Characterization of a Spin-Locked Spin-Echo EPI Sequence for pH-Sensitive Dynamic T1rho Imaging of the Brain

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PURPOSE: T1 relaxation in the rotating frame **(**T1ρ) has been shown to be sensitive to pH [1,2]. In the brain, pH is an indicator of metabolic state and may have a significant role in the pathophysiology of psychiatric diseases such as panic disorder [3]. Recently, T1ρ has been utilized to image brain pH dynamics [2]. In this prior work, a spin-lock-prepared spin-echo EPI (SLEPI) sequence, similar to that used for quantitative T1ρ mapping [4], was used in conjunction with a flashing checkerboard fMRI block design to measure changes in T1ρ as a result of brain activation in the visual cortex. The results suggested that, compared to BOLD, T1ρ provides unique and more localized functional imaging contrast generated by activity-evoked acidosis. In the present work, we aim to more fully characterize this dynamic T1ρ sequence. Specifically, saturation effects, sequence pH sensitivity, time series processing methods, and the utility for *in vivo* brain imaging are investigated in simulation, phantom, and *in vivo* experiments.

METHODS: A multislice 2D single-shot spin-echo SLEPI sequence was implemented on a 3T Siemens Trio MR system. Imaging parameters common to all SLEPI experiments were: spin-lock times (TSLs)={10,50}ms; $B1_{SL}$=260Hz; imaging matrix=64×64; slice thickness=5mm; 10 slices; and TR/TE=2000/12ms (intra-slice TR=200ms). A non-selective spin-lock pulse was applied prior to each shot. T1ρ and S(0) were calculated using the following model: S(TSL)=S(0)*exp(-TSL/T1ρ). ***Simulations:*** The longitudinal magnetization Mz of each slice of the SLEPI sequence was simulated over time using Bloch equations. Typical relaxation values for brain matter were assumed: T1=1000ms [5] and T1ρ=75ms [6]. The value of Mz for each TSL at the time of excitation was used to estimate the measured T1ρ. Simulated T1ρ values were compared to the true values to estimate the effects of dynamic changes in T1ρ and S(0). ***Phantom Experiments:*** Two solid egg white vial phantoms were prepared with unique pH values: (i) 8.4 and (ii) 7.7. Solid egg white was chosen due to its similar relaxation parameters to brain matter. To verify this, the T1, T2, and T1ρ of the phantoms were measured using 2D IR-SE, SE, and spin-locked SE sequences, respectively. The phantoms were then imaged with the SLEPI sequence and 70 T1ρ maps were generated to estimate pH sensitivity. ***In Vivo Experiments:*** The brain of a healthy subject was imaged using the SLEPI sequence both with and without the spin-lock prep pulse, yielding T1ρ and BOLD images, respectively. The imaging FOV was 24×24 cm^2, and the slices were placed axially through the visual cortex. A flashing checkerboard paradigm was used to elicit neural activation in the visual cortex. For the spin-lock sequence, new T1ρ and S(0) maps were generated every 4.0 sec. Four runs of 140 measurements were performed for both T1ρ and BOLD, yielding a total of 280 T1ρ and S(0) maps and 560 BOLD images. Each run consisted of seven 40sec blocks with alternating baseline and stimulation states. T1ρ, S(0), and BOLD activation maps were generated using AFNI and Matlab with the following processing steps: registration; spatial smoothing; calculation of T1ρ and S(0) maps (for SLEPI); and GLM model fitting. Temporal interpolation was investigated as a means to estimate TSL=10ms images at the acquisition times of the TSL=50ms images to reduce the effects of inter-TSL changes in T1ρ and S(0).

RESULTS: ***Simulations*:** Since the spin-lock pulse is non-selective, Mz approaches a steady state that is a function of T1, T1ρ, and TSL. T1ρ is therefore incorrectly quantified using the mono-exponential decay model, particularly for early slices that do not have time to reach steady state between switching of TSLs. However, if there is a change in T1ρ, the percent change in the measured value varies similarly at steady state to that of the true value, and thus relative changes in T1ρ can be readily quantified. High temporal resolution is important in part to reduce T1ρ measurement errors due to inter-TSL changes in S(0). ***Phantom Experiments:*** The T1, T2, and T1ρ values of the phantoms were found to be close to those of brain matter (vials (i)/(ii): T1=1445/1418ms; T2=80/105ms; T1ρ=76/102ms). For the SLEPI data, the mean pixel T1ρ values for vials (i) and (ii) were 32.2±1.3 and 38.8±1.3ms, respectively. This suggests a 0.1 unit change in pH will produce a 1ms change in SLEPI-measured T1ρ, resulting in effect sizes of ~0.77 and 0.38 for ΔpH=0.10 and 0.05 units, respectively. ***In Vivo Experiments:*** Temporal interpolation increased S(0) activation but had negligible effect on T1ρ. Regions of T1ρ activation became better defined with more runs. Figure 1 shows comparable activation maps for T1ρ, S(0), and BOLD using all four runs of data. It can be seen that BOLD activation is effectively measured in the S(0) parameter, whereas T1ρ shows different and more localized regions of activation.

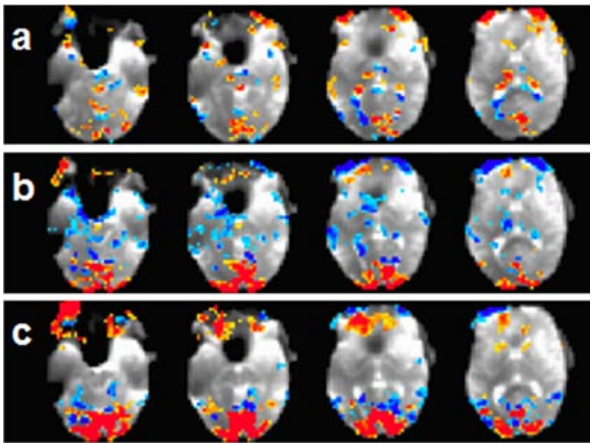

Figure 1: (**a**) T1ρ, (**b**) S(0), and (**c**) BOLD activation maps generated from an equivalent number of samples (p<0.01, uncorrected). The T1ρ and S(0) maps used the same source data. Results are shown for four consecutive slices passing through the visual cortex. S(0) activation closely resembles that of BOLD, whereas T1ρ activation is distinct and more localized.

DISCUSSION: Short-TR SLEPI dynamic imaging has been shown to be sensitive to changes in T1ρ and with sufficient samples (>30) can detect physiologically-relevant pH changes of 0.1 units. The method effectively separates T1ρ and BOLD activation with high temporal resolution (4.0sec). Significant limitations of the current implementation include low SNR, poor absolute T1ρ quantification, and susceptibility to changes in T1.

CONCLUSION: Dynamic T1ρ imaging of the brain using a rapid SLEPI sequence provides unique and more localized functional activation compared to BOLD. The technique is sensitive to physiological changes in pH and can simultaneously measure both T1ρ and BOLD activation.

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