Rapid and Accurate Variable Flip Angle T1 Mapping with Correction of On-Resonance MT Effects

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INTRODUCTION: Variable flip angle (VFA) acquisition using spoiled gradient echo (SPGR) [1] has become a widely accepted approach for fast high resolution mapping of longitudinal relaxation rate $R1=1/T1$. Recent studies have shown that magnetization transfer (MT) between free and bound protons due to the application of an on-resonance excitation pulses causes a significant bias in steady state MR signal in tissues with natural abundance of macromolecular content [2]. Ou et al predict up to 14% error in white matter (WM) VFA *T1* values [3], an effect comparable to white matter *T1* changes observed in multiple sclerosis [4]. Explicit consideration of a two-pool MT model in VFA experiments may improve the accuracy of *T1* estimation [3]. However, due to very low sensitivity of the modified VFA signal model to parameters of the two pool MT model such as bound pool fraction *(f)*, cross-relaxation rate *(k)*, transverse relaxation times of the bound pool T_2^B, and free pool T_2^F, the feasibility of MT-corrected *in vivo T1* mapping using VFA measurements only is limited. Cross-relaxation imaging (CRI) provides a convenient framework to model the effect of both off-resonance MT and on-resonance excitation pulses on bound and free proton pools [5]. It was recently demonstrated that combination of VFA and pulsed MT SPGR measurements within modified CRI framework may be used to remove bias due to on-resonance MT in both VFA *R1* values and two-pool MT parameters [6]. However, this approach requires augmenting VFA measurements with multiple MT acquisitions to allow estimation of the full set of parameters. Here, we propose a method to obtain accurate *T1* maps of clinical quality using a standard VFA datasets augmented with a single off-resonance MT SPGR scan (VFA-MT).

METHODS: The simultaneous fit of SPGR data (VFA part) and off-resonance MT SPGR (MT part) data to the modified CRI equation accurately yields all parameters of the model ($PD,R1,f,k,T_2^B$)[6]. To achieve fast *T1* mapping, we simplify the full model by setting T_2^B, $T_2^F R_1^F$, and $R=k(1-f)/f$ to constrained values as proposed in [7] (11μs, 0.022, and 19s^{-1}, respectively), which leaves only three free parameters ($PD,R1,f$) for estimation. These parameters may be in principle determined using only three measurements (two VFA and one MT). The accuracy of this simplified 3-parameters/3-measurements approach (VFA-MT) was studied in simulations, phantom imaging, and *in vivo*. *Simulations:* We run simulations to identify the ranges of an offset frequency and an MT flip angle of a VFA-augmenting MT scan for which the effect of such constraints on accuracy of *R1* and *f* is minimal. *Phantom Studies:* Phantom (25% gelatin) and *in vivo* experiments were run on a 3.0T GE MR750 (Waukesha, WI), and flip angle and field maps for all data were measured by an optimized AFI method [7] and IDEAL [8], respectively. Phantom protocol included acquisition of 3D VFA data FAs=[7,15,35,50]˚ and MT SPGR data (FA=15˚, Δ=2.5,5,9,13kHz, α_{MT}=[850,1300]˚, 18ms Fermi pulse, 120×120×88mm FOV, 128×128×44 matrix, TR/TE=37/2.3ms). Single-slice, 2D inversion-prepared spin-echo (IR) data was collected to determine a reference *T1* value in the phantom (TR/TE=5000/8.2ms, TI=0.05,0.1,0.2,0.3,0.5,0.7,0.9,1.2,1.6,2s). *In Vivo Studies:* Volunteer brain data included 3D VFA (FAs=[5,10,20,30]˚) and MT SPGR(FA=10˚, Δ=2.5,5,9,13kHz, α_{MT}=[500,1100]˚, 18ms Fermi pulse, 240×180×80mm FOV, 128×96×40 matrix, TR/TE=40/2.0ms). The reference MT-corrected *T1* maps were obtained by simultaneous fit of all VFA and MT data to the modified CRI model [6]. All processing was done by in-house nonlinear optimization routines.

RESULTS AND DISCUSSION: *Simulations:* Figure 1 illustrates the effect of two-pool MT model parameters on observable *T1* values when calculated using standard VFA method. The error in *T1* increases almost linearly with *f* for typical values of *k* observed in neural tissues (>1) and hence is expected to be most biased in macromolecular-rich tissues such as white matter. The sensitivity of *T1* to T_2^B was negligible. Figure 2 shows the effect of off-resonance frequency and MT flip angle of a VFA-augmenting MT scan on the average loss in *R1* and *f* for the proposed simultaneous constrained estimation of these parameters. Similar to observations in [7], there is a range of Δ and MT flip angle with low sensitivity to the fixed parameters (Δ=4-6kHz, α_{MT}=400-600˚). Therefore, the optimized set of measurements (SPGR α=[5,30]˚; Δ=5kHz, α_{MT}=500˚) were used for *in vivo* validation of the constrained model. *Phantom Studies:* The proposed method was applied to correct *T1* mapping in the phantom (*f*≈4%). Examination of mean phantom *T1* values obtained with full CRI (12 measurements), proposed constrained VFA-MT (3 measurements) and VFA (2 measurements) confirmed that both full CRI and VFA-MT provide excellent agreement with the reference IR *T1* measurement (Fig. 3). At the same time, VFA *T1* was biased by approximately *f*%, which is consistent with simulations in Fig. 1. *In Vivo Studies:* Images in Fig. 4 reveal that there is a visible bias in *T1* map obtained with regular VFA compared to *T1* maps obtained with on-resonance MT effect correction. The MT-corrected values ($T1_{WM}$=1050±25, $T1_{GM}$=1537±25) agree well with literature [10] ($T1_{WM}$≈1060, $T1_{GM}$≈1630), while VFA underestimated them ($T1_{WM}$=931±34, $T1_{GM}$=1462±28). The whole brain *T1* histograms (Fig. 5) show excellent correlation between reference full CRI values and proposed VFA-MT approach. The method corrected VFA *T1* values by 11.5% in WM and 6.2% in GM, which agrees well with the bias predicted by [3]. Analysis of ROI *T1* measurements (Table 2) demonstrated excellent preservation of *T1* mapping accuracy in both WM and GM (error<1%) when moving from full CRI (12 measurements) to constrained VFA-MT (three measurements) estimation. The errors in *f* maps (not shown here) were more significant but always <10%, which is consistent with results in [7].

CONCLUSIONS: Accurate estimation of *T1* values from VFA measurements requires consideration of MT effects, which may introduce *T1* bias roughly proportional to the macromolecular content. The fast *T1* correction protocol developed in this work (VFA-MT) requires a single MT scan in addition to regular VFA measurements for accurate *T1* mapping. The presented approach is promising for fast high-resolution whole brain *T1* mapping within clinically acceptable scan times.

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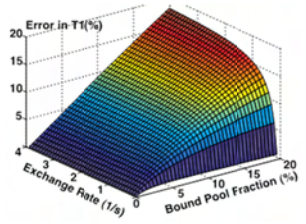

Fig. 1: Error of VFA *T1* values vs. quantitative MT parameters *f* and *k*.

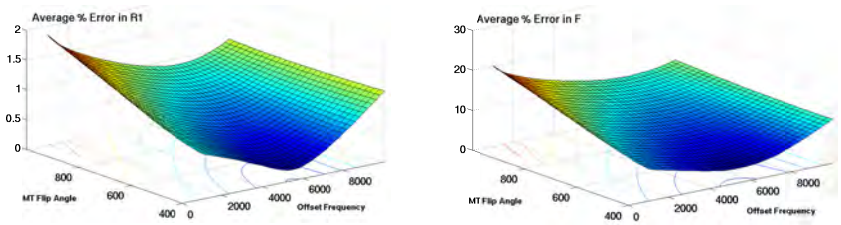

Fig. 2: Dependence of error in estimation of $R1=1/T1$ (left) and *f* (right) due to constraining vs. offset frequency and MT flip angle of a MT SPGR acquisition of proposed 3-point protocol.

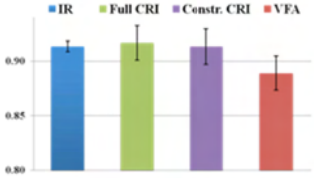

Fig. 3: Phantom *T1* values calculated by different methods.

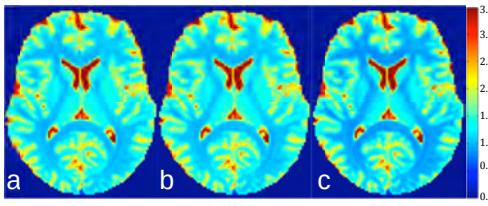

Fig. 4: *In vivo T1* maps estimated by modified full (a) and constrained CRI (b), and *VFA* (c).

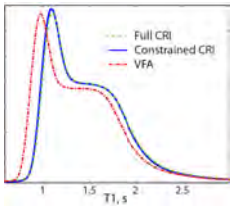

Fig. 5: Brain *T1* histograms

	CC	IC	PT	CN
T1	0.77%	0.73%	0.45%	0.43%
f	3.05%	5.89%	4.22%	9.73%

Table 1: Errors of constrained method in brain structures (CC: Corpus Callosum, IC: Internal Capsule, PT: Putamen, CN: Caudate Nucleus)