Measurement of Apparent Long-Range Diffusion of ^{3}He using Pulsed Gradient Spin Echo T_2 in the Rat Lung at Low Magnetic Field Strength

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Introduction: Measurement of Apparent Diffusion Coefficients (ADC) of hyperpolarized ^{3}He gas in the lungs, can provide information on the micro-anatomical changes associated with disease over length scales permitted by the diffusion time. Improved sensitivity of ADC to chronic obstructive pulmonary disease (COPD) has recently been demonstrated using diffusion times on the order of seconds. These long diffusion times are generally not possible using pulsed-gradient echo methods at clinical field strengths due to short transverse relaxation times in the lung, thereby requiring alternative approaches (e.g. stimulated echoes) [1]. However, pulsed-gradient echo methods may be extended to longer diffusion times at low magnetic field strengths, taking advantage of the long transverse relaxation time (i.e. reduced susceptibility gradients) and independence of the available magnetization on field strength [2]. Low fields have previously been used to reduce susceptibility gradients in the lungs for measurement of T_2 relaxation of hyperpolarized gases in the presence of oxygen [3]. The purpose of this work was to explore, theoretically and experimentally, the measurement of long range ^{3}He ADC using a Pulsed Gradient Spin Echo (PGSE) approach at low magnetic field strength.

Methods: *Animal experiments were performed following a University-approved animal care protocol.* Hyperpolarized ^{3}He gas was produced using a turn-key polarizer (HeliSpin, GEHC). T_2* relaxation times *in vivo* in rat lungs were measured at 3.0 T (GE Healthcare). T_2 and T_2*relaxation times were also measured *in vivo* at low field (74 mT) using a custom built, variable field strength animal imaging system [2]. Healthy Sprague-Dawley rats (~350 g), ventilated with a custom ventilation system compatible with hyperpolarized gases, were used. Simulations were performed using custom algorithms written in MATLAB. Assuming a long range ADC of 0.019 cm^2/s *in vivo* in healthy rat lungs, and a susceptibility difference between air spaces and lung tissue of 9 ppm [4], observed spin-spin relaxation time in the PGSE sequence ($T_{2,PGSE}$) was calculated using the formalism of [5]: $T_{2,PGSE} = T_2 + \left\{\gamma^2 ADC\left\{(2/3)\Delta^3 g_0^2 + \delta^2(\Delta - (1/3)\delta)g^2\right\}\right\}^{-1}$, where g_0 is the susceptibility induced gradient, which is dependent on field strength [6]; γ is the gyromagnetic ratio; Δ is the diffusion time (i.e. spacing between the 90º and 180º RF pulses); T_2 is the relaxation time due primarily to paramagnetic oxygen present in the lung [3]; and g and δ are the magnitude and duration of the applied pulsed gradient, respectively. In all the calculations, it was assumed $g_0 << g$ and $\delta << \Delta$. In order to determine the range of diffusion times accessible at a given field strength, $T_{2,PGSE}$ was calculated as a function of Δ for varying B_0 fields with g = 0 (Fig. 1). At the lowest field strength (1 mT), $T_{2,PGSE}$ was also calculated as a function of g (Fig. 2), for long-range ADC values previously measured for asthma and COPD [1].

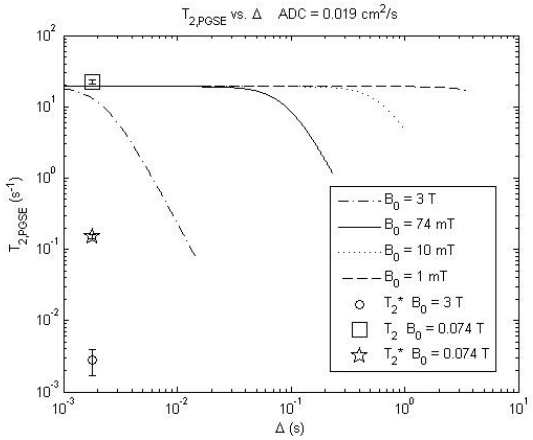

Figure 1. $T_{2,PGSE}$ vs. Δ at varying B_0

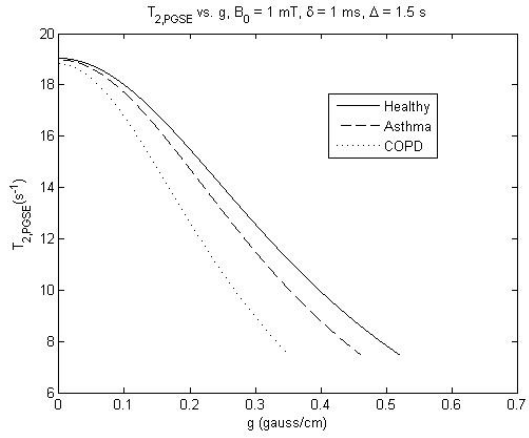

Figure 2. $T_{2,PGSE}$ vs. g at B_0=1 mT

Results: Figure 1 shows that with decreasing field strength, longer (i.e. observable) $T_{2,PGSE}$ values are obtained, due to the significantly lower susceptibility gradients. This agrees with *in vivo* data obtained at 74 mT, motivating the use of ultra-low field strengths (~ 1 mT) to probe long range diffusion. This is confirmed by measurement of T_2* at high field, also shown in Fig. 1. Figure 2 displays the dependence of $T_{2,PGSE}$ on applied gradient strength, simulating a PGSE experiment with Δ = 1.5 s, δ = 1 ms, at a B_0 field of 1 mT. Fig. 2 reveals that with increasing gradient strength, a decrease in $T_{2,\ PGSE}$ is observed. It is also clear that there is a difference in the $T_{2,PGSE}$ dependence on pulsed gradient strength between healthy and diseased lungs due to differences in long-range diffusion.

Discussion: ^{3}He T_2* measurements at 3.0 T, as well as T_2 and T_2* measurements at 74 mT, in rat lungs *in vivo* confirm that susceptibility gradients in the lung can be substantially reduced at low field, permitting long diffusion times (~ several seconds) with the PGSE method. Theoretical PGSE calculations of long range (Δ ~1.5 s) diffusion at 1 mT demonstrate a strong dependence of $T_{2,PGSE}$ on the applied gradient strength, suggesting that measurement of ADC using $T_{2,PGSE}$ is possible. It is also demonstrated that there is an observable difference in $T_{2,PGSE}$ between healthy and diseased lungs, which is due to the expected increased sensitivity of long range ADC to lung disease. Although the lowest field strengths (< 1 mT) will achieve the longest diffusion times (> 1 s), slightly higher field strengths (e.g. 10 – 100 mT) are also expected to extend diffusion times up to several hundred milliseconds without the loss in signal-to-noise ratio expected at very low magnetic field strength.

References: 1) Wang et al. ISMRM 16th Scientific Meeting, #393 (2008). 2) Dominguez-Viqueira et al. *Conc Magn Res B* (33) 124, 2008. 3) Kraayvanger et al. ISMRM 16th Scientific Meeting, #396 (2008). 4) Case et al. *J Magn* Res (73) 304, 1987. 5) Stejksal and Tanner. *J Chem Phys* (42) 288, 1964. 6) Hurlimann. *J Magn Res* (131) 232, 1997.

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