameters: FOV:300mm; slice thickness:100mm; TR/TE:10/6.26ms; Base resolution: 64x64. Nonlinear fitting of the data was implemented using the Nelder-Mead Simplex Method (Matlab optimization toolbox). As shown in fig. 2, the average PO2 is in good agreement with the nominal value 137 Torr and the ODR averages to the expected 0.0 Torr/s. The ADC slightly greater than 1.5cm^2/s, acceptably close to the expected 1.6cm^2/s.

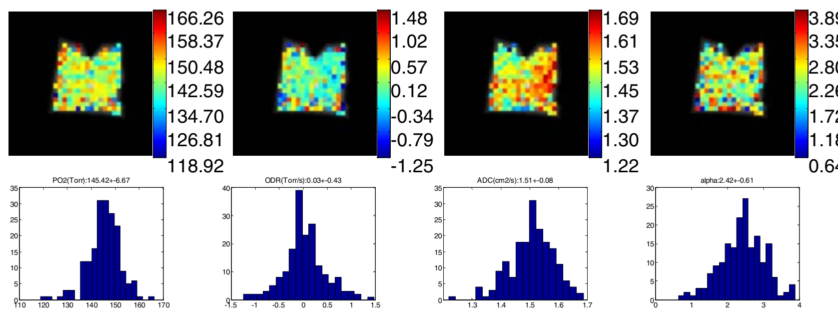

Fig.2. Phantom experiment results: PO2=145.42+-6.67 Torr; ODR = 0.03+-0.43 Torr/s; ADC = 1.51+-0.08cm^2/s; alpha = 2.42+-0.61;

This method was also tested in an animal model. 22 kg Yorkshire pigs was placed supine position in a birdcage coil and positioned in a 1.5 T whole-body imager (Sonata, Siemens). MR imaging began immediately after administration of a gas mixture consisting of 100 ml O_2, 400 ml of ^{3}He that was polarized to a level of about 30%. 6 images were acquired with the timing scheme [0 1.9225 13.2425 24.5625 30.8825 35.2025] (seconds), and the gradient factor group [0 1.7305 1.1506 0.7056 0.3305 0](s/cm^2). The key parameters of the GRE sequence were: flip angle 3.0°; TR/TE 6.4/2.9 ms; FOV 240mm; base resolution 64×64; slice thickness 30 mm. Figure 2 shows the static images and the map of P_AO_2, ODR ADC values for one slice of the pig lung. Also shown in this figure are the histograms of the measured parameters. The mean and standard deviations of the parameters is in consistence with the separated measurements. It should be pointed out that this technique requires a relatively large signal-noise ratio for accurate results.

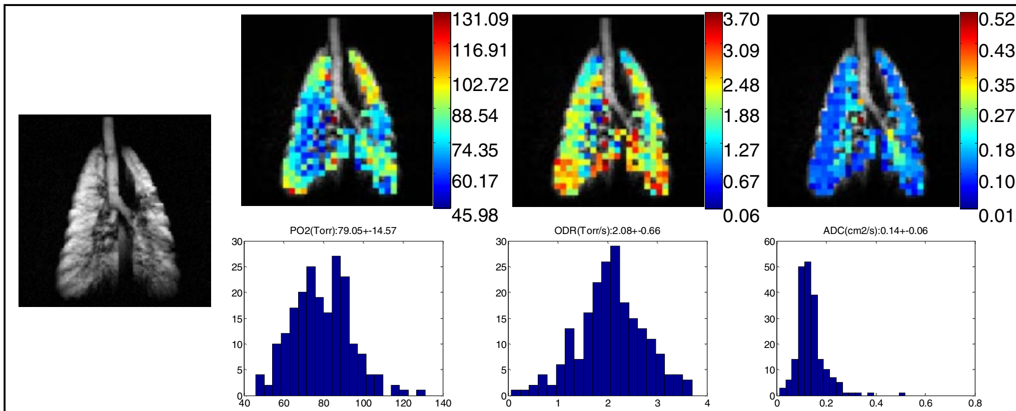

Fig.3. simultaneous measurements of PO2,ODR&ADC in the pig experiment. From the left to right on the top: PO2, ODR and ADC maps; on the bottom: PO2, ODR and ADC histograms. The statistical values of each parameter are shown in the histogram.

Conclusion: In this study we demonstrate a new scan scheme with the nonlinear fitting method for the simultaneous measurement of P_AO_2, ODR and ADC. The phantom and animal experiments shows the validity of this technique.

References: 1.) Deninger, A. J. *et al.*, *J Mag Res* **141**, 207 (1999). 2.) Fischer, M.C. *et al.*, *Mag Res Med* **52**, 766 (2004). 3.) Yablonskiy D. A.. *et al.*, *PNAS* **99**, 3111(2002).