Long-time-scale hyperpolarized ^{3}He and ^{129}Xe diffusion in human lungs: Experimental measurements and computer simulation

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Introduction: Hyperpolarized noble-gas diffusion MRI measures the degree to which diffusion-driven displacement of inhaled gases molecules is restricted by the walls of the airspaces of the lung, from which information about lung microstructure can be derived [e.g.. 1,2]. In a prior study [3,4,5], there was a factor of 20 disagreement between the long-time-scale ^{3}He apparent diffusion coefficient (ADC) measured in the lung and the results of a simulation that modeled the largest (or most proximal) 15 generations of the airway tree, and the discrepancy was postulated to be due to the presence and importance of collateral ventilation (inter-acinar channels) within the lung. However, they chose not to include the more distal 9 generations of the airways and the alveolei, and 95% of the gas within the lung resides in the distal airspaces. The purpose of this study is to compare the measured diffusion-time dependence of the ^{3}He and ^{129}Xe long-time scale ADC in human lungs with the results from a computer simulation that models the most distal airspaces of the lung, the acini which contain a respiratory bronchiole and its alveolar ducts and alveolar sacs. The effects of intra- and inter-acinar collateral channels were also simulated.

Methods: A series of global (i.e., integrated over the entire lung) ADC values were measured at diffusion times ranging from about 0.1 to 5.0 seconds in a single breath hold using a stimulated-echo-based method as described in ref. 1. The measurements were obtained from all subjects following inhalation of ~1L of a gas mixture containing either hyperpolarized ^{3}He or ^{129}Xe. **^{3}He**: ^{3}He diffusion MRI was performed in 29 healthy volunteers (Age: 57±9; 12M, 17F). The tag wavelength was 10 mm. **^{129}Xe**: ^{129}Xe diffusion MRI was performed in 5 healthy volunteers (Age: 32±12; 1M, 4F). The tag wavelength was 5 mm. **Simulation**: An acinar structure model based-on histological data was created and the number of inter-acinar (collateral) channels could be varied. The diffusion of the atoms in the acinar model with different initial conditions was assessed by numerically solving a one-dimensional gas transport equation [6]. The free diffusion coefficients for ^{3}He and ^{129}Xe mixed in the air were assumed to be 0.88 cm^2/s and 0.14 cm^2/s, respectively.

Results: The experimentally measured and simulated ^{3}He and ^{129}Xe ADC values normalized by the corresponding free diffusion coefficients in air are plotted in Figs. 1 and 2. The measured ^{3}He and ^{129}Xe ADC values agree well with the simulated ADC values even in the absence of collateral channels. Both the experimental measurements and the computer simulation reveal a distinct biphasic time-dependence with the ADC markedly decreasing with diffusion time up to about 1 s, and then decreasing more slowly beyond 1 s. The computer simulation also revealed that just one collateral pathway per generation within the acinus led to ADC increases of ~25%, while similar collateral pathways between two acini led to ADC increases of 45-65%.

Discussion: There is excellent agreement for both magnitude and biphasic time-dependence of ADC between computer simulation in an acinar model and experimental ADC measurements in human lung even in the absence of simulated collateral channels (intra and inter-acinar channels). However, the simulation shows that the presence of collateral ventilation can increase the ADC considerably suggesting that the ADC may be sensitive to changes in collateral ventilation that are thought to occur in early smoking related lung disease. Interestingly, the experimental long-time-scale ^{129}Xe ADC was smaller while the experimental ^{3}He ADC was mostly greater than the simulated ADC. This may be due to differences in the physical properties of the two gases (xenon is 20 times more soluble in human tissue and 2 times more viscous than helium), and the source of this discrepancy deserves further research.

Conclusion: The experimentally measured long-time-scale ^{3}He and ^{129}Xe ADC can be explained using only the intra-acinar structures in the lung, but other factors such as the physical properties of the gases and collateral ventilation may play a secondary role. The importance of the intra-acinar structure and collateral channels may vary with varying parameters such as tag wavelength. The ADC may be sensitive to increases in collateral channels as is thought to occur in early smoking related lung disease.

References:

[1] Wang C, et al. Magn Reson Med 2006; 56:296-309.
[2] Woods JC, et al. Magn Reson Med 2004; 51:1002-1008.
[3] Conradi MS, et al. Acad Radio 2008;15(6):675-682.
[4] Bartel ST, et al. J Appl Physiol 2008;104:1495-1503.
[5] Bartel ST, et al. J Appl Physiol 2009 ;106 :1024.
[6] Verbanck S, et al. J Appl Physiol 2007; 103:249-254.

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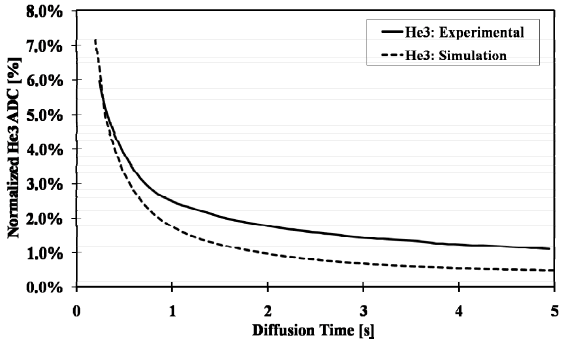

Figure 1. Plot of experimental and simulated ^{3}He ADC Vs diffusion time after normalizing each by the ^{3}He free coefficient in air (^{3}He in the air: 0.88 cm^2/s)

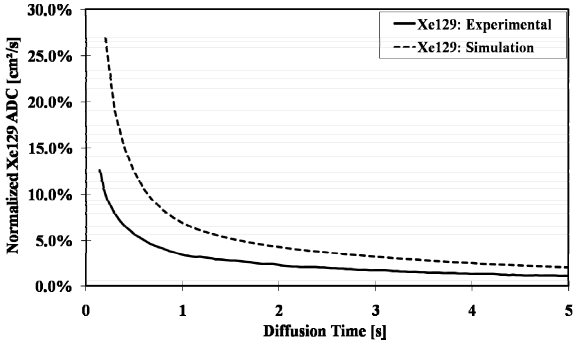

Figure 2. Plot of experimental and simulated ^{129}Xe ADC Vs diffusion time after normalizing each by the ^{129}Xe free coefficient in air (^{129}Xe in the air: 0.14 cm^2/s)