A Low Field Dual Channel Heteronuclear RF Probe For Hyperpolarized Magnetic Resonance Imaging At 0.0475 T

Aaron M. Coffey[1,2], Roman V. Shchepin[1], Ken Wilkens[1], Kevin W. Waddell[1], and Eduard Y. Chekmenev[1]

[1]*Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States,* [2]*Biomedical Engineering, Vanderbilt University, Nashville, TN, United States*

Introduction The advent of hyperpolarization technologies has lead to increased ability to assay cellular metabolism at the molecular level [1; 2] at sensitivities greater than conventional MR or MRS by several orders of magnitude. Dynamic Nuclear Polarization (DNP) is the most common hyperpolarization method owing to commercial instrument availability, while methods based on parahydrogen are proving advantageous such as chemical addition by Parahydrogen And Synthesis Allow Dramatically Enhanced Nuclear Alignment (PASADENA) [3]. Hyperpolarization reopens examination of imaging at low field resonance frequencies. The signal voltage detected by MR [4-5], or electromotive force (*Emf*) arising from Faraday's law of induction, is $|Emf| = N \bullet |\Delta\Phi_B/\Delta t|$ where N is the number of turns and Φ_B the change in magnetic flux through a singe loop. Consequently, there could be additional *RF* benefits for low field detection of hyperpolarized compounds using multi-turn resonators. Moreover, dielectric losses dominate MR noise *in vivo* with $SNR \propto \omega$ at high field, while the scaling rule applicable to non-conductive samples in low field MR is $SNR \propto \omega^{7/4}$ [7].

Methods RF coil channel separation via individual transmit-receive coils permits optimizing sensitivity for the resonance frequency. Low frequency RF coil design leverages the multi-turn inductors permitted by long allowable coil lengths; e.g. $\lambda/10$ = 60 meters at 0.5 MHz, the 0.0475 T ^{13}C Larmor frequency. In initial work, a 50 mm x 170 mm single layer solenoid coil for ^{13}C was wound from 34 meters of 20 AWG magnet wire to form 206 turns with inductance 550 µH as measured by an Agilent E5071C network analyzer. The RF tuning and matching network was constructed from fixed C22CF series capacitors (Dielectric Laboratories, Cazenovia, NY) used in parallel with variable capacitors (model NMTM120C, Voltronics, Denville, NJ). The ^{1}H Helmholtz saddle coil, Fig. 1D, was previously described [6].

Results 1-^{13}C-succinate-d2 was polarized with PASADENA [3] using up to 97% enriched parahydrogen with Fig. 1B and 1C showing *in situ* hyperpolarized (P = 15 %, ^{13}C SNR = 500, and FWHM = 22 Hz) and direct Boltzmann signal detection via the solenoid coil. For ^{13}C spectroscopy signal comparisons at high and low field, Fig. 1E and 1F, the phantom consisted of 1.0 g sodium 1-^{13}C acetate dissolved in 2.8 mL 99.8% D_2O. To obtain polarization equivalent to 4.7 T equilibrium level at low field, the sample was prepolarized at 7 T to account for T_1 decay after ~7 s transfer delay. The condition of identical sample with identical polarization simulating conditions of the magnetic field independent hyperpolarized state was fulfilled. Using the same spectral widths and other acquisition parameters, the Doty volume coil (4.7 T) yielded SNR = 120 with FWHM = 6 Hz and the ^{13}C solenoid coil (0.0475 T) SNR = 30 with FWHM = 25 Hz.

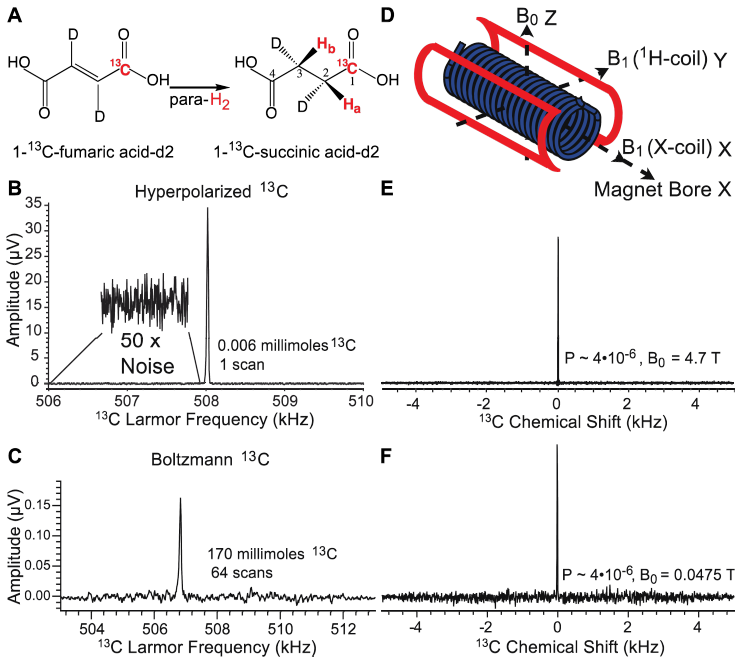

Figure 1. (A) Conversion of fumaric acid to succinic acid via the PASADENA hyperpolarization process leading to hyperpolarized 1-^{13}C carbon (red). (B) Single acquisition of 6.1 micromoles (< 1 mg) of hyperpolarized succinate contrast agent with P ~ 15 % or enhancement ε ~ 3,600,000 at 0.0475 T. (C) ^{13}C spectroscopy of a ^{13}C reference sample containing 0.17 moles sodium 1-^{13}C-acetate using Boltzmann polarization and 64 averages. (D) Coil layout and coordinate system of probe and magnet. (E) ^{13}C spectrum acquired at 4.7 T, SNR = 120 using commercial RF coil (Doty Scientific, SC). (F) ^{13}C spectrum acquired at 0.0475 T signal with SNR = 30 using the H-X RF coil.

Conclusions With the emergent technologies for hyperpolarizing nuclear spins, polarization levels become extrinsic to the static B_0 field. Specifically, hyperpolarized nuclear spin states are independent of the applied magnetic field and ω_0. Consequently, magnetic flux Φ_B is approximately field independent with the result that the induced *Emf* with multi-turn coils at low B_0 field can provide a sensitive means for MR detection of hyperpolarized compounds. This approach is demonstrated here for ^{13}C at 0.0475 T using hyperpolarized succinate, compared to high field ^{13}C detection at 4.7 T under conditions of equal nuclear spin polarization. The $\omega^{7/4}$ dependence is likely to cause a SNR maximum at a particular resonant frequency for a specific coil geometry and subject size and properties [8]. While the low field affords little if any opportunity for chemical shift imaging, other mechanisms such as *J*-couplings can be potentially used to resolve multiple metabolites. A low field MR imaging system for heteronuclear hyperpolarized contrast agents *in vivo* at 0.0475 T is under development to demonstrate utility for human scale.

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