

Spin-lock sodium MRI of the human brain: a preliminary study

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Introduction: Proton $T_{1\rho}$ MRI studies have shown that spin-locking can provide unique and clinically-useful contrast correlated to macromolecular content due to its ability to probe slow molecular motion (1). Although spin-locking spectroscopy of sodium has been investigated as a means to selectively detect sodium nuclei involved in slow molecular motion and anisotropic environments (2), to knowledge there is currently no literature reporting spin-lock sodium MRI data. A large fraction of sodium ions in biological tissue are complexed to macromolecules through electrostatic binding sites and their interactions with the bound water fraction. Several disease states, e.g. stroke and osteoarthritis, involve substantial changes to motional characteristics of the complexed fraction of sodium spins. Measurements of T_2 or T_2^* are sensitive to slow motion only through the spectral density at zero frequency; slow dynamics are probed more efficiently through the application of a strong RF field near the kilohertz range (3). We hypothesize that spin-lock sodium MRI will generate significant contrast based on macromolecular content in biological tissue due to its sensitivity to slow molecular motion. The purpose of this study was to characterize the effect of spin-locking in sodium MRI in agarose and human brain.

Materials and Methods: A spin-lock pulse cluster was used with a rotary echo spin-lock pair and with frequency offset ($\Delta\omega$) equal to 200 Hz (Fig. 1). Spin-lock duration τ was set to 3 ms; high and low B_1 amplitudes were performed corresponding to $\omega_1 \approx 465.4$ and 116.4 Hz, respectively. A ramp-sampled 3D radial acquisition (ramp/total points = 12/64, BW/Px \approx 500 Hz) with spirally distributed radial views was performed immediately after the last pulse with a dead time delay of 50 μ s. RF spoiling with pseudorandom phase cycling was performed. An ultra-short echo (UTE) acquisition was also performed with the same α pulse and a TE=200 μ s. All sequences had a TR=50 ms, and all were obtained at 3 Tesla Siemens Trio scanner. Phantoms of 1 M [Na⁺] of saline and 2, 4, and 8% agarose were imaged with UTE, 507 Hz spin-lock, and 231 Hz spin-lock with 2500 radial views. A healthy, 27 year-old male subject's brain was imaged with the same three sequences and the same coil as with the agarose experiments, but with 25,000 radial views (scan time = 20.8 min). Brain images were intensity standardized using fluid signal from the ventricles and vitreous humor, and phantom images were standardized to the saline signal. Image intensities were evaluated from ROIs drawn in ImageJ (NIH). All image slices and their ROIs were coregistered and drawn manually. Brain scans were analyzed by drawing an ROI in the ventricular fluid and a large ROI in medial lobe of the axial slice in Fig. 2. The normalized tissue contrast was determined by subtracting the mean tissue ROI intensity from the mean fluid ROI intensity and dividing by the fluid ROI intensity (the standard deviations of the ROIs were carried through).

Results: 3D radial sodium MRI scans using UTE and spin-locking in brain and agarose phantoms are shown in Fig. 2. Fig. 2A is the UTE sequence, and Fig. 2B and Fig. 2C are the high (507 Hz) and low (231 Hz) spin-lock amplitude images, respectively. Standard intensities versus agarose concentration are shown in Fig. 3. The normalized tissue contrast values (measured as described above) were: $26.0 \pm 2.6\%$ for UTE, $28.2 \pm 2.5\%$ for 507 Hz, and $32.5 \pm 2.7\%$ for 231 Hz.

Discussion: We have demonstrated that off-resonance spin-lock sodium MRI is capable of providing contrast directly related to macromolecular content due to its sensitivity to spins in slow molecular motion regimes. Agarose and tissue show substantially different sodium signal amplitudes under high and low amplitude spin-lock pulses (Figs 2 and 3). Normalized tissue contrast showed a 4% greater decrease in amplitude in under 231 Hz spin-lock versus 507 Hz. Although we are currently operating at the SAR limit, it may be possible to apply even higher amplitude pulses if TR is increased or the hard pulse is altered. In that case, it should be possible to further separate signal intensities of spins at low frequencies so that a difference image could be made with signal almost entirely from motionally-restricted spins. Although UTE produces more SNR than the spin-lock sequence, it is much less sensitive to relaxation changes. While slow molecular motion can be probed with sequences weighting with T_2 and T_2^* such as spin echo and gradient echo, these suffer from a number of problems including SAR limits (180 deg refocusing pulses) and B_0 imaging artifacts (gradient echo). Spin locking produces less SAR than a refocusing pulse and is relatively insensitive to B_0 , while providing a sensitive means to probe relaxation induced changes. Since disease states correspond to changes primarily in sodium spins complexed to macromolecules, we believe this technique could prove valuable as a biomarker for those pathologies. Future investigations will also investigate spin-lock effects in heavily anisotropic environments, such as cartilage, where the observed signal changes under spin-locking are likely to be even greater in magnitude.

References: (1) Witschey, et al. *Magn Reson Med* (2006), (2) Hancu, et al. *Magn Reson Med* (2002), (3) van der Maarel, *Concepts Magn Reson Part A* (2003)

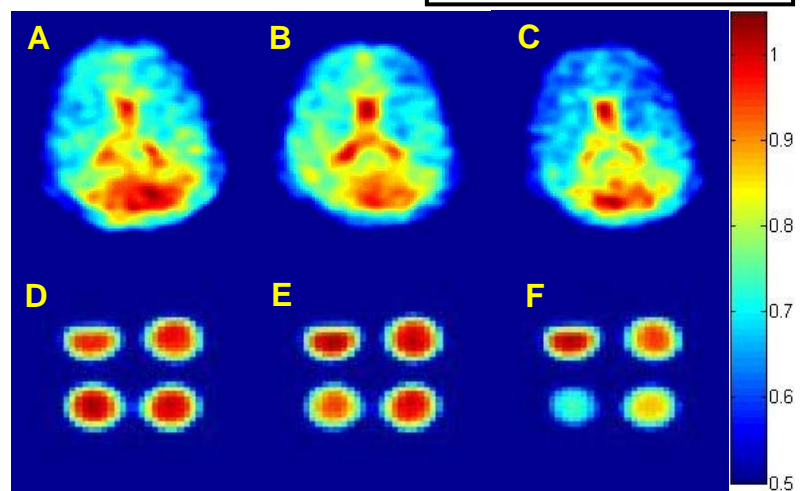
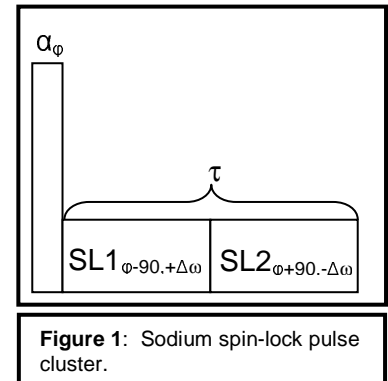


Figure 2. Brain scans using UTE (A) versus off-resonance spin locking at high (B) and low (C) B_1 amplitude. Phantom images below (D-F) have same sequence parameter as those above. Saline is at top left, with 2, 4, and 8% agarose arranged clockwise. Note the decreased tissue and agarose signal in the low amplitude (231 Hz) spin-lock images.

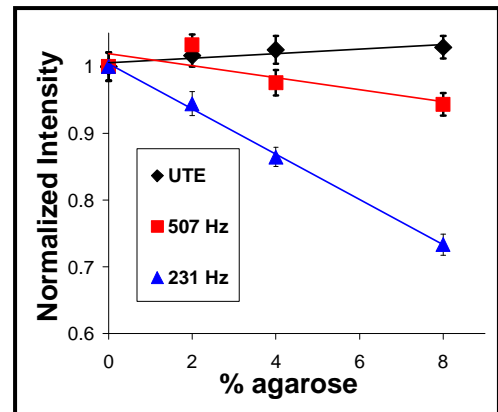


Figure 3. Effect of spin-locking in different motional regimes. Average phantom (1 M [Na⁺]) signal intensity. Zero percent agarose corresponds to saline.