Determination of Alveolar Oxygen Partial Pressure in Rat Lung using Spin-Spin Relaxation Times of ^{3}He and ^{129}Xe at Low Magnetic Field Strength

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Introduction: Quantitative assessment of alveolar oxygen partial pressure (p_AO_2) in the lung has the potential to become a remarkably useful tool in the diagnosis and monitoring of respiratory disease. Previously, quantification of p_AO_2 has been demonstrated, both in vivo and in vitro, through the study of oxygen's effect on the spin-lattice relaxation time, T_1, of hyperpolarized ^{3}He [1]. However, this approach requires careful calibration of the RF pulses, and can be time consuming. More recently, it has been demonstrated that p_AO_2 can be measured using the spin-spin relaxation time, T_2, of ^{3}He at very low magnetic field strengths [2] where the contribution of susceptibility-induced relaxation is insignificant. T_2 can be measured with the Carr-Purcell-Meiboom-Gill (CPMG) sequence which has the inherent advantage of being able to reduce experiment time, increase experiment accuracy, and eliminate the need for extremely precise flip angle calibrations. To our knowledge, CPMG has not been applied to hyperpolarized ^{129}Xe measurement of p_AO_2 at low fields. ^{129}Xe has the advantage of being highly abundant (i.e. inexpensive) compared to ^{3}He and therefore may permit widespread use of the technique. We explore further the use of CPMG measurements for the determination of alveolar oxygen partial pressure using both hyperpolarized ^{3}He and ^{129}Xe gases in phantoms and in vivo in rat lung at low magnetic field (0.07T). We present relaxivity relationships for oxygen's effect on ^{3}He and ^{129}Xe spin-spin relaxation, and test the assertion that T_2=T_1 in the limit of rapid CPMG pulse rates at low magnetic field strength [2,3].

Methods: Hyperpolarized ^{3}He gas was produced using a turn-key polarizer (HeliSpin, GEHC). Hyperpolarized ^{129}Xe gas was produced using a home-built spin exchange optical pumping system [4]. Plastic syringes were prepared with varying amounts of pure O_2 gas and the remaining volume filled with hyperpolarized gas just prior to signal acquisition. NMR experiments were performed on a home-built resistive MR imaging system [5] at a field strength of 0.07T, and controlled using an Apollo console (TecMag, Houston, TX, USA). In vivo spin-spin relaxation times were measured using ^{3}He gas in a 364g Sprague-Dawley rat ventilated with a custom ventilation system and a known p_AO_2 of ~11% using a University-approved animal care protocol. A CPMG pulse sequence [6] with an inter-echo time of 2.64ms and 8192 echoes was used to measure T_2 for varying concentrations of O_2 in vitro, and in vivo. Polarizations at the time of initial signal acquisition were estimated to be 25-30% for ^{3}He and 5-10% for ^{129}Xe. Total experiment time was 20-25 seconds. T_2 was determined from the exponential decay of the echo amplitudes using a non-linear least squares fit.

Results and Discussion: The decay time measured by the CPMG sequence ($T_{2,CPMG}$) can be broken down into constituent decay mechanisms according to: $1/T_{2,CPMG} = 1/T_2 + 1/T_{2,diff}$ [2] , where T_2 is the true transverse relaxation time, which is assumed to be dominated by dipolar coupling with paramagnetic oxygen [3], and $T_{2,diff}$ is the decay due to diffusion through magnetic field non-uniformities (principally susceptibility in the lung). Though low magnetic field reduces the diffusion term, it can still be significant due to the high diffusivity of gases. Therefore, we derive a linear relationship of the form: $1/T_{2,CPMG} = \kappa P_{O2} + \chi$ for both ^{3}He and ^{129}Xe (Fig.1), where the y-intercept χ is proportional to the effect of diffusion on our measurements; κ is the slope of our linear fit; and P_{O2} is the oxygen partial pressure in Pascals. The slope, κ, is calculated as $5.80 \times 10^{-6}\ s^{-1}Pa^{-1}$ for ^{3}He and $4.20 \times 10^{-6}\ s^{-1}Pa^{-1}$ for ^{129}Xe. A spin-spin relaxation time of 22.6 ± 1.6s was measured in vivo in the rat lung for ^{3}He. A lengthening of the measured $T_{2,CPMG}$ in vivo compared to phantom studies is seen and is attributed to the limited diffusion of the ^{3}He gas within the lung. This value is equal, within experimental uncertainty, to the spin-lattice relaxation time measured previously for ^{3}He under comparable ventilation conditions [1], demonstrating the feasibility of performing p_AO_2 measurements of the lung in vivo using measurements of low field T_2 of ^{3}He or ^{129}Xe in the lung. This also supports the assertion that when diffusion induced relaxation through susceptibilities becomes negligible using a combination of low field and fast CPMG, a regime in which T_2=T_1 is reached.

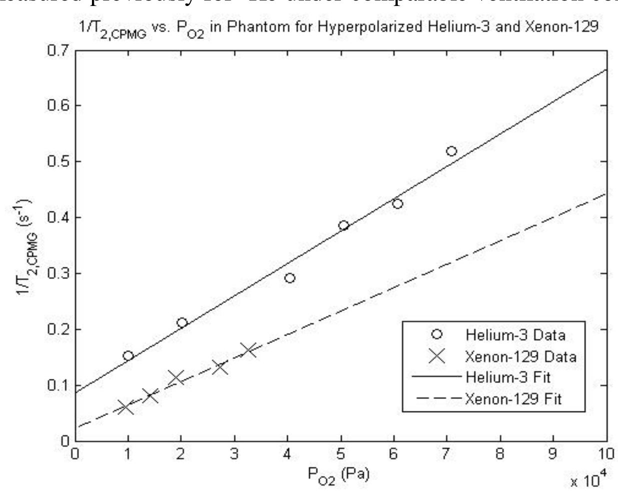

Figure 1. $1/T_{2,CPMG}$ vs. P_{O2} for ^{3}He and ^{129}Xe

Conclusions: We have presented a method of measuring oxygen partial pressure at low fields with hyperpolarized gases using spin-spin relaxation times in vitro obtained with CPMG. We obtain a linear relationship between $1/T_{2,CPMG}$ and the oxygen partial pressure, with values of $5.80 \times 10^{-6}\ s^{-1}Pa^{-1}$ and $4.20 \times 10^{-6}\ s^{-1}Pa^{-1}$ for the relaxivity of ^{3}He and ^{129}Xe in the presence of O_2, respectively. κ for ^{3}He is greater than that for ^{129}Xe, however the low cost of using ^{129}Xe in experiment makes it a more desirable candidate for p_AO_2 measurement in the future. A T_2 of 2.6 ± 1.6s was also measured using ^{3}He in rat lung.

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