Optimizing Single-Breath Xenon Transfer Contrast MRI: Experimental Results, Theory, and Stochastic Modeling
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Introduction
Xenon Transfer Contrast (XTC) measures the rate of gas depolarization due to gas mixing between the dissolved and gas phases; providing information about gas exchange (1). As demonstrated by Ruppert, et al., parameter optimization is essential (2). Using a single breath-hold XTC (SB-XTC) protocol, Patz et al. demonstrated the same information can be obtained with a single breath-hold of gas rather than the original two breath-hold protocol (3). This modification eliminates errors due to misregistration between image sets. It also reduces the number of images from 4 to 3 and the required amount of hyperpolarized gas.

In this work, we determined the optimal parameters for SB-XTC and compared our analytic results with experimental data as well as simulations. We found the optimal parameters for the SB-XTC protocol were different from (2) and we compared our data to those results. Unlike (2), we considered the effect of the number of phase encoding pulses. By halving (doubling) the in-plane resolution, we determined the minimum uncertainty is reduced (increased) by 82% (466%).

Theory
The SB-XTC MRI protocol generates contrast using a train of selective RF pulses applied at ±200ppm with a fixed time between each excitation. The equations relating the signal intensities of the three images (Si, S2, and S3) are:

\[ S_i = \rho \sin(\alpha_i) \cos(\alpha_i) \frac{1}{N} \]  Equation 1a

\[ S_i = S_i \beta_n^n \left(1 - D_n\right)^m \]  Equation 1b

\[ S_i = S_i \beta_n^n \left(1 - D_n\right)^m \left(1 - D_n + F_n\right)^{1-N_n} \]  Equation 1c

where \( \rho \) is the initial SNR density (arbitrary units (a.u.) pixel\(^{-1}\)), \( \beta_n = \cos(\alpha_i) \exp(-TR\beta_n) \), \( \beta_n = \cos(\alpha_i) \exp(-TR\beta_n) \), \( f_n = \sin(\alpha_i) / \sin(\alpha_n) \), and \( \alpha_n \) are the flip angles for the images, \( N_n \) is the number of phase encoding RF pulses, \( D_n \) is the effective depolarization fraction due to T1 relaxation and RF attenuation, and \( F_n \) is the effective depolarization rate due to gas mixing. The depolarization due to gas mixing (1) and relative measurement uncertainty (determined by error propagation and substitution) were calculated using:

\[ F_n = 1 - \frac{S_3}{S_2} \frac{1}{F_n} \frac{1}{N_n F_n} \frac{1}{\text{SNR}} \]  Equation 2

\[ \sigma_n = \frac{1 - F_n}{N_n F_n} \frac{1}{\text{SNR}} \left[ 1 + \frac{2}{\left(1 - D_n\right)^m} \right]^{1/2} \]  Equation 3

Methods
MRI experiments - A standard 2D gradient recalled echo (GRE) pulse sequence with no slice selection was used to acquire images from a single healthy volunteer. The data matrix was 64×32 with FOV = 30cm, TE = 6.6ms, TR = 35.5ms, and the flip angles were 3°, 3°, and 10° for the first, second, and third images, respectively. The number of contrast generating inversions varied from 10 to 54 and a total of eight data sets were acquired. The RF pulse width of each inversion was 10ms and each inversion was separated by 62ms. All images were reconstructed using Matlab.

Computer Simulations - Monte Carlo simulations were performed to verify Equation 3 using \( \alpha_1 = 1-16^° \), \( \alpha_2 = 1-30^° \), \( \alpha_3 = 1-100^° \), \( N_n = 32, 64, 128 \), \( D_n = 0.5-10^% \), and \( F_n = 0.5-10^% \). To ensure the simulations were comparable to the MRI data, we calculated the average SNR of the first image to be 65 a.u.-pixel\(^{-1}\). Using this result, we estimated: \( \sigma_n \) = 0.5\( \sin(3°) \cos(3°) = 1.270 = 1.000 \) a.u.-pixel\(^{-1}\). We performed the Monte Carlo simulations using Equations 1a-c) by adding a different normally distributed pseudo-random number to each signal using Matlab’s randn function with a mean of zero and a variance of one. Each simulation was repeated 16,384 times. We then generated histograms of \( F_n \) and calculated \( \sigma_n / F_n \). For a given \( N_n \), Matlab’s min function was used to find the global minimum in \( \sigma_n / F_n \).

Results
A colormap of \( \sigma_n / F_n \) for a given pair of flip angles is displayed in Figure 1-a) to demonstrate the local minima along \( N_n \). In Figure 1-b), the global minimum in \( \sigma_n / F_n \) was 6.9%, 9.2%, and 13% for \( N_n = 32, 64, \) and 128, respectively. In Figure 1c), the optimal choice for \( \alpha_3 \) depended on \( F_n \) and our simulations indicate \( \alpha_3 \) also depended on \( D_n \), and \( N_n \). Interestingly, the optimal choice for \( \alpha_2 \) depended only on \( N_n \). In Figure 2a), we observe an offset between the MRI data (black ‘*’) and Equation 3. A similar offset is observed between Figure 2b) and the equation in (2). The offset between the predicted values and the data may be mostly due to physiological variations due to the observed gravitational gradient (2). We estimated these effects to be 11% using literature values (4).

Discussion
We compared our experimental data with Equation 3 and the equation reported in (2). While the concept of a finite magnetization reservoir is well-known, the initial SNR density was not considered in the previous study (2) and this observation allowed us to compare our results to the predicted values. From Figure 1b), we note the minimum uncertainty is reduced by 5.5%. The difference between the simulations and recovery of SNR density was not considered in the previous study (2) and the difference may be mostly due to the data may be mostly due to errors in the MRI data, we calculated the average SNR density of the first image to be 65 a.u.-pixel\(^{-1}\).

References

Figure-1a Colormap of \( \sigma_n / F_n \) vs \( \alpha_1 \) and \( \alpha_2 \) for \( N_n = 44, F_n = 2.5\% \), \( D_n = 1\% \) depicting a local minimum along \( N_n \). b) Plot of the local minima in \( \sigma_n / F_n \) for \( F_n = 2.5\% \), \( D_n = 1\% \) and different values of \( N_n \). Plots of c) optimal \( \alpha_1 \) and d) global minimum in \( \sigma_n / F_n \) versus \( F_n \) for \( N_n = 32 \) and \( D_n = 1\% \). Interestingly, \( \alpha_2 \) was determined by \( N_n \) and \( \alpha_3 \) was 14 ± 0.5° for the simulated results.

Figure-2. Relative uncertainty (‘*’) for in vivo MRI experiments versus \( N_n \). Dashed lines were created using Equation 3 with a) SNR = 65 a.u.-pixel\(^{-1}\), \( F_n = 2.15\% \), and \( D_n = 1\% \) b) Equation reported in (2) with \( f_1 = 1.00\% \), SNR = 65 a.u.-pixel\(^{-1}\) and \( f_3 = 3.03\% \), SNR = 50a.u.-pixel\(^{-1}\).