B1 and B0 Sensitivity of Spin-Lock Preparation Pulses for Whole-Brain Quantitative T1rho Mapping

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Introduction: Quantitative T1ρ mapping of the brain is an emerging technique to image psychiatric and neurological diseases including Alzheimer's disease [1,2], Parkinson's disease [2,3], multiple sclerosis [4], and bipolar disorder [5]. T1ρ mapping is of interest due to its sensitivity to a variety of factors influenced by disease processes including cellular density, pH, and glucose concentration [6-8] as well as its ability to image with high spatial resolution in a reasonable scan time. Whole-brain T1ρ mapping may be useful for a variety of diseases and has recently been demonstrated with 1.8 mm isotropic resolution in 14 minutes [9]. Recently, new cerebellar abnormalities in bipolar disorder were found using whole-brain T1ρ mapping because of its volumetric coverage [5]. Although whole-brain T1ρ mapping is promising, there are a number of technical challenges that still need to be addressed. One of these issues is accuracy of T1ρ quantification across the entire brain, especially in regions of inhomogeneous RF transmit (ΔB_1) and main magnet (ΔB_0) fields. T1ρ prep pulses typically consist of the following steps: (i) 90º excitation of the longitudinal magnetization (M_z); (ii) alignment of a spin-locking pulse with the transverse magnetization (M_{xy}) for duration TSL with optional refocusing; and (iii) a second 90º excitation yielding the spin-lock-prepared M_z. Excitation and refocusing pulse errors and/or M_{xy} off-resonance can lead to signal loss and/or inefficient spin locking, thereby generating T1ρ quantification errors. A number of spin-lock prep pulse methods have been developed to reduce sensitivity to ΔB_1 and ΔB_0 [10-12]. However, the effectiveness of these pulses to accurately quantify T1ρ throughout the entire brain has not been evaluated. This is particularly pertinent for challenging regions near air-tissue interfaces such as the orbitofrontal and temporal pole regions. In this study, we simulated the T1ρ quantification accuracy of a variety of spin-lock prep pulses over an expected range of ΔB_1 and ΔB_0 as measured *in vivo* using whole-brain ΔB_1 and ΔB_0 mapping of 24 participants. We also introduce prep pulse variants using adiabatic excitation and refocusing pulses to better address ΔB_1 and ΔB_0 compared to existing methods at the expense of signal loss and RF heating.

Methods: *In vivo whole-brain ΔB_1 and ΔB_0 mapping:* 24 participants were imaged as part of an Institutional Review Board-approved study of bipolar disorder where written informed consent was obtained. Imaging was done on a Siemens 3T TIM Trio scanner using the body coil for transmit and a vendor-provided 12-channel head coil for receive. The imaging session included 3D T1- and T2-weighted anatomical brain scans and whole-brain ΔB_1 and ΔB_0 mapping sequences. ΔB_1 maps were calculated using the 180º null method [13] (3D GRE; FOV=24×24×16cm^3; 3.8×3.8×4.0mm^3; TR/TE=60/3.3ms; FAs=145/180/215º). ΔB_0 maps were calculated using a stock field mapping sequence (multi-slice GRE; FOV=24×24×16cm^3; 3.8×3.8×4.0mm^3; TR/TEs=420/4.9/7.4ms). Using the anatomical scans as a reference, the ΔB_1 and ΔB_0 maps for all participants were transformed a common brain atlas. The group ΔB_1 (prescribed flip angle scale factor) and ΔB_0 (Hz) mean and standard deviation (σ) were calculated on a voxel-by-voxel basis. *Simulations:* The Bloch equations were used to simulate rotation and T1ρ relaxation of the magnetization vector under the influence of spin-lock and other preparation RF pulses. Five prep pulse methods were considered: (**A**) self-compensating spin-lock [10]; (**B**) Method A with adiabatic excitation pulses (B_1=1000 Hz; Tp=3.1ms; R=30); (**C**) self-compensating spin-lock with refocusing pulse for reduced B_0 sensitivity (magnetization flipped to –z axis) [11]; (**D**) Method C with adiabatic excitation pulses (magnetization returned to +z axis); and (**E**) Method D with an adiabatic refocusing pulse (B_1=1000 Hz; Tp=12.3ms; R=25). A spin-lock pulse amplitude of 350 Hz and TSLs=0 and 80ms were used. Relaxation was only considered during the spin-lock pulse, with M_{xy} parallel to the spin-lock pulse decaying with T1ρ (75ms) and M_{xy} perpendicular to the spin-lock pulse decaying with T2ρ (130ms based on T2=70ms and T1=1000ms). Thus, T1ρ quantification errors could result from either (i) inefficient return of the magnetization vector to the z-axis (residual M_{xy} assumed to be spoiled) or (ii) inefficient spin locking resulting in T2ρ contamination. ΔB_1 and ΔB_0 were varied over the range observed in the *in vivo* study. T1ρ was calculated using a mono-exponential fit of the resultant TSL M_z signals at the end of the prep pulse. *Signal loss and SAR*: Percent signal loss due to relaxation under the influence of the RF excitation and refocusing pulses was estimated assuming T1ρ and T2ρ as before for the hard pulses and adiabatic T1ρ=170ms and T2ρ=80ms for the adiabatic pulses [4]. RF energy deposited by each preparation pulse was estimated in arbitrary units relative to a 250μs, 1000 Hz, 90º hard pulse with energy=1.0au.

Results: Fig. 1 shows a scatter plot of all brain tissue voxel (ΔB_0, ΔB_1) pairs in the *in vivo* 24-participant-averaged inhomogeneity maps. Mean value (black) ranges are ΔB_0=[-100,+75] Hz and ΔB_1 =[0.8,1.2], and ±2σ value (red) ranges are ΔB_0=[-200,+150] Hz and ΔB_1=[0.5,1.6]. Simulation results are shown in Fig. 2 for Methods C and D over the same ΔB_0 and ΔB_1 range plotted in Fig. 1 (black dashed lines: ΔB_0=0 and ΔB_1=0; white dashed box: bounds for average ΔB_0 and ΔB_1 values). Method D outperformed C in terms of T1ρ quantification accuracy due primarily to reduced T2ρ weighting during the TSL=80ms pulse. Method B outperformed A, but it did not perform as well as D. Method E did not perform as well as D due to adiabatic refocusing errors. Table 1 shows estimated signal loss and energy for all methods.

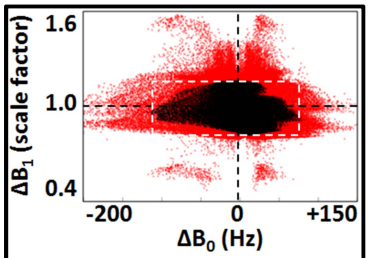

Fig. 1: ΔB_1 vs. ΔB_0 scatter plot for 24 whole brains. Black = mean. Red = ±2σ.

Discussion: Adiabatic excitation pulses improve T1ρ accuracy in regions of ΔB_1 and ΔB_0 inhomogeneity and may be useful when imaging portions of the brain susceptible to these effects such as the orbitofrontal region. However, this advantage comes at the cost of some signal loss and RF energy deposition, which may necessitate longer scans to allow more time between spin-lock prep pulses for greater M_z signal T1 recovery and reduced SAR. Optimization of the adiabatic pulses for the required ΔB_0 and ΔB_1 range, which was not done here, may further improve their performance. This work focused on continuous-wave spin-locking, but adiabatic spin-locking [14] offers a potentially efficient alternative solution. The methods and (ΔB_0, ΔB_1) data reported here will help evaluate these new techniques for accurate quantification of T1ρ throughout the brain.

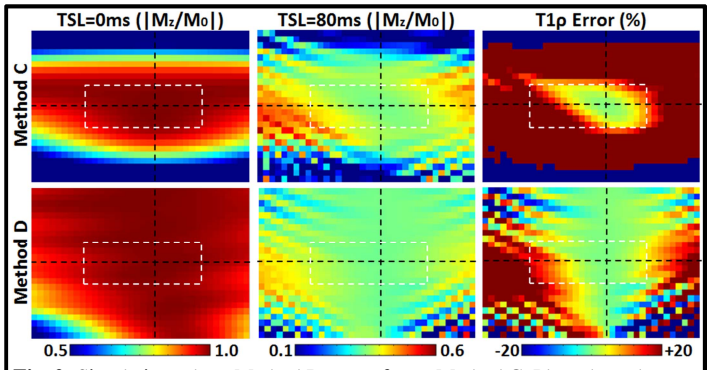

Fig. 2: Simulations show Method D outperforms Method C. Plots show the same ΔB_1 vs. ΔB_0 range as Fig. 1 (same dashed lines). Ideally, $|M_z/M_0|$=1.0 for TSL=0ms and $|M_z/M_0|$=0.34 for TSL=80ms, yielding T1ρ=75ms. Method D has lower T1ρ errors, both for average ΔB_0 and ΔB_1 values (white box) and beyond.

Table 1

Method	Signal Loss	Energy (a.u.) TSL=0	Energy (a.u.) TSL=80
A	0.7%	2.0	41.2
B	3.5%	18.1	57.3
C	1.0%	4.0	43.2
D	4.2%	20.1	59.3
E	17.3%	42.7	81.9

References: **[1]** Borthakur A, *et al*. NeuroImage 2008. **[2]** Haris M, *et al*. J Neurol 2011. **[3]** Michaeli S, *et al*. Mov Disord 2007. **[4]** Mangia S, *et al*. Mult Scler 2014. **[5]** Johnson CP, *et al*. Mol Psychiatry (in press). **[6]** Michaeli S, *et al*. J Neurosci Methods 2009. **[7]** Kettunen MI, *et al*. MRM 2002. **[8]** Jin T, *et al*. MRM 2011. **[9]** Watts R, *et al*. JMRI 2013. **[10]** Charagundla S, *et al*. JMR 2003. **[11]** Witschey WRT, *et al*. JMR 2007. **[12]** Chen W, *et al*. MRI 2011. **[13]** Dowell NG, *et al*. MRM 2007. **[14]** Mangia S, *et al*. MRI 2009.