Correlation between the apparent diffusion coefficient and the oxygen depletion rate in COPD disease: a case study

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Introduction: Hyperpolarized helium-3 magnetic resonance imaging (HP ^{3}He MRI) shows promise as an ideal imaging tool for quantitative assessments of pulmonary parameters. This technique is capable of providing both structural and functional lung information. In terms of structural imaging, the apparent diffusion coefficient (ADC), which is a function of alveolar size and geometry, has the potential to characterize the lung's microstructure at the alveolar level. In terms of functional imaging, the regional alveolar partial pressure of oxygen (P_AO_2) and oxygen depletion rate (ODR) give a measurement of the oxygen exchange efficiency and how quickly oxygen is depleted from the alveoli. Since alveolar dimension increases as a function of tissue destruction in chronic obstructive disease, the disease provides a good model for ADC measurement. Consequently, an intensive interest in the use of the HP ^{3}He MRI ADC technique to diagnosis this disease has been developed over recent years [1,2]. A number of studies have clearly demonstrated substantial ADC difference between healthy and emphysematous lungs[3]. Although few studies are reported, the function parameters P_AO_2 and ODR should also be affected in the COPD because this disease changes the regional ventilation-perfusion ratio. It is of clinical importance to measure ADC, P_AO_2 and ODR simultaneously, particularly in human trials, to provide a direct correlation between the lung's microstructure and lung function and to give a new insight into COPD.

Method: During the HP ^{3}He MRI simultaneous measurement, the signal decay in a series of images is dominated by three major factors (RF depolarization, oxygen effect and diffusion effect) and can be expressed as: $S_n = S_0 \cdot \exp[\,Nn\ln(\cos\alpha) - \frac{1}{\xi}\int_0^{t_n} p_{O_2}(t)dt - b(n)\cdot D\,]$. Assuming a linear oxygen decay inside the lung $p_{O_2}(t) = p_0 - Rt$, the normalized signal is $E_n = \varepsilon\cdot n - \frac{1}{\xi}p_0\cdot t(n) + \frac{1}{2\xi}R\cdot t^2(n) - b(n)\cdot D$, where p_0 is the initial oxygen pressure, R is the oxygen decay rate, D is the apparent diffusion coefficient, n is the image number, $t(n)$, and $b(n)$ are the acquisition end time and gradient factor of the n^{th} image, $\varepsilon = N\cdot ln(cos(\alpha))$ is flip angle factor, N is the image resolution, α is the flip angle and ξ is the relaxation constant. We notice that E_n is a linear combination of the four unknowns ε, p_0, R and D multiplied by the associated functions n, $t(n)$, $t^2(n)$ and $b(n)$. By applying the multiple regression method we can retrieve ε, p_0, R and D from a series measured signal y_n. The problem is equivalent to the minimization of $\chi^2 = \sum_{n=1}^{M}\frac{1}{\sigma_n^2}(y_n - E_n)^2 = \sum_{n=1}^{M}\frac{1}{\sigma_n^2}\left[y_n - \left(\varepsilon\cdot n - \frac{1}{\xi}p_0\cdot t(n) + \frac{1}{2\xi}R\cdot t^2(n) - b(n)\cdot D\right)\right]^2$. By setting the partial derivatives of $\chi 2$ with each unknown to zero, a set of four linear equations can be obtained. Solving this set of linear equations will yield the solutions for ε, p_0, R and D. From the solutions we notice that the associated functions n, $t(n)$, $t^2(n)$ and $b(n)$ have to be different in order to make the solution non-trivial, i.e., $t(n)$ and $b(n)$ can not be a linear function of n. Although there exists a flexibility in choosing $t(n)$ and $b(n)$, as long as they are not linear functions of n, different choice of $t(n)$ and $b(n)$ will give different measurement uncertainties on ε, p_0, R and D in the presence of noise. The measurement uncertainties can be analytically derived from the solutions by applying the error propagation theorem. Based on the uncertainty expression we can find an optimal choice for $t(n)$ and $b(n)$ at a given measurement condition. In the human experiment below, we choose an optimal measurement timing $t(n)$ = [0 1.32 9.04 16.06 21.08 24.10] (seconds), which gives a full development to the oxygen effect. The gradient factor $b(n)$= [1.7305 1.1506 0.7056 0.3305 0] (s/cm^2) is calculated from $b(n) = 1.4 * (\sqrt{6} - \sqrt{n})$ in order to achieve a good signal-to-noise ratio at the end of the measurement.

Result and Discussion: The human experiment was conducted under approved IRB and US FDA IND protocols. Hyperpolarized ^{3}He gas was generated using a prototype commercial polarizer (Amersham Health, Durham, NC). A severe COPD patient (female, age 52 years, weight ~50kg) was imaged with a transmit-receiver ^{3}He saddle coil set (IGC Medical Advances Inc. Milwaukee, USA) consisting of 2 pairs of coils (each coil 23x25cm) operating in quadrature mode. The total lung capacity (TLC) of the subject was 6.08L and the tidal volume was 15%*TLC≈900ml. A bag of 500ml ^{3}He and 400ml N2 gas mixture was inhaled by the subject in the measurement. The imaging sequence is a 2D Gradient Echo sequence with the following key parameters: FOV 350 mm, slice thickness 50mm, TR/TE:10ms/6.96ms, pixel bandwidth 260Hz, k-space matrix size 64×64, and flip angle ~4.6 degrees. Figure 1 shows the measured P_AO_2, ODR and ADC maps and histograms. The statistical values, as listed above the corresponding histograms, are consistent with the published values. In the figure, we can notice the ODR shows a relatively low value (2.0Torr/s) in the upper-right region of lung where ADC has a higher value (~0.85cm^2/s). This observation means the oxygen exchanges at a lower rate where alveolar tissue is destructed by COPD and this correlates the functional abnormality with the structure destruction.

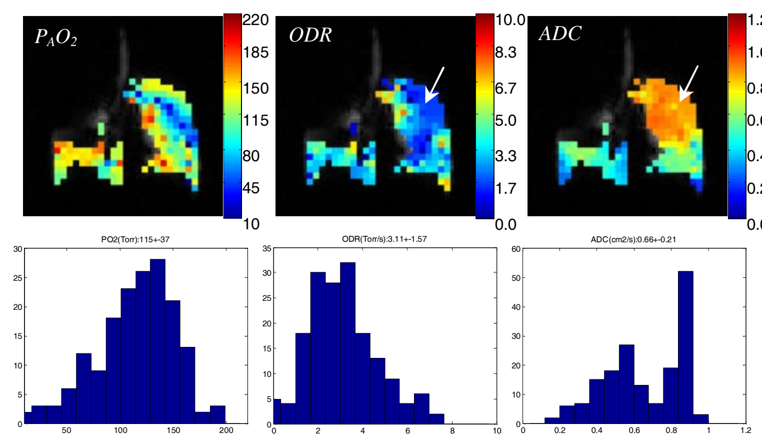

Fig.1. The P_AO_2, ODR and ADC maps and histograms of the COPD patient. The statistical values (average ± standard deviation) are listed above the corresponding histograms. In the arrow-pointed region, ODR shows a relative lower value (2.0Torr/s) while ADC has a higher value (~0.85cm^2/s)

Conclusion: In this work we present a case study on the simultaneous measurement of the apparent diffusion coefficient (ADC), partial pressure of oxygen (P_AO_2) and the oxygen depletion rate (ODR) on COPD human subjects by HP ^{3}He MRI. We observed a correlation between the functional abnormality and the alveolar structure destruction caused by the disease.

References: 1 Yablonskiy DA, *et al.*, *Proc Natl Acad Sci U S A* 2002;99:3111-3116. 2.) Chen XJ, *et al.*, *Magn Reson Med* 1999;42(4):721-728. 3.) Saam BT, *et al.*, *Magn Reson Med 2000*;44:174-179.