Real time liquid state polarization measurements for in vivo exams using hyperpolarized ^{13}C compounds

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Introduction

Hyperpolarized, ^{13}C labeled molecules can advance MRI into the realm of metabolic imaging [1]. Exams involving hyperpolarized compounds, however, require more complex hardware. Accurate liquid state polarization (LSP) measurements prior to patient injection are needed to insure the success of the ^{13}C exam and for quantification purposes. Although such measurements can be done outside the MR suite, immediately after the dissolution process, they would require an additional NMR spectrometer. Moreover, as the timing of the injection with respect to the dissolution time is not constant, measurement of the LSP at dissolution time does not guarantee exact knowledge of LSP at injection time, potentially introducing errors in quantification. We present a hardware setup that allows LSP measurements in the MRI magnet, immediately prior to patient infusion, using the scanner's magnet, electronics and software. This setup consists of 3 miniature transmit/receive (T/R) Helmholtz coils, creating mutually orthogonal fields, rigidly mounted to each other, and intended to surround the injection tube leading to the patient. We demonstrate the sensitivity of this setup in measuring single-shot signals from as little as 0.1ml of non-hyperpolarized ^{13}C-enriched samples (which can constitute a reference for LSP measurements, if needed). We also demonstrate that the signals measured are invariant to the orientation of the tube/coils in the magnet within the measurement error, confirming that the setup has the sensitivity and orientation invariance needed for accurate, real-time LSP measurements.

Methods

Three identical Helmholtz coils (tuned to 32.12MHz, ^{13}C resonance frequency at 3T) were built out of 2mm silver wire and rigidly mounted 2cm apart (to avoid coupling). The coils provide B_1 fields along 3 mutually orthogonal directions. A 1cm diameter collinear hole was drilled through the middle of coil formers, for the injection tube/ reference phantoms. Figure 1a displays a picture of one of the coils, next to a dime; the average quality factor of the coils was 191, and changed 20% (on average) between the loaded and unloaded states. Figure 1b displays a schematic of the coil setup. The red arrows in Figure 1b represent the direction of the B_1 fields generated by each coil, the green rectangle the bar used for rigid mounting, and the blue line the infusion line, through which hyperpolarized substance flows toward the patient. A single T/R channel and a 3-way, zero degree power splitter were used to operate this setup. Calculations were performed to understand the sensitivity of the setup to spatial orientation within the magnet. 2-ml phantoms filled with labeled 1-^{13}C lactate (Lac) (1-1.4M) and/or 1-^{13}C acetate (Ace) (1.5M-6M) were used to assess the sensitivity of the coils. A 30cm long, 8 ml cylindrical phantom filled with 6M 1-^{13}C Ace was used to assess the orientation dependence of the system.

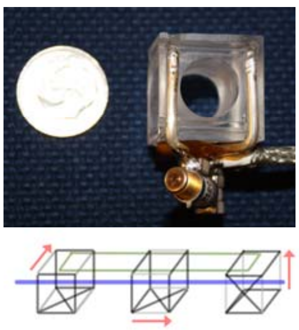

Figure 1: a) picture of a Helmholtz coil, next to a dime **b)** schematic of the 3 coil setup

Flip Angle	Min	Max
90	2	2.35
60	1.73	1.85
45	1.42	1.47
30	1	1.02

Table 1: Calculated orientation dependence

[theta,phi]	Measured signal
[90,330]	1.01
[90,345]	1
[90,0]	0.84
[90,15]	0.88
[90,30]	0.99
[90,45]	0.92
[90,60]	0.96
[90,75]	1.19
[90,90]	1.25
[0,0]	1.15
[45,0]	0.97
[90,180]	0.95

Table 2: Measured orientation dependence

Results

Experiments indicated that single shot signal is observable with this coil setup for phantoms containing 2ml of 1.4M sodium lactate for flip angles of 10°, at SNR>30, and for any coil assembly orientation. This indicates that <0.1ml of 6M 1-^{13}C Ace will be visible at 10° flip angle. A phantom containing this amount of (chemically stable) fluid easily fits inside the coil former (next to the infusion tube), and can constitute a reliable reference for LSP measurements. Table 1 depicts simulation results indicating the maximum and minimum signals (over 4π solid angle) expected when using excitation flip angles in excess of 30°. Lower flip angles (typical for an experiment involving hyperpolarized compounds) translate into smaller orientation dependence. Table 2 displays the signals (spectrum integrals) measured from this coil system and the 30cm long phantom, with a 20° flip angle, over a large number of orientations within the solid angle. Shim values were kept constant over the entire measurement period. The variability of these measurements is ~15%, only slightly larger than the variability of a measurement along a single direction (~13%). Note that these measurements were performed with the coils being significantly translated/rotated and occasionally removed from the magnet between repeat measurements. Levene's homogeneity of variance test indicates that the two variances are not statistically different, confirming that the signals measured with this coil are invariant to orientation --within the measurement error.

Discussion and conclusions

The slight measurement inconsistency observed for a single orientation is due to variable shimming (depending on the exact position of the coils and coil cables), and will likely be present in situations encountered in vivo, when such coil might end up operating in the magnet's fringe field, and would likely not be shimmed. This fact will probably preclude using absolute LSP measurements (in the absence of a reference phantom) with such setup, but will create no impediment for LSP measurements with a reference phantom. A smaller signal from a reference phantom due to improper shimming will also translate in a smaller signal from the hyperpolarized signal, but will maintain the ratio of the two signals, which will give the LSP measure.

A hardware setup that can allow real-time liquid state polarization (LSP) measurements from hyperpolarized compounds in the MRI magnet was presented. A system of three rigidly fixed miniature transmit/receive Helmholtz coils, creating mutually orthogonal fields, was designed to surround the patient injection tube. The sensitivity of this setup in measuring signals from small ^{13}C enriched samples (which will constitute the reference for the hyperpolarization measurements) was demonstrated. The spatial invariance (within measurement error) of the signal measurements was also shown, confirming that LSP measurements can be achieved with such setup. Operation in the magnet's fringe field, or in the absence of shimming is also possible. The presence of a reference phantom for LSP referencing will probably be required under these circumstances.

References

1. Ardenkjaer-Larsen et al, PNAS (2003), 100(18):10158-63.