## A robust transmitter calibration procedure for NMR of hyperpolarized nuclei

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**Introduction**: Calibration of the relationship between the voltage applied to the RF coil and the resulting flip angle is a standard part of any <sup>1</sup>H imaging procedure, and is an automated feature on commercial MR systems. Calibration methods designed for thermally polarized <sup>1</sup>H are not applicable to hyperpolarized substances, however, requiring custom calibration procedures to be implemented by the practitioner of hyperpolarized NMR. The simplest and most straightforward method of transmitter calibration for hyperpolarized nuclei is to observe the decay of the NMR signal as a function of RF pulse number for a series of constant, low-flip-angle excitation RF pulses. The accuracy and precision of the resulting calibration, however, depends on the flip angle used, which must be large enough to yield good SNR and avoid contamination of the measurement by  $T_1$  decay, but must be small enough to keep later signal measurements for becoming buried in the noise floor. That is, it helps to know the correct calibration before measuring it. The purpose of the present work is to demonstrate a robust, easily implemented calibration procedure using low-flip-angle RF pulses that circumvents this difficulty, requiring virtually no a priori knowledge of the proper calibration and thus minimal operator intervention.

## Methods:

*Calibration Pulse Sequence*: The iterative calibration procedure described here is meant to be performed in a dedicated in vivo acquisition and will entirely consume a small hyperpolarized sample. Starting with a transmitter voltage that is nonzero but can be confidently assumed to generate a flip angle less than  $12^{\circ}$  (much less is okay), a series of 32 excitation RF pulses are applied (TR=9.1ms), each using the same transmitter voltage. The magnitude of the NMR signal is sampled following each excitation, and spoiler gradients are applied before application of the next RF pulse. TR is kept small in order to avoid unnecessary  $T_1$  contamination of the flip angle measurement. After each block of 32 RF pulses, the transmitter voltage setting is doubled, and another calibration block is performed. This procedure is repeated until the transmitter voltage setting reaches a pre-set limit that can be confidently assumed to generate a flip angle greater than  $12^{\circ}$  (for instance, the maximum operational voltage specification of the RF coil can be used), at which point the sequence ends.

*Data Analysis*: The data from each calibration block consists of an exponentially decaying sequence of 32 signal measurements that, in the absence of  $T_1$  relaxation, is proportional to  $\cos^n \theta$  (n = 0,...,31). Early in the pulse sequence, the first signal measurement of a given calibration block will be greater than the first signal measurement of the previous block. However, once the flip angle becomes large enough that more than half of the remaining magnetization is consumed by 32 excitations ( $\theta$ -12°), the first signal measurement of subsequent blocks will decrease. A good balance between SNR and insensitivity to finite  $T_1$ , should be obtained from the block containing the peak signal measurement. The data from this block is fit to  $A\cos^n \theta$  to determine the corresponding flip angle. This flip angle is divided by the known transmitter voltage setting to arrive at the proper transmitter calibration.

*Theoretical and Experimental Tests*: Theoretical performance of the calibration procedure was evaluated by comparing numerical simulations of the iterative pulse sequence described above with a non-iterative implementation consisting of a single calibration block. Measurement noise was added to the simulated signal decay, and a  $T_1$  value of 22s was assumed. The iterative calibration pulse sequence was implemented on a 1.5T whole-body scanner (Siemens Sonata) and was performed in 30 subjects as the first scan of a <sup>3</sup>He imaging session. Each subject's weight was recorded. Calibration was performed at breath hold following inhalation of mixture of 30-50ml 35%-polarized <sup>3</sup>He and ~1L N<sub>2</sub> gas. The same flexible vest-shaped Tx/Rx RF coil was used for all scans.

**Results/Discussion**: Simulation results are shown in Figs. 1 and 2. Systematic error due to  $T_1$  contamination and statistical error due to measurement noise are displayed. For the non-iterative procedure, the systematic error is significant at low flip angles but decreases with increasing flip angle as the rate of RF consumption outstrips the longitudinal relaxation rate. At the TR and  $T_1$  assumed here, the systematic error is less than 1% for flip angles greater than 12°. By contrast, the iterative method yields systematic error less than 1% for any starting point. It is apparent from this plot that the effect of doubling the flip angle at each iteration in combination with using the peak signal measurement to derive the calibration, is to map any initial starting location into the optimum range  $12^\circ < \theta < 24^\circ$ . A similar pattern of behavior is seen in the noise error plot. It is noteworthy that the calibration error due to measurement noise is only slightly higher for very low initial flip angles than for initial flip angles in the optimum range. The key is that only a small amount of the available magnetization is consumed by flip angles below the optimum range.

Figure 3 shows experimentally measured signal amplitudes versus excitation number from a representative calibration scan. Each continuous piece represents one block of 32 excitation RF pulses at the same transmitter voltage. Note that the first signal measurement peaks in the next-to-last calibration block and the signal measurements decline rapidly in the final calibration block, illustrating that most of the hyperpolarized magnetization is consumed in the calibration block of interest.

A histogram of the experimentally measured calibration values is shown in Fig. 4. For our scanner, the calibration value corresponds to the amplitude of a 1ms rectangular RF pulse that generates 180° flip angle, given in Volts. The mean  $\pm$  standard deviation is 389  $\pm$  62 V, with a maximum deviation from the mean of 128V. Thus if the mean value had been used instead of performing an individual calibration for each subject, the flip angles would have been in error by as much as 30% in some cases. A weak correlation was observed between the measured calibration and subject weight, as shown in Fig. 5.

<u>Conclusions</u>: The iterative calibration procedure was found to be extremely robust in routine use. For the RF coil used in this study, the correct calibration varied among subjects by a factor of two from the highest to lowest measured value, with a standard deviation of 16% about the mean. Flip-angle errors of this magnitude are large enough to affect the quality of the study for many hyperpolarized gas applications, in which image quality often depends on careful rationing of the available hyperpolarized magnetization. The range of errors could be reduced somewhat by choosing calibration value based on weight, but only after the relationship has been established through many calibration scans. These results highlight the importance of calibration as a standard part of a hyperpolarized-gas imaging session. The primary advantage of the iterative calibration procedure presented here is that is requires virtually no a priori knowledge of the correct transmitter calibration, and thus the exact same sequence can be used across a wide range of RF coils without operator intervention, thereby minimizing the possibility of procedural error.

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