Finite Element Modeling and Experimental Validation of Transverse Relaxation and Apparent Diffusion Coefficients of Hyperpolarized Noble Gases in Rodent Lung

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Introduction

Hyperpolarized noble gases (HNG), helium (^{3}He) and xenon (^{129}Xe) have become promising contrast agents for lung MR imaging. MR parameters, such as the apparent transverse relaxation time (T_2*) and apparent diffusion coefficient (ADC) are sensitive to the geometric and physiological properties of the airways and can be used to estimate the dimensions and geometry of the airways which may provide a means of diagnosing lung diseases [1, 2]. Furthermore, it is expected that helium and xenon will be sensitive to different length scales of airways due to differences in diffusion coefficients. To investigate the diffusional properties of these gases and validate the performance of the different techniques used for ADC and T_2* measurements, computer simulations using the finite element method and phantoms (using capillary tubing) with geometric properties similar to the airways were developed. Preliminary computer simulation of T_2* and ADC experiments of xenon in phantoms and models of lung airways are described. The results of these simulations are compared to preliminary experimental data obtained in rat lungs at 1.89 and 3 T.

Methods

Computer simulations of the behavior of the HNG MR signal of xenon in the lung airways and phantoms were implemented using the finite element method. The static field inhomogeneities induced by susceptibility differences at the tissue-gas interface were calculated using the AC/DC module of Comsol Multiphysics (COMSOL AB, Stockholm, Sweden). To simulate the behavior of the magnetization in the transverse plane, the Bloch-Torrey equation [3] was solved using the PDE modeling module of Comsol Multiphysics and Comsol Script. Computer models of alveolar ducts and capillary phantoms are shown in Fig. 1. Three different dialysis modules (Spectrum Labs, Rancho Dominguez, CA, USA) with polysulfone capillary tubing of inner diameter 0.1 mm and 0.5 mm were used as phantoms. These modules had surface areas that range from 1175 cm^2 to 3500 cm^2. Phantom and live rat lung experiments were performed using a 1.89 T superconducting magnet (Magnex, Exon, England) and a 3 T GE Signa system (GE Healthcare, USA) using hyperpolarized xenon. At 1.89 T the T_2* and ADC estimates were obtained from gas spectra. At 3 T, ADC and T_2* maps were obtained. Hyperpolarized natural abundance xenon gas (26.4% ^{129}Xe) was produced from a gas mixture (1% xenon, 10% nitrogen and 89% helium) using a home-built, continuous-flow polarization system that used a 60W diode array laser (Coherent, Santa Clara, USA) and produced xenon polarizations of up to 22% [4, 5].

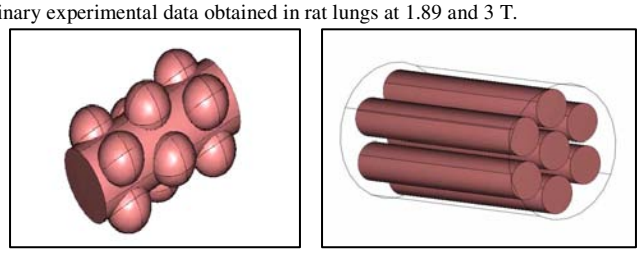

Figure 1. Computer models of an alveolar duct (left) and capillary phantom used in this work. The alveolar duct and the capillary are surrounded by tissue-like material (water).

Results and Discussion

Figure 2 shows the magnetic field distributions produced by susceptibility differences in the alveolar duct and phantom models. Field gradients are stronger inside the alveoli, in the direction of the external magnetic field (x axis, horizontal direction). Significant field gradients are also introduced by neighboring airways (capillaries in Fig. 2b). Computer simulations show that these regions of large susceptibility-induced gradients contribute significantly to the observed T_2*, which may be sensitive to changes in alveolar structure (e.g. emphysema). Figure 3 shows the field dependence of T_2* resulting from the computer simulations. These results are in relatively good agreement with previously reported results using a semi-empirical T_2* model [6] and measured values at 1.89 T and 3 T. The measured T_2* of 18 ms at 1.89 T for the dialysis module with the 0.1 mm diameter capillaries is close to the T_2* values measured in rat lungs (21.5 +/- 1.2 ms). This suggests that the dialysis module may be a useful physical model system to mimic the rat lung airways.

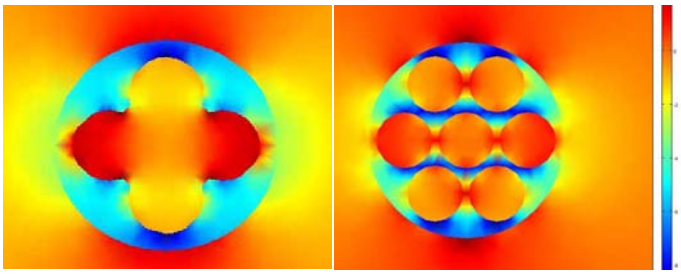

Figure 2. Computer simulation of the magnetic field strength variation (transverse plane, in ppm) induced by susceptibility differences in the alveolar duct (left, outer diameter 0.7 mm) and capillary phantom (right, outer diameter 0.35 mm) models.

The ADC values measured in the phantoms were 0.078 +/- 0.009 cm^2/s for the 0.5 mm capillary phantom and 0.027 +/- 0.004 cm^2/s for the 0.1 mm capillary phantom (Fig. 4), in good agreement with the simulation results (0.066 cm^2/s and 0.024 cm^2/s, respectively). These results show a significant reduction in the diffusion coefficient (from 0.14 cm^2/s for free diffusion [1]) due to motional averaging due to the restriction imposed to diffusion by the capillary walls. This reduction of the ADC is greater for the smaller diameter capillaries. These ADC values are in good agreement with measured values in rat lungs [1, 6]. The effects of emphysema in airway geometry were simulated by increasing the inner diameter of the alveolar duct [3] from 0.34 mm to 0.56 mm. The increase of ADC values obtained from the simulations is similar to reported experimental results [7]. These simulations suggest that xenon may be more sensitive than helium to changes in small airway structure (e.g. alveolar geometry) due to its smaller diffusion coefficient. In future, airway size variability should be incorporated in to the model to assess the sensitivity of T_2* and ADC to those changes when a large number of airways contribute to the signal.

Conclusions

The theoretical model is successful in predicting the T_2* and ADC for xenon in simple and complex geometries and can approximate the changes observed in emphysema. The results show that dialysis modules can be used as phantoms to validate the methods to estimate T_2* and ADC of hyperpolarized noble gases in the lungs. The fact that xenon diffuses into the liquid media that surrounds the capillaries can be used to assess the effects of gas exchange, which can also be incorporated in to the computer models.

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References

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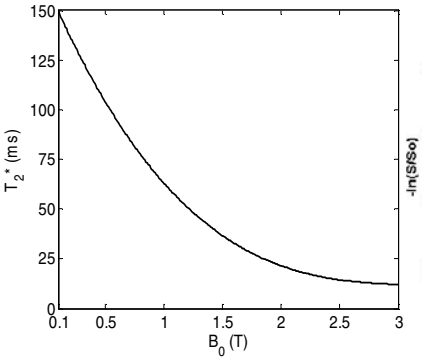

Figure 3. Field dependence of xenon T_2* in lung airways obtained from the computer simulations.

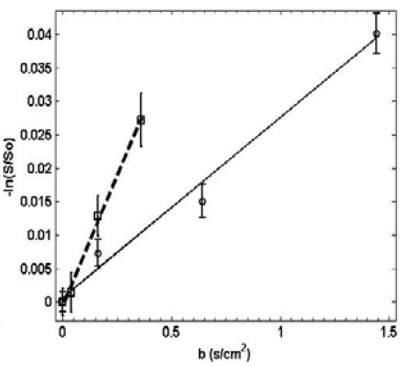

Figure 4. Results of the diffusion experiments for phantoms of different capillary diameters (0.1mm, circles; 0.5mm, squares), with the diffusion gradient perpendicular to the capillary axis.