Accurate tracking of pulmonary O_2 partial pressure using hyperpolarized ^{3}He at very low field

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INTRODUCTION: Taking advantage of the negligible power deposition at very low RF frequency, fast repetition CPMG sequences can be used with zero applied gradient to monitor the global O_2 partial pressure in the human lung. At very low magnetic field, where tissue susceptibility gradients play no role, the CPMG relaxation time T_2' of ^{3}He in the lung is constant at short repetition time T_{CP} and is only limited by the oxygen dependent magnetization lifetime T_1 [1]; at longer T_{CP}, diffusion in residual magnet gradients dominate the relaxation. The basic features of this idea are illustrated in Figure 1 using the simple model $T_2' = (1/T_1 + 1/T_d)^{-1}$, where $T_d = D(\gamma G T_{CP})^2/12$ for diffusion in a uniform background gradient G.

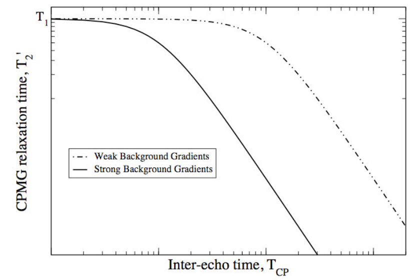
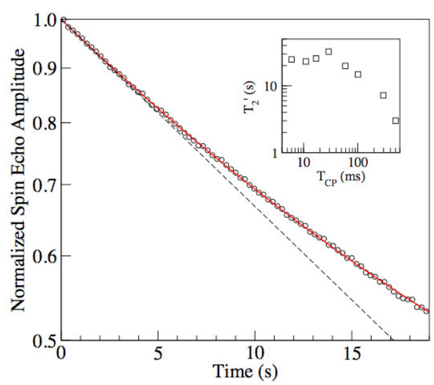


Figure 1: The relaxation of ^{3}He in the lung is limited by T_1 at short T_{CP}. The onset of this regime depends on the strength of the background gradients. It is inaccessible at 1.5 T where fast RF pulse rates would exceed safety limits on power deposition.

METHOD: In vivo measurements were performed (with governmental approval) at 3.2 mT (105 kHz) in a whole body scanner operating at reduced current. Each measurement used ~ 50 standard cm^3 of ~ 20 - 30% polarized ^{3}He diluted to 1 litre with N_2. While lying supine in the imager, a healthy subject (fully informed about the procedures) exhaled normally, inhaled the gas mixture, then further inhaled air to fill the lung and held his breath during CPMG signal acquisition (~ 20 s). The CPMG sequences were made in zero applied gradient using an initial 90^o RF pulse (0.5 ms duration) followed by a train of 180^o RF pulses (1.0 ms duration) at regular interval (T_{CP} ranging from 6 to 500 ms). Homebuilt RF transmit and receive coils suitable for low frequency operation [1] were used.



RESULTS – EXPERIMENTAL (SNR ~ 50): The ^{3}He spin-echo amplitudes of a CPMG sequence made with T_{CP} = 6 ms and zero applied gradient is shown in Figure 2; for clarity each circle represents the average of 40 points. The signal decay was fit assuming a constant uptake of O_2 into the blood (ie. $P_{O2} = P_o - Rt$) as observed in ^{3}He MRI measurements of T_1 at 1.5 T [2]. For the results shown here, the initial O_2 partial pressure P_o in the lung was found to be 106.7 (5) mbar and the uptake rate R was 1.01 (3) mbar/s. The corresponding initial exponential decay time T_2' was 24.8 s; the inset of Figure 2 shows T_2' for the various T_{CP} values examined here. The regime $T_2' = T_1$ exists for $T_{CP} < 50$ ms. The value of T_1 depends on the concentration of O_2 in the lung and was ~ 25 s for the ^{3}He inhalation protocol used here. For $T_{CP} > 50$ ms, the effect of diffusion in B_0 field inhomogeneities leads to shorter relaxation times (in qualitative agreement with Figure 1).

Figure 2: Normalized echo amplitude versus time. Dashed line: initial exponential decay. Red line: nonlinear least squares (NLLS) fit to exp(-□$P_O t$ + □ Rt^2) where □ = 3.8 x 10^{-4} s^{-1} per mbar of O_2 at 37 ^{o}C [3]. Inset: initial exponential decay time T_2' versus T_{CP}.

RESULTS – SIMULATION (SNR = 1000): To accommodate the fast RF pulse rate, preamplifier gain had to be reduced at the expense of Signal-to-Noise Ratio (SNR). When this technical difficulty is overcome, and if more ^{3}He is used, SNR values up to 1000 will become routine, which will allow a reliable determination [4] of P_o and R to be made using shorter acquisition times (see Figure 3). A short CPMG sequence will then leave sufficient time and ^{3}He magnetization (see Figure 2) for a second MR acquisition to be performed within the same breath hold.

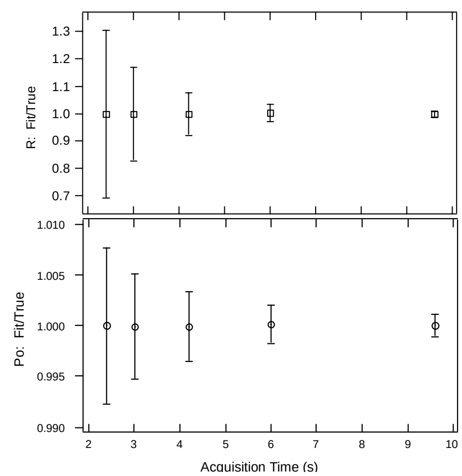


Figure 3: Fit parameters P_O and R extracted from data simulations using input values P_O = 100 mbar and R = 1 mbar/s, T_{CP} = 6 ms, and having SNR = 1000. Results are the mean (data point) and standard deviation (error bar) determined from 1000 trials. The accuracy of the NLLS fit is very good, however uncertainty in R becomes prohibitive for acquisition times as short as 2 seconds (see comment [4]).

DISCUSSION: At very low B_0, a fast repetition CPMG sequence can be used to accurately measure the global O_2 partial pressure P_o and uptake rate R in the human lung. We have shown that with a readily achievable increase in SNR, these measurements will only require a few seconds of acquisition time and use up only a small amount of the initial ^{3}He magnetization. We plan to use the remaining magnetization to obtain a subsequent image (diffusion or distribution) immediately following the global O_2 determination. This will allow both structural and functional information about the lung to be collected in a single breath hold: an approach that will reduce examination time and make for a most efficient use of ^{3}He, which is a non-renewable resource. To extend this technique so as to obtain regional O_2 information as well, we envision the use of small local coils arrayed across the chest. Being at low frequency where Johnson noise of the detection coils dominates SNR, further improvements will be explored through the use of cooled normal coils, superconducting coils, or SQUID detectors and amplifiers.

REFERENCES:

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[3] B. Saam *et al.*, Phys Rev A **52**, 862 (1995).
[4] Precision can also be improved by decreasing T_{CP} (*i.e.* increasing the number of data in the fit).