Supporting Information

Sub-second Proton Imaging of ^{13}C Hyperpolarized Contrast Agents in Water

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3.1. Heteronuclear Polarization From Three Methyl Protons to ^{13}C in Isolated Methyl Group,

Sodium 1-^{13}C-Acetate Phantom in D$_2$O: Imaging and Spectroscopy

Polarization transfer from ^{13}C spin storage with long T_1 to protons was tested and optimized

using sodium 1-^{13}C-acetate in 99.8% D$_2$O. ^{1}H polarization was transferred from three methyl

protons of acetate using an INEPT transfer block to enhance polarization of the 1-^{13}C site of

acetate. This ^{13}C pre-polarization step was useful, because it increases the overall experimental

sensitivity and reduces repetition time between experiments due to ^{1}H T_1 << ^{13}C T_1. Methyl

protons served as a source of polarization and therefore experiments were repeated every 10

seconds versus minutes, because acetate's long ^{13}C$_1$ T_1 relaxation period can be avoided.

Furthermore, these experiments with INEPT preparation step to increase ^{13}C polarization above

thermal equilibrium conveniently simulate the non-equilibrium polarization enhancements

achieved via hyperpolarization.

For sodium 1-^{13}C-acetate, ^{13}C polarization transfer from methyl protons using the refocused

INEPT sequence, Fig. 1, can be expressed analytically according the following equation:

$$P_{13C} = 3 \bullet \sin(2\pi J_{HC} \tau_{INEPT}) \bullet \sin(2\pi J_{HC} \tau_{refocus}) \bullet \cos^2(2\pi J_{HC} \tau_{refocus}) \bullet P_{1H} , \quad (1)$$

where P_{13C} refers to ^{13}C polarization and J_{HC} to the two-bond heteronuclear spin-spin coupling

between 1-^{13}C and the methyl protons (J_{HC} = 6.0 Hz). The factor of 3 accounts for coherence

transfer from three protons of the methyl group to one ^{13}C. The first sin term represents INEPT

evolution and the second sin and cos^2 terms represent evolution during refocusing. The INEPT

part of the equation is maximized when τ_{INEPT} = 1/(4J_{HC}), while the refocus part is maximal at

$\tau_{refocus} \sim 1/(10J_{HC})$. Theoretically, if the polarization from all three methyl protons were fully refocused, i. e. $\sin(2\pi J_{HC}\tau_{refocus}) \cdot \cos^2(2\pi J_{HC}\tau_{refocus}) = 1$ (Eq. 1), then the enhancement factor would be 3, however, this is not the case, because this term has a maximum < 1, and therefore, the maximum theoretical enhancement is significantly less. When 42 ms and 16 ms respective delays were used for τ_{INEPT} and $\tau_{refocus}$, $P_{13C}^{INEPT} = 1.15 \cdot P_{1H}$, providing the largest $^{1}H \rightarrow ^{13}C$ polarization transfer when compared to the signal from ^{13}C Boltzmann polarization, Fig. 1. The equilibrium P_{1H} is 3.9772 times greater than equilibrium of P_{13C}, or $P_{1H} = 3.9772 \cdot P_{13C}$, resulting in $P_{13C}^{INEPT} = 1.15 \cdot 3.9772 \cdot P_{13C} = 4.59 \cdot P_{13C}$, where 4.59 is the theoretical enhancement, ε.

3.2. ^{1}H Background Suppression Using Multiband RF Excitation Pulses and ^{1}H Pre-saturation:

Imaging and Spectroscopy

With refocused INEPT optimized as a pre-polarization sequence for ^{13}C, a second INEPT pulse sequence block was then utilized to transfer polarization from ^{13}C to the contrast agent's protons. In aqueous solutions, a proton presaturation pulse alone, placed prior to ^{13}C magnetization transfer, was found to be ineffective for suppressing water. Frequency selective RF pulses provide an elegant solution to further minimize water ^{1}H background signal, because they excite a specific frequency range while ignoring extraneous regions. The excitation bandwidth for a typical 90° rectangular hard pulse can be defined as $1/t_p$, where t_p is the duration of the pulse. In examining protons with a typical spectral width of 12 ppm or 2.4 kHz at 4.7 T, a 90° hard pulse with $t_p = 50$ μs has an excitation bandwidth of 20 kHz, which exceeds the needed bandwidth by almost eight folds. Moreover, an RF pulse with such a large excitation bandwidth has almost no spectral selectivity. A potential solution to achieve spectral excitation selectivity when using square RF pulse is (i) to decrease $1/t_p$ by reducing RF power and (ii) to apply frequency offset so that only non-water spins are excited. However, a hard pulse excitation profile in frequency domain is described by a sinc function, sin(x)/x, where the maximum amplitude is located at the center of the pulse, with noticeable oscillations similar to an FID. These oscillations are problematic even at reduced excitation bandwidth, because they can excite water ^{1}H resonance. The water excitation would still occur resulting in significant water ^{1}H background signal.

A Gaussian shaped RF pulse provides a suitable alternative to a hard pulse since its excitation profile in the frequency domain is also symmetrical, and it does not display the oscillations observed in the hard pulse, and decays quickly to zero. As a result, it enables

exciting primarily proton(s) of interest in the contrast agent, while having minimal to no excitation of water ^{1}H resonance. Sinc excitation pulses can potentially offer another excitation selectivity method.

Water Background Suppression and Frequency Selective Excitation Pulse
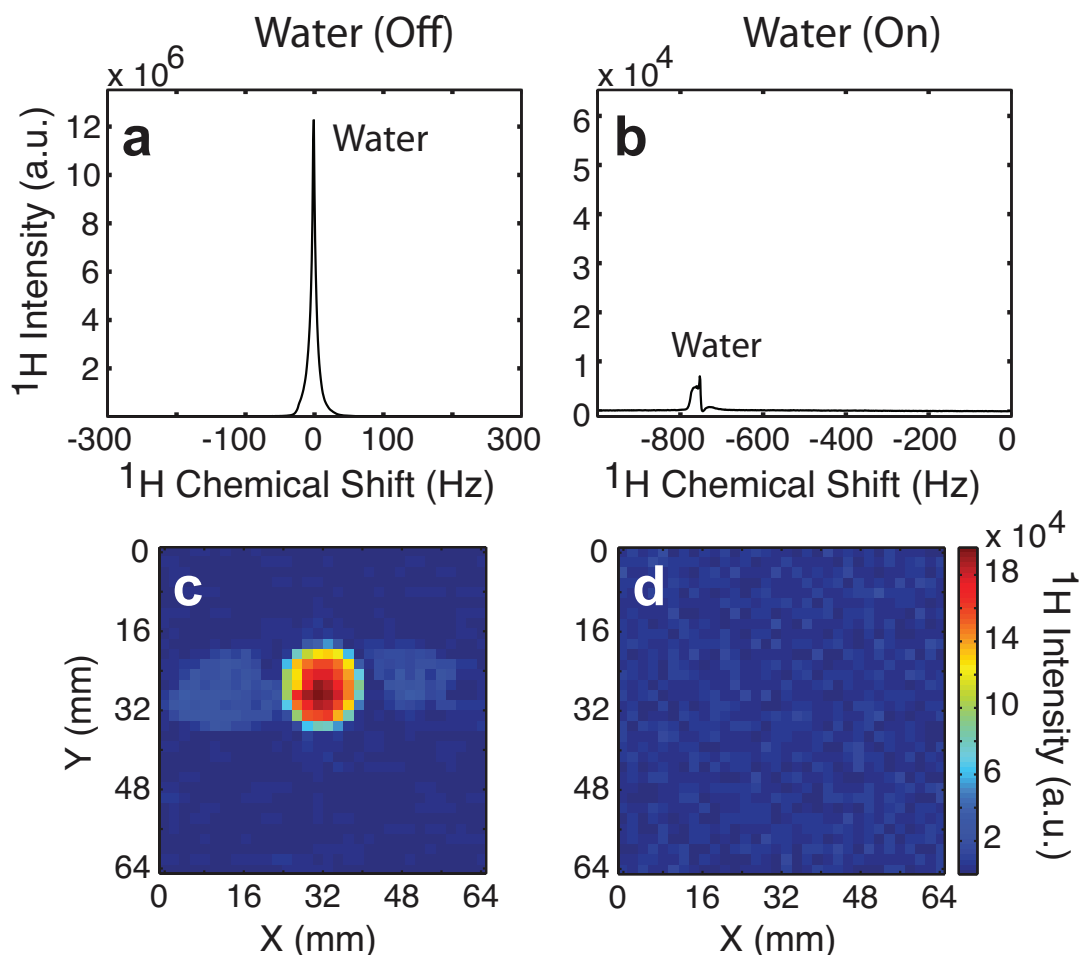
Figure S1. **Water Background Suppression.** Single scan proton spectroscopic and imaging detection of a 2.8 mL water phantom, without (**a** and **c**) and with (**b** and **d**) water suppression. Suppression was observed for the water signal. The water FSSFP images were acquired using TR = 5.95 ms, TE = 2.97 ms, FOV = 64x64 mm^2, and an in-plane resolution of 2x2 mm^2.