**INTRODUCTION:** B1 mapping is an important measurement used in quantitative magnetization transfer (qMT) imaging, particularly at high field strengths (≥ 3.0 T) where B1 can vary by ± 30% in a human brain (Fig. 1). For pulsed spoiled gradient echo (SPGR) qMT imaging experiments, B1 maps are used as a corrective factor for the excitation flip angle (~5° to 15°) and MT saturation power (flip angles ~150° to 700°). Additional measurements necessary for qMT (e.g. T1 mapping) may also require B1 maps as a corrective factor; variable flip angle (VFA) T1 mapping requires B1 maps, while inversion recovery (IR) or Look-Locker typically do not1. Thus, local (e.g. artifacts) or global (e.g. systemic biases) inaccuracies in B1 mapping2 will propagate to the fitted qMT parameters differently, depending on the chosen T1 mapping method.

We recently reported that the qMT pool-size ratio (F), an important myelin biomarker, is insensitive to a large range of B1 inaccuracies when using VFA for T1 mapping3 (Fig. 1). Here we present a simulation-based analysis of the B1 sensitivity of qMT, comparing how different T1 mapping methods (VFA vs. IR) propagate the B1 error to the qMT parameters. We show that the F parameter is very robust and insensitive to B1 inaccuracies when VFA T1 mapping is used, but this comes at the expense of a substantial increase in error of kf.

**METHODS:** The Bloch-McConnell equations for magnetization exchange were solved using MATLAB (MATLAB2011a, The Mathworks Inc.) for a pulsed SPGR experiment by decomposing the pulse sequence into periods of instantaneous saturation of the free pool, constant irradiation of the restricted pool, and free precession4.Healthy white matter tissue parameters were fixed to the following values: F = 0.122, kf = 3.97 s-1, R1f = 1.11 s-1, R1r = 1.0 s-1, T2f = 27.2 ms, T2r = 10.96 μs.The MT signal was simulated from the solution of the Bloch-McConnell equation for the following MT protocol: TR = 25 ms, αexcitation = 7°, Gaussian-Hanning MT pulses with a pulse duration of 10.2 ms, αMT = 142° and 426°, logarithmically spaced off-resonance frequencies = 423.9 Hz, 1,087.5 Hz, 2,731.6 Hz, 6,861.6 Hz, and 17,235.4 Hz. The MT signal was subsequently fitted using the Sled and Pike method5 for a linear range of 100 B1 and 100 T1 values (10,000 points in total); T1 varied independently of B1 for this step, and without any assumptions on the measurement method. B1 ranged from 0.5 to 2 (B1,true = 1), and T1 ranged from 0.1 s to 4 s (T1,true = 0.9 s). VFA signals were also simulated from the analytical SPGR equation1: TR =25 ms, α = 3° and 20°, T1 = T1,true. T1 values were fitted from the VFA data for the B1 error range. The fitted T1 values were subsequently used in conjunction with their respective B1 values to fit the MT signal.

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| **Figure 2.**  Percent error in fitted qMT F values in the presence of a wide range of B1 and T1 errors (B1,true = 1 n.u., T1,true = 0.9 s). The superimposed lines plot the T1 distribution for a B1-independent T1 mapping method (IR, solid line) and VFA (dashed line). | **Figure 3.** Percent error in fitted qMT parameters for a range of B1 errors (**a** – pool size ratio (F), **b** – magnetization exchange rate (kf), **c** – free pool T2 (T2f), **d** – restricted pool T2 (T2r)). Fits using a B1-independent T1 measure (IR) are shown in red, and those using VFA T1 mapping are shown in blue. See solid and dashed lines in Fig. 2 for B1 dependence of IR and VFA T1. |

**RESULTS:** Figure 2 shows the error (%) of the fitted qMT pool-size ratio, F, in the presence of a wide range of B1 and T1 inaccuracies (B1,true = 1, T1,true = 0.9 s). The superimposed lines show the range of errors expected from an experiment using a B1 independent T1 method like IR (solid line), and from VFA T1 mapping (dashed line). Figure 3 plots the errors in qMT fitted parameters (F, kf, T2f, T2r) using B1-independent (IR) and VFA measured T1 (see lines in Fig. 2), for a range of B1 inaccuracies typically observed in vivo. Errors in F induced by B1 errors were greatly reduced using VFA T1 mapping (Fig. 3a). A substantial increase in errors in kf occurs for VFA relative to IR (Fig. 3b), while T2r remains insensitive to B1 inaccuracies for both cases.

**DISCUSSION:** The qMT pool size ratio F was shown to be nearly B1-errorinsensitive when using VFA T1 mapping (Fig. 3a - blue). Using a B1-independent T1 measure such as IR produces large qMT F errors (from >100% to -45% for B1 errors ranging from -30% to 30%, Fig 3a - red), while VFA T1 mapping kept qMT F errors within a moderate range (7% to -3%, Fig. 3a - blue). The B1 errors for the case of VFA were mostly absorbed by the kf parameters (Fig. 3b), in agreement with observations from previous in vivo work3. These results suggest that qMT imaging using B1-independent T1 measurement, and qMT methods that fixes qMT model parameters, may have increased sensitivity to B1-inaccuracies. However, for applications where kf may be the biomarker of interest (e.g. cartilage imaging6, systemic inflammation7), a B1-independent measure of T1 may be preferred instead of the VFA method. Further analytical sensitivity analysis of the qMT equations for different qMT measurement protocols could help determine optimal qMT protocols for reduced B1-inaccuracy sensitivity.

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