Sensitivity Enhancement of Hyperpolarized Nuclei through Polarization Transfer

S. Kadlecek[1], K. Emami[1], V. Vadhat[1], J. Yu[1], R. A. Guyer[1], R. V. Cadman[1], M. Ishii[1,2], J. M. Woodburn[1], H. H. Kim[3], W. Gefter[1], and R. R. Rizi[1]

[1]Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Otolaryngology, Johns Hopkins University, Baltimore, MD, United States, [3]Department of Chemistry, University of Pennsylvania, Philadelphia, PA, United States

Introduction: Hyperpolarized (HP) ^{13}C contrast agents have several unique characteristics which hold great promise for qualitatively new angiography and molecular imaging applications. They have intrinsically large signal-to-noise, are non-ionizing and may in principle be very benign, and the large ^{13}C chemical shift offers the opportunity for molecule- and conformation/environment sensitivity. We have begun preliminary studies to investigate the feasibility of increasing the sensitivity and molecular specificity of HP ^{13}C imaging through polarization transfer. These phantom studies are specifically designed to assess the difficulties encountered when performing polarization transfer in a normal clinical imaging environment. The eventual goal is to use low-gyromagnetic-ratio HP agents as long-T_1 'carriers' of spin order, and polarization transfer to realize the larger signal available from higher-gamma nuclei.

Methods: Samples of HP ^{13}C contrast agent were prepared using a prototype polarizer (GE Healthcare, Malmö, Sweden) and the method of Parahydrogen-Induced Polarization [1,2]. The techniques were also developed and demonstrated using a thermal phantom of 5 ml neat ^{13}C-labeled methanol. Polarization transfer and imaging was performed using a double-tuned ^{13}C/^{1}H birdcage coil (Stark Contrast MRI Coils, Erlangen, Germany) in a Siemens (Erlangen, Germany) Sonata 1.5T scanner. The scanner has an unavoidable 100 μs delay between pulses on both proton and carbon frequencies. Figure 1 shows a typical setup, in which a syringe of ^{13}C-labeled material is placed near a syringe of water, used as surrogate for tissue in *in vivo* applications. Several sequences were investigated, and the most effective polarization transfer scheme is shown in Figure 2. This pulse sequence is very similar to traditional 'INEPT' polarization transfer, except that polarization is transferred from the ^{13}C nucleus to a nearby proton. The sequence timing is determined by the number of nearby protons and the ^{13}C-^{1}H scalar coupling, with additional refocusing pulses and delays added to accommodate the low RF powers and long pulses encountered in a clinical scanner. The polarization transfer step is preceded by a 90-degree ^{1}H pulse and dephasing gradients, to minimize signal from the more numerous water protons, and is followed by either a ^{1}H spectroscopy acquisition or ^{1}H true-FISP imaging.

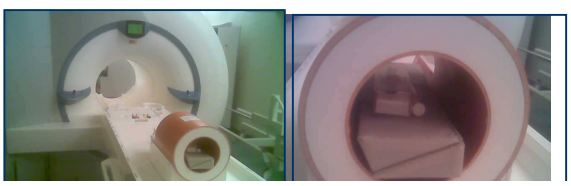

Figure 1: phantom placement in the double-tuned MRI coil

Results: Figure 3 shows the results of a normal ^{1}H spectrum acquisition (A), which is dominated by the water phantom, the spectrum after water suppression (B), and after polarization transfer from the methanol ^{13}C (C). Note that the water and hydroxyl protons' signal is eliminated and, as expected, the methyl protons are re-polarized using the sequence of figure 2. The expected signal-to-noise enhancement of ~16 is achieved over direct spectroscopy of the carbon nucleus despite the additional complexity and non-ideal aspects of the polarization transfer sequence on a clinical scanner. The corresponding imaging results are shown in figure 4. Again, the water signal is suppressed to near-invisibility and signal-to-noise is considerably superior to direct imaging of the carbon nucleus, although the enhancement is not quite as large due to the shorter proton T_2 during SSFP imaging.

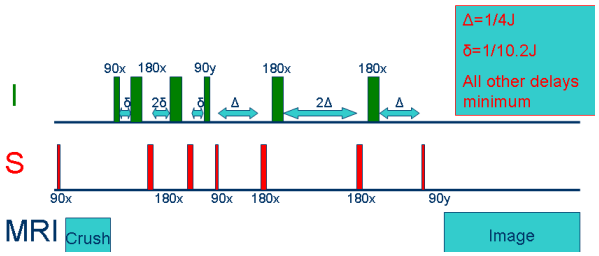

Figure 2: MRI imaging sequence for HP nucleus (I) to large-gamma ('sensitive', or S) nucleus

A 1.5 ml, 50 mM hyperpolarized sample of partially deuterated 2-hydroxyethyl propionate (HEP, Figure 5) was prepared at approximately 0.5% polarization. A polarization transfer sequence, modified to reflect the smaller scalar couplings of HEP was applied and imaging results are shown in Figure 6. Despite the low level of polarization and extremely low concentration, the signal from the propionate protons is enhanced by approximately 300, while the water phantom is suppressed by a factor of >600. This combination more than makes up for large concentration difference. Comparison of the relative signal intensities suggests a final proton hyperpolarization of 0.15% and an increase in imaging signal-to-noise of approximately a factor of two as compared to direct HP ^{13}C imaging.

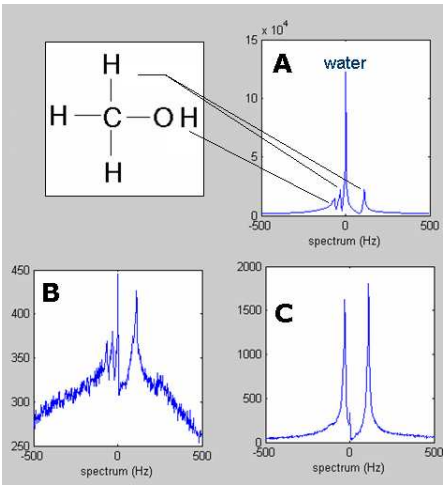

Figure 3: Spectra showing selective enhancement of MeOH methyl protons using modified reverse-INEPT spectroscopy on a clinical MRI scanner.

Discussion and Conclusion: Although still significant, the realized signal gains polarization transfer in the HP sample less than is achieved in the thermal phantom. This is partially due to the decreased efficiency of SSFP imaging in a situation where the T_2 is reduced and the polarization is not replenished. In addition, polarization transfer in the HP sample is less efficient because of the relatively long time that the nuclei spend in the transverse plane. This is in turn determined by the reduced scalar couplings (2-7 Hz) of HEP as compared to methanol (141 Hz).

The technique remains of great interest in situations where imaging sensitivity is of primary importance, or the unique scalar couplings of a metabolite allow it to be highlighted by polarization transfer.

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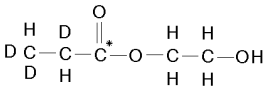

Figure 5: Structure of D_3,^{13}C-HEP

References:

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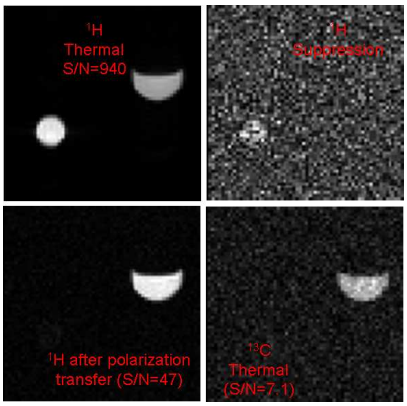

Figure 4 (left): Images showing the increased S/N achievable using polarization transfer from ^{13}C to the more sensitive ^{1}H, while effectively maintaining insensitivity to concentrated ^{1}Hs in H_2O.

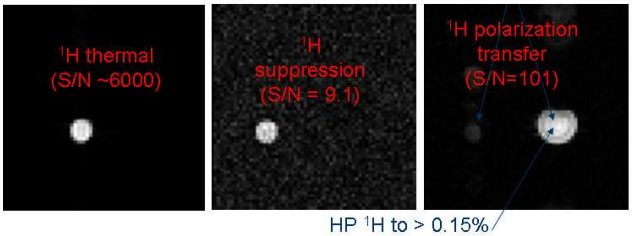

Figure 6(right): Images showing ^{1}H hyperpolarization derived from hyperpolarized ^{13}C.