An SSFP-based Pulse Sequence for Measuring Hyperpolarized Gas Diffusion

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Introduction: SSFP sequences provide very high SNR by recycling transverse magnetization at the end of each TR, through the repeated application of RF pulses (usually with alternating phase) at a rate that is much faster than T1 and T2 relaxation. This sequence results in a steady state equilibrium where the signal level is the same after each RF pulse. The equations governing this equilibrium are well studied, and depend on both relaxation rates and flip angle. When SSFP pulse sequences are applied to hyperpolarized magnetization [1, 2], the system reaches a different kind of steady state in which the magnetization declines by a constant factor at each RF pulse. As in proton MRI, the steady state signal depends on relaxation and flip angle [3], however in hyperpolarized-gas MRI the transverse magnetization decay during each TR window is usually dominated by diffusion attenuation due to the imaging gradients rather than T2 relaxation. In a system where the amount of signal attenuation within each TR window is asymmetric between the two RF phases, the resulting steady state splits into two constant levels for both thermal-equilibrium [4] and hyper-polarization. The sensitivity of hyperpolarized helium to diffusion provides an opportunity to generate diffusion weighting based on asymmetric signal attenuation in a balanced SSFP sequence, by placing diffusion-sensitizing gradients in selected TR windows. The purpose of the present work is to derive the equations that govern the steady state signal ratio of hyperpolarized magnetization in SSFP with asymmetric signal attenuation, demonstrate the signal behavior in helium phantoms, and use this framework to extract quantitative measurements of the helium diffusion coefficient.

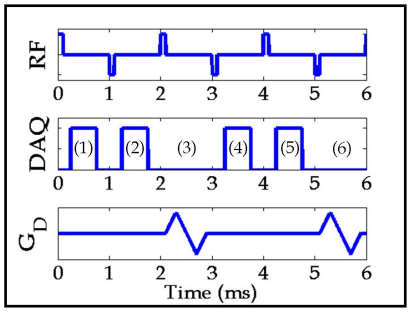

Figure 1: SSFP with asymmetric attenuation through diffusion gradients.

Theory: We have calculated the steady state ratio of consecutive transverse signals in an SSFP sequence applied to hyperpolarized magnetization $M_y(n+1)/M_y(n)$. In the equations below $E_1=\exp(-TR/T1)$, $E_2=\exp(-TR/T2)$, and we have assumed on-resonance for all spins. The ratio of consecutive pulses is a complicated expression,

$$\frac{M_y(n+1)}{M_y(n)} = \frac{\cos\alpha}{2}(E_2 - E_1) \mp \frac{\sqrt{\cos^2\alpha(E_2^2+E_1^2)+2E_1E_2(1+\sin^2\alpha)}}{2} \approx 1$$

, for values of α, T1, T2, and TR common in HPG MR (TR<< T1, T2).

In a standard SSFP imaging pulse sequence, diffusion attenuation is the same in all TR windows and can be folded into the T2 dependence. We have developed an asymmetric diffusion weighted SSFP sequence, which contains a bi-polar diffusion gradient after every third pulse as shown in Figure 1. This alters the steady state condition and produces a new transverse ratio where diffusion attenuation is represented by $E_D=\exp(-b*ADC)$,

$$\frac{M_y(2)}{M_y(1)} = \cos\alpha E_2 - \frac{\cos^3\alpha(E_1^3+E_2^3E_D)+\cos\alpha\sin^2\alpha(E_1^2E_2E_D+E_1E_2^2)\pm\sqrt{X}}{2(\sin^2\alpha E_1E_2+\cos^2\alpha(E_2^2E_D+E_1^2-E_1E_2E_D))} \approx E_D,$$

$$X = \cos^6\alpha[E_1^3+E_2^3E_D]^2 + 4\sin^6\alpha E_1^3E_2^3E_D + 2\cos^4\alpha\sin^2\alpha E_1E_2\left([E_1^4-E_1E_2^3E_D][E_D+2]+[E_2^4E_D-E_1^3E_2][1+2E_D]+6E_1^2E_2^2E_D\right)$$
$$+\cos^2\alpha\sin^4\alpha E_1^2E_2^2\left(E_1^2[E_D^2+4(1+E_D)]+2E_1E_2[E_D-2(1+E_D^2)]+E_2^2[1+4E_D(1+E_D)]\right)$$

The ratio of transverse signals once again has a very complicated dependence on system parameters, but is dominated by the diffusion attenuation in the regime of hyperpolarized-gas MR (E_D>>E1, E2). In this regime, this complicated expression reduces to My2/My1 = Ed.

Materials and Methods: To verify this effect we made global measurements of the diffusion coefficient of helium-3 in two 100mL glass cells, one of which is filled with 3mm diameter glass beads to inhibit diffusion. The helium-3 was polarized to ~60% using a hybrid rubidium-potassium SEOP polarizer [5]. Data was collected on a 1.5T scanner (Avanto, Siemens Medical Solutions, Malvern, PA) using a homebuilt CP birdcage coil. The basic block of measurements consists of 6 RF pulses: 2 diffusion periods and 4 DAQ periods which are labeled (1-6) in Figure 1. The data is combined (2+5)/(1+4) to compensate for any systematic differences between the two RF phases. The sequence has TR=1.76ms, α=8°, and a slice thickness of 20mm. Diffusion measurements were made at several very short diffusion times (Δ=360μs, 480μs, and 600μs). At each value of Δ, the gradient amplitude was stepped up in twenty discrete steps from zero to a maximum value determined by either a hardware limit or an attenuation restriction of b-value ≤0.08s/cm^2. Multiple groups of 6 pulses were taken at each amplitude step to ensure system was in a steady state. Data was analyzed using MatLab software (The Mathworks, Inc.). Once the average ratio at a given b-value was calculated, the natural log of the data was fit to a line. The slope of this line is the measured ADC value for the sample.

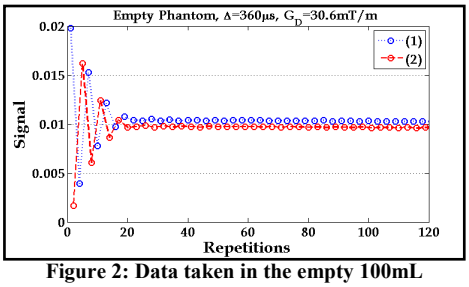

Figure 2: Data taken in the empty 100mL phantom which shows how the signal level oscillates toward the steady state of (2-red) lower than (1-blue) due to the diffusion gradients.

Results: Figure 2 shows the transverse signal in one of the phantoms during the approach to steady state. After ~20 RF pulses, the asymmetric application of a diffusion gradient has resulted in two distinct signal levels. In figure 3 the steady state ratio of the levels is plotted versus b-value in each of our phantoms at a particular value of delta, Δ=360μs. There is a clear separation of the ratios due to the different diffusion coefficients in the two phantoms. The measured ADC values from this data and the other values of Δ are presented in Table 1.

The values measured in the empty cell are consistent with previous measurements of the 3-helium self-diffusion coefficient of 1.8~1.9cm^2/s [6]. The values measured in the bead phantom are less than the free diffusion coefficient, demonstrating restricted diffusion. These values also have the expected time dependence that measurements at shorter times are closer to free diffusion, and thus have larger ADC values.

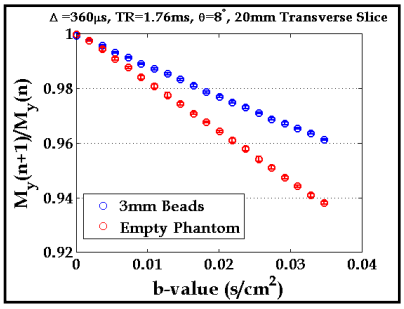

Figure 3: Ratio vs b-value for each phantom at Δ=360μs.

Conclusion: We have demonstrated that incorporating asymmetric diffusion attenuation into a balanced SSFP pulse sequence alters the steady state behavior of hyperpolarized magnetization. When the diffusion attenuation (exp-bD) is applied during every third TR window, the ratio of the signal magnitudes in the other two windows is very nearly equal to exp(-bD), allowing accurate diffusivity measurements to be made at extremely short diffusion times (where the achievable diffusion attenuation is much smaller, due to gradient slew-rate and amplitude limits), by using the high signal provided by the SSFP pulse sequence. We think this effect can be further developed for a range of potential uses. For example, by adding balanced imaging gradients to each window of the acquisition, one should be able to generate high-SNR diffusion-weighted images at much shorter diffusion times than are currently practical, which may be useful for probing much shorter length scales in the lung.

ADC (cm^2/s)	Empty Phantom	3mm Bead Phantom
Δ=360μs	1.884±0.010	1.124±0.006
Δ=480μs	1.873±0.005	1.064±0.004
Δ=600μs	1.875±0.005	1.029±0.008

Table 1: Self-diffusion of 3He in Phantoms

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