Improved Accuracy of Cross-Relaxation Imaging Using On-Resonance MT Effect Correction

Pouria Mossahebi[1], Vasily L. Yarnykh[2], and Alexey A. Samsonov[3]

[1]*Biomedical Engineering, University of Wisconsin, Madison, WI, United States,* [2]*Radiology, University of Washington, Seattle, WA, United States,* [3]*Radiology, University of Wisconsin, Madison, WI, United States*

INTRODUCTION: Over past years, several methods have been proposed for quantitative mapping of molecular parameters describing the magnetization transfer (MT) effect within the two-pool model (bound pool fraction *f*, cross-relaxation rate *k*, and transverse relaxation times of the bound pool T_2^B and free pool T_2^F) from a series of images with variable off-resonance saturation [1-4]. Resulting parametric maps are expected to provide new biomarkers in various neurological conditions. Particularly encouraging results were reported for the bound pool fraction, which provides strong associations with myelin content in neural tissues [5,6]. The common feature of the above methods is the need for complementary *T1* mapping, which allows decoupling of the two-pool model parameters from the longitudinal relaxation rate *R1*=1/*T1*. One of such methods, cross-relaxation imaging (CRI) [4] allows 3D acquisition with excellent speed and resolution based on combination of a limited number of MT-weighted images and variable flip angle (VFA) *T1* maps obtained using a fast spoiled gradient-echo (SPGR) sequence. However, recent studies showed that the on-resonance MT effect may cause a significant bias in the steady-state MR signal [7,8], if the model does not account for bi-exponential behavior of longitudinal relaxation occurring due to MT. This bias unavoidably introduces errors in VFA *R1* measurements [8], which may propagate into the two-pool model parameters measured by CRI. In this study, we theoretically and experimentally characterize systematic errors in CRI caused by MT-related bias in VFA *R1* mapping and propose a modified processing algorithm, which corrects for such errors and yields accurate quantitative MT parametric maps.

THEORY: In the standard CRI approach, reconstruction of parametric maps is performed in two steps [4]. During the first step, *R1* and proton density (*PD*) maps are calculated from VFA data by fitting the Ernst equation. This approach ignores coupling between *R1* and the rest of two-pool model parameters. During the second step, the matrix model of pulsed MT [4] is fitted to MT-weighted data, while *R1* is supplied as an external parameter. Prior to fit, MT data are normalized to the signal intensity obtained without saturation to exclude *PD*. Depending on the sampling scheme and constraints imposed on certain two-pool model parameters, either all four parameters *(f, k,* T_2^B*,* T_2^F*)* or their subsets can be fitted [4,5,9]. As an alternative to this approach, we modified the CRI model to simultaneously perform global fit of VFA and MT data, which yields all parameters *(PD, R1, f, k,* T_2^B*,* T_2^F*)* with full consideration of coupling between them. Theoretically, MR-related errors in *R1* measured by the VFA method can be caused by the two mechanisms unaccounted within the standard single-pool signal model. These are on-resonance saturation of the bound pool by the excitation pulse and bi-exponential relaxation during TR, where a contribution of the fast-relaxing component becomes more significant at short TR. To estimate relative roles of these factors, the model was further modified to include an additional term to account for the effect of excitation pulse on semisolid pool [7] calculated by Bloch equation simulations.

METHODS: Volunteer data were obtained on a 3.0T GE MR750 (Waukesha, WI) scanner. To correct for B1 and B0 inhomogeneity, flip angle (B1) and field (B0) maps were measured by optimized AFI method [10] and IDEAL [11], respectively. 3D VFA data were acquired with FAs α=[5,10,20,30]°. Ten MT SPGR datasets were acquired (α=10°, Δ =0.8, 2.5,5,9,13 kHz, α_{MT}=[500,1100]°, 18ms Fermi pulse). Additional dataset without saturation was acquired at offset frequency 200kHz to normalize MT data for the original CRI approach. All data were acquired with TR/TE=40/2.0ms, 240×180×80mm FOV, 128×96×40 matrix. The standard CRI processing workflow was implemented according to [4,9]. In modified CRI, all parametric maps were generated by fitting the SPGR and MT data simultaneously to the general signal equation based on the two-pool matrix steady-state MT model [2,4] using in-house-written C and MATLAB (MathWorks, Natick, MA) software utilizing a trust-region-reflective algorithm for nonlinear least squares fitting of each voxel.

RESULTS: Synthetic MT and SPGR data for white matter (WM) and gray matter (GM) ROIs were generated based on the parameters given in [9]. Table 1 shows that on-resonance MT effect introduces significant bias to all quantitative MT parameters except T_2^B when estimated with original CRI method. The dominant cause of errors was found to originate from effective shortening of T1 in the two-pool system due to bi-exponential relaxation, whereas saturation of the bound pool by the excitation pulse produced an almost negligible effect (~1%). Qualitative (Table 2) and quantitative in vivo comparisons (Fig. 1) of original and modified CRI methods are consistent with simulations and demonstrate compatible effect sizes in all parameters.

DISCUSSION: We showed that errors caused by unaccounted effect of MT on VFA R1 measurements result in significant bias in estimates of CRI parameters. Generally, this bias depends on the values of the two-pool model parameters, which makes it inconsistent for different tissues types and in different pathological conditions. Approximately, this type of errors can be characterized as overestimation of *R1*, *f*, and *k*, and underestimation of T_2^F with a relative effect size on the order of *f*%. Our results show that accuracy of the original CRI approach is noticeably improved with the proposed combined data fit to the modified CRI model, which accounts for MT effects on the apparent *R1*. In brain imaging, the method also corrected VFA *R1* values by approximately 15% in WM and 6% in GM, which agrees well with the bias predicted by [8]. Finally, the modified CRI fit does not require acquisition of normalizing

CONCLUSIONS: This study demonstrates that separate treatment of VFA and MT data in the CRI method causes non-negligible systematic errors in both *R1* and cross-relaxation parameters. Our modified CRI data processing approach effectively corrects these errors and does not require any additional measurements, thus maintaining time-efficiency of the original CRI technique.

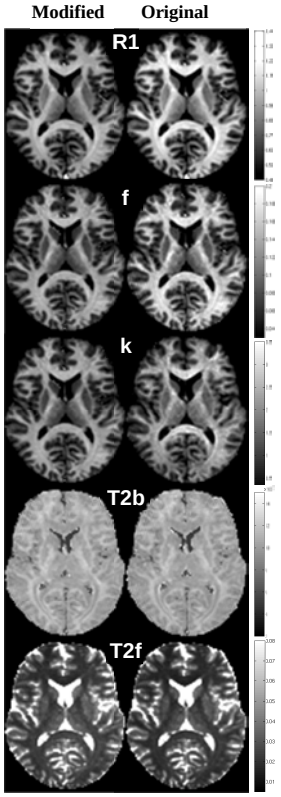

Figure 1. Parametric MT maps estimated using modified (left) and original (right) CRI.

	R1	*f*	*k*	*T2b*	*T2f*
WM (Corpus Callosum)	15.27%	11.24%	13.97%	2.76e-4%	-11.49%
GM (Putamen)	8.16%	5.65%	6.49%	2.63e-4%	-5.64%

Table 1. Errors in two-pool MT model parameters in original CRI fit due to unaccounted on-resonance MT effects (simulations).

	Modified CRI					Original CRI				
	R1 (s^{-1})	*f* (%)	*k* (s^{-1})	*T2b* (μs)	*T2f* (ms)	*R1* (s^{-1})	*f* (%)	*k* (s^{-1})	*T2b* (μs)	*T2f* (ms)
WM (Corpus Callosum)	0.977±0.032	14.00±0.46	2.635±0.218	10.31±0.32	25.06±2.23	1.104±0.038	16.62±0.78	2.815±0.242	10.15±0.32	21.77±1.95
GM (Putamen)	0.726±0.039	7.21±0.39	1.359±0.094	10.40±0.31	33.06±2.89	0.774±0.044	8.12±0.49	1.363±0.098	10.24±0.30	30.95±2.70

Table 2. In vivo measurements of CRI parameters using modified and original CRI.

REFERENCES: [1] Sled JG. et al. MRM 2001; 46. [2] Yarnykh VL. MRM 2002; 47:929. [3] Tozer D. et al. MRM 2003; 50. [4] Yarnykh VL. et al. Neuroimage 2004; 23:409. [5] Underhill HR. et al. NeuroImage 2011; 54:2052. [6] Samsonov A et al. ISMRM 2010, 4876. [7] Bieri O. et al. MRM 2006; 56:1067. [8] Ou X. et al. MRM 2008; 59:835. [9] Underhill HR. et al. NeuroImage 2009; 47:1568. [10] Yarnykh VL. MRM 2007; 57:192. [11] Reeder SB. et al. MRM 2005; 52.

ACKNOWLEDGEMENTS: This work was supported by NIH (R01NS065034).