

## A B<sub>1</sub> Insensitive qMT Protocol

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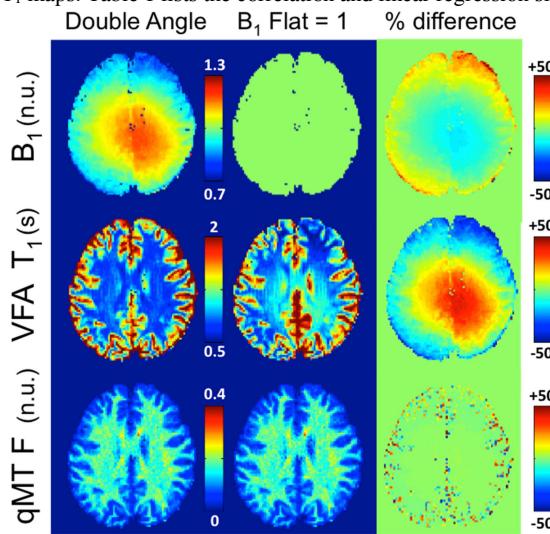
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**INTRODUCTION:** Quantitative magnetization transfer (qMT) imaging requires several additional measurements to correct for instrumental biases (B<sub>0</sub>, B<sub>1</sub>) and to constrain parameters in the fitting model (T<sub>1</sub>). These three extra measurements are typically independent of each other, but certain T<sub>1</sub> mapping techniques also require B<sub>1</sub> maps (e.g. variable flip angle – VFA<sup>1</sup>). In this case, B<sub>1</sub> is used twice before fitting the qMT parameters: to correct the flip angles for T<sub>1</sub> mapping, and to scale the nominal MT saturation powers. Inaccuracies in B<sub>1</sub> would propagate to the fitting of the qMT parameters through two pathways – through errors induced in T<sub>1</sub>, and errors in MT saturation powers. This work demonstrates that for the Sled and Pike qMT model<sup>2</sup>, certain qMT parameters (F – pool ratio, and T<sub>2r</sub>) are insensitive to a large range of B<sub>1</sub> inaccuracies when using VFA for T<sub>1</sub> mapping.

**METHODS:** Three healthy adults were scanned with a 3T Siemens Tim Trio MRI using a 32-channel receive-only head coil. Single slices (2x2x5 mm<sup>3</sup>) were acquired parallel to the AC-PC line, superior to the corpus callosum. Whole-brain T<sub>1w</sub> MPRAGE images (1x1x1 mm<sup>3</sup>) were acquired for image registration and skull stripping. **T<sub>1</sub> maps:** VFA T<sub>1</sub> maps were acquired using an optimally spoiled<sup>3</sup> 3D gradient echo sequence (TE/TR 2.89/15 ms,  $\alpha = 3^\circ/20^\circ$ , A<sub>G</sub> = 280 mT•ms/m,  $\varphi = 169^\circ$ ), and the flip angles were scaled voxel-wise with each B<sub>1</sub> map prior to fitting for T<sub>1</sub>. Inversion recovery (IR) T<sub>1</sub> data was collected from a four inversion time spin echo sequence (TE/TR = 11/1550 ms, TI = 30, 530, 1030, 1530 ms), using an open source robust inversion recovery fitting methodology<sup>4,5</sup>. **qMT maps:** MT data was acquired using the spoiled gradient echo two-TR (25/60 ms) optimal 10-point protocol for 3T using Gaussian-Hanning MT pulses (the full protocol including the 10 off-resonance frequency and MT saturation power pairs can be found in Levesque et al 2011<sup>6</sup>). qMT parameter maps were fitted using the Sled and Pike model<sup>2</sup>. B<sub>0</sub> was mapped using a two-point phase-difference gradient echo method (TE1/TE2/TR = 4/8.48/25 ms). **B<sub>1</sub> maps:** A double angle (DA) B<sub>1</sub> map was acquired using a turbo spin echo readout (TE/TR12/1550 ms,  $\alpha = 60^\circ/120^\circ$ ). To simulate a wide range of B<sub>1</sub> inaccuracies, flat (homogenous) B<sub>1</sub> maps were simulated for a range of values (B<sub>1</sub> Flat = 0.5, 0.75, 0.9, 1, 1.1, 1.25, 1.5, 2 n.u.). VFA T<sub>1</sub> maps and corrected MT saturation powers were then calculated from these flat B<sub>1</sub> maps to provide a wide range of inaccurate T<sub>1</sub> and MT saturation powers. Note that VFA T<sub>1</sub> calculated with a flat B<sub>1</sub> factor of 1 is equivalent to fitting VFA T<sub>1</sub> maps using the nominal flip angles.

qMT maps were fitted with combinations of B<sub>1</sub> maps using DA and flat B<sub>1</sub>, as well as IR T<sub>1</sub> maps and VFA T<sub>1</sub> maps corrected with the corresponding B<sub>1</sub> maps. Voxel data from all subjects were pooled for each qMT/T1/B<sub>1</sub> sets, and linear regressions and correlations were calculated between qMT/T1/(B<sub>1</sub>=DA) and qMT/T1/(B<sub>1</sub> Flat) for all B<sub>1</sub> flat maps and both T<sub>1</sub> methods.

**RESULTS:** Figure 1 shows a comparison between B<sub>1</sub> maps (measured DA and simulated B<sub>1</sub> flat = 1, the latter being equivalent to assuming true nominal angles) for a single subject; VFA T<sub>1</sub> maps calculated using each B<sub>1</sub> map; and fitted qMT F maps. Figure 2 shows the pooled whole brain Pearson correlation coefficients (a) and linear regression slopes (b) for qMT F values between the measured DA B<sub>1</sub> maps and simulated flat B<sub>1</sub> maps, for VFA (blue) and IR (red) T<sub>1</sub> maps. Table 1 lists the correlation and linear regression slope for all fitted qMT parameters and both T<sub>1</sub> methods (VFA, IR) between DA and B<sub>1</sub> flat = 1.



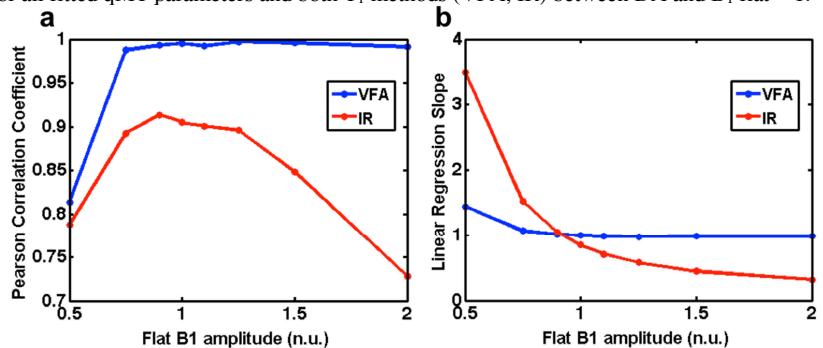
**Figure 1:** A single subject comparison of qMT F maps fitted using DA and flat (B<sub>1</sub> = 1) B<sub>1</sub> maps and VFA T<sub>1</sub> maps corrected using the corresponding B<sub>1</sub> map.

**DISCUSSION:** As can be observed from Fig. 1, processing qMT F maps using a flat B<sub>1</sub> map (nominal flip angle assumption, large B<sub>1</sub> inaccuracies) and the corresponding VFA T<sub>1</sub> map results in nearly identical qMT F maps using DA B<sub>1</sub> maps, except for cortical regions where partial volume with CSF is present due to the voxel size (2x2x5 mm<sup>3</sup>). Severe overestimation of B<sub>1</sub> is better tolerated than severe underestimation for the qMT parameter F (Fig. 2). As expected, inaccurate B<sub>1</sub> values lead to severe qMT parameters errors when IR T<sub>1</sub> maps are used (Fig. 2 and Table 1). Poor correlation in R<sub>1f</sub> values for VFA, and strong correlations for IR R<sub>1f</sub> (Table 1), can be easily explained because the measured T<sub>1</sub> is used to constrain the fitted R<sub>1f</sub><sup>2</sup>.

The exact origin of the erroneous B<sub>1</sub> and VFA T<sub>1</sub> nearly cancelling out in qMT F maps remains to be clarified, and simulations may provide a better understanding this insensitivity. It may be possible that k<sub>f</sub>, which has the lowest correlation (Table 1 - VFA), is absorbing some errors instead of F during the fitting procedure, when the effects of inaccurate B<sub>1</sub> and T<sub>1</sub> compensate each other. F has been observed to be the best qMT correlate with myelin content using histology<sup>7</sup>, and some qMT methods have recently been developed to fix most qMT parameters except F to reduce the number of acquisitions<sup>8</sup>. A likely source of the insensitivity of F and T<sub>2r</sub> to B<sub>1</sub> may also be that the measured MT signal is inversely proportional to the MT saturation powers, while measured MT signal is proportional to T<sub>1</sub>, and it can be seen from Figure 1 that B<sub>1</sub> and VFA T<sub>1</sub> are inversely proportional. qMT protocols with different TRs or parameter constrained methods<sup>8</sup> may be more sensitive to B<sub>1</sub> inaccuracies than the protocol presented in this work.

**CONCLUSION:** We have demonstrated that qMT F maps fitted using VFA T<sub>1</sub> can be insensitive to B<sub>1</sub> inaccuracies. Thus, faster and lower resolution B<sub>1</sub> maps can be used without sacrificing qMT F accuracy or precision when VFA T<sub>1</sub> maps are used. More work in simulating the effects of B<sub>1</sub> and VFA T<sub>1</sub> inaccuracies on qMT parameter estimation is needed to have a clearer understanding of the limitations of this observation.

**REFERENCES:** [1] Deoni S. et al, MRM 49:515-526 (2003) [2] Sled J. and Pike G. B., MRM 46:923-931 (2001) [3] Yarnykh V., MRM 63:1610-26 (2010) [4] Barral J. et al, MRM 64:1057-1067 (2010) [5] <http://www-mrsrl.stanford.edu/jbarral/t1map.html> (Accessed: October 2012) [6] Levesque I. et al, MRM 66:635-643 (2011) [7] Schmierer K. et al, JMRI 26:41-51 (2007) [8] Yarnykh V., MRM 68:166-178 (2012)



**Figure 2:** Pooled (all subjects) whole brain Pearson correlation coefficients (a) and linear regression slopes (b) for qMT F values between the measured DA B<sub>1</sub> maps and simulated flat B<sub>1</sub> maps.

		F	k <sub>f</sub>	R <sub>1f</sub>	T <sub>2r</sub>	T <sub>2f</sub>
DA B <sub>1</sub> , VFA T <sub>1</sub> vs Flat B <sub>1</sub> = 1, VFA T <sub>1</sub>	Pearson $\rho$	<b>0.99</b>	0.32	0.81	<b>0.99</b>	0.92
	Slope	<b>0.99</b>	0.31	0.98	<b>0.95</b>	0.90
DA B <sub>1</sub> , IR T <sub>1</sub> vs Flat B <sub>1</sub> = 1, IR T <sub>1</sub>	Pearson $\rho$	0.90	0.36	0.99	0.96	0.90
	Slope	0.84	0.37	0.97	1.16	0.89

**Table 1:** Pooled (all subjects) whole brain Pearson correlation coefficients and linear regression slopes for qMT F values between the measured DA B<sub>1</sub> maps and simulated flat B<sub>1</sub> maps.