Application of HSn Low Peak B1 Adiabatic Refocusing Pulses to Hyperpolarized ^{13}C Spectroscopic Imaging

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Introduction: High polarization of nuclear spins in liquid state through hyperpolarized technology utilizing DNP has enabled the direct monitoring of ^{13}C metabolites *in vivo* at very high SNR [1]. In our preclinical spectroscopy and spectroscopic imaging animal studies, we have routinely used a 1.7 gauss peak B1 adiabatic double spin-echo sequence to acquire full spin-echo data [2]. The advantages of acquiring a spin-echo are: insensitivity to T2* effects, higher signal from collecting both halves of the echo, and easier data processing due to the full echo magnitude spectra linewidth being the same as that from half echo phased spectra [2,3]. The adiabatic pulses provide uniform refocusing over a range of B1 values, but the commonly used hyperbolic secant (HS) pulse can have a relatively high peak B1 [4]. The coil and amplifier combination proposed for upcoming clinical hyperpolarized ^{13}C studies can output approximately 0.5 gauss after loading [5,6]. To accommodate this B1 constraint, we designed stretched hyperbolic secant refocusing pulses to operate at a nominal B1 of 0.4 gauss. We validated the new pulses in simulations, phantom tests, and *in vivo* experiments by comparing them to the previously reported 1.7 gauss pulses. We also acquired 3D-MRSI phantom data using the clinical setup and the low B1 pulses.

Pulse Design and Simulation: The specific forms we used for the HSn pulse envelope and instantaneous frequency, which have been described previously [7], were

Envelope: $$B1(\tau) = (B1_{max}) * \mathrm{sech}(\beta\tau^n)$$

Instantaneous frequency: $$\omega(\tau) = AB\int_0^{\tau} \mathrm{sech}^2(\beta(\tau')^n)d\tau'$$

where τ is the normalized time scale [-1,1], $B1_{max}$ is the nominal peak B1 in gauss, n is the stretch factor, $A = -\mu\beta$, and $B = \left[\int_0^1 \mathrm{sech}^2(\beta\tau^n)d\tau\right]^{-1}$.

This form reduces to a standard hyperbolic secant for n = 1. For our 0.4 gauss pulse, shown in Figure 1, the design parameters were: n = 3 (HS3), μ = 8, β = 4.725, and pulse length = 15 ms. We performed off-resonance and B1 sensitivity simulations with a Bloch simulator. As shown in Figure 1, the simulated profile is flat and equal to unity over the range of -500 Hz to 500 Hz and down to 0.25 gauss. We obtained very similar performance in phantom (single ^{13}C metabolite) experimental measurements of off-resonance and B1 sensitivity at 3T, which are also shown in Figure 1.

Methods: All experiments were performed on a General Electric EXCITE 3T (Waukesha, WI) MR scanner equipped with 40 mT/m, 150 mT/m/ms gradients and a broadband RF amplifier. For studies using spherical and syringe ^{13}C phantoms, the acquisition parameters were: 10 degree flip angle, centric phase encoding order, TE = 150 ms, TR = 2 s, FOV = 8x8 cm, and 8x8 spatial resolution. The mouse experiment acquisition parameters were: variable flip angle, centric phase encoding order, TE = 150 ms, TR = 215 ms, FOV = 4x4 cm, and 8x8 spatial resolution. For the *in vivo* experiments, we achieved ~20% liquid state polarization of [1-^{13}C]pyruvate (with 0.5 mM gadolinium) using a DNP polarizer. We injected ~350µL (~80 mM) over 12 seconds followed by a saline flush, with acquisitions starting 35 seconds from the start of injection. Custom built, dual-tuned ^{1}H/^{13}C transmit/receive coils were used for all spherical phantom and animal experiments.

Results: Figure 2 shows a 3D-MRSI phantom comparison between 1.7 gauss and 0.4 gauss acquisitions on a small animal coil. The top part of Figure 2 shows a single slice comparison, and the bottom part of Figure 2 shows spectra summed over all signal containing voxels. There was nearly perfect agreement between the two acquisitions. Figure 3 shows an *in vivo* comparison between 1.7 gauss and 0.4 gauss acquisitions. Once again, there was equally good spectral quality in the 0.4 gauss acquisition. Figure 4 shows a slice from a lactate/urea syringe phantom acquisition using our prostate clinical setup of a clamshell ^{13}C transmit coil (capable of ~0.5 gauss with proper loading) and a single channel endorectal receive coil. Figure 4 shows the feasibility of a full spin-echo 3D-MRSI acquisition with a human ^{13}C coil setup.

Discussion: The simulation, phantom, and *in vivo* data suggest that the 0.4 gauss HS3 pulses performed as well as the previously reported 1.7 gauss HS pulses. Although the 1.7 gauss pulses do have a higher bandwidth [2], the new pulses' bandwidth is sufficient to cover pyruvate and its products, including bicarbonate but not CO_2. In general, the primary disadvantage of a spin-echo acquisition is signal loss for short T2 species, but fortunately, the T2's of pyruvate, lactate, and alanine are relatively long [8]. In addition, a full echo requires a longer TR, but most of that extra time is used collecting data from the additional first half of the echo. For the clinical setup, we acquired data from reference samples and verified that sufficient B1 can be attained. Although the human studies have not yet started, with the newly designed HSn pulses, spin-echo acquisitions as done in previous animal experiments will now be an option.

References: [1] Ardenkjaer-Larsen et al., Proc Natl Acad Sci USA 2003;100:10158-10163 [2] Cunningham et al., JMR 2007;187:357-362 [3] Chen et al., ISMRM 2007 #538 [4] Tunnus et al., NMR in Biomed 1997;10:423-434 [5] Tropp et al., ISMRM 2006 #2594 [6] Nelson et al., ISMRM 2007 #536 [7] Park et al, MRM 2006;55:848-857 [8] Yen et al, ISMRM 2008 #1747

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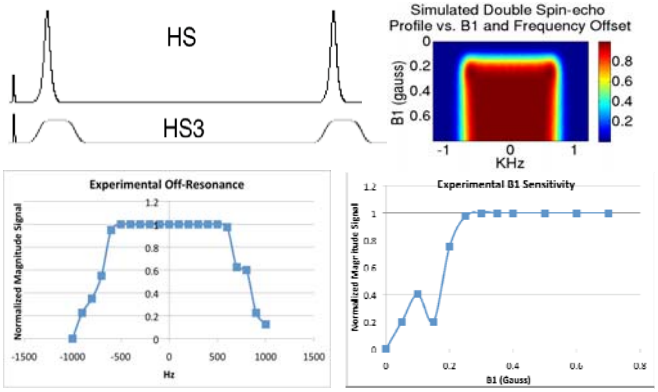

Figure 1: *The top left shows the double spin-echo RF sequence (90-180-180) with the 1.7 gauss HS and 0.4 gauss HS3 pulses. Only the envelopes of the 180s are shown. The 0.4 gauss peak B1 HS3 pulse has a duration of 15 ms. The top right shows the simulated off-resonance/B1 sensitivity map. The bottom left shows the experimental off-resonance profile at 0.4 gauss. The bottom right shows the experimental B1 sensitivity profile on resonance.*

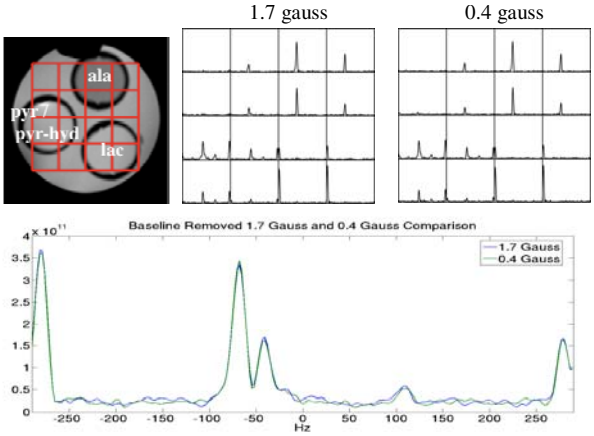

Figure 2: *Phantom comparison between acquisitions with 1.7 gauss and 0.4 gauss pulses, showing nearly perfect agreement. The top shows spectra from a single slice, and the bottom shows summed spectra over all voxels containing signal.*

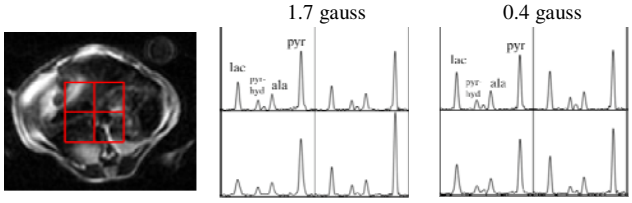

Figure 3: *In vivo spectra from a normal white mouse showing good spectral quality in both 1.7 gauss and 0.4 gauss acquisitions.*

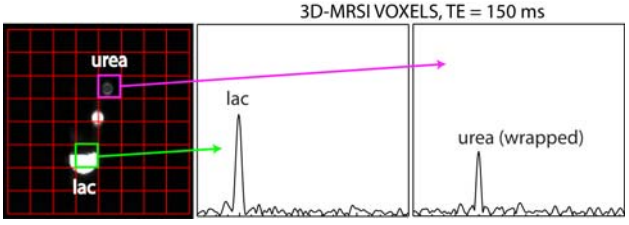

Figure 4: *Slice of syringe phantom data using clinical setup of clamshell transmit and endorectal receive, showing the feasibility of a full spin-echo 3D-MRSI acquisition.*