Biexponential T_1 Relaxation at 7T: Characterization and Impact on T_1 Mapping

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Target Audience: Researchers and clinicians interested in quantitative T_1 mapping that is independent of scan parameters and models signal behavior more reliably.

Purpose: Quantitative T_1 maps can provide insight into disease processes or early markers of pathology. In white matter, there is significant variability among reported T_1 values, especially at high field, making it difficult to establish a baseline for healthy populations. Some of this variation arises from differences between sequences[1], but there can be disagreement between T_1 values obtained even with the same sequence[2,3]. We hypothesized that a major source of variation arises from biexponential T_1 relaxation related to magnetization transfer. MT effects are well established[4] but their impact on T_1 mapping is not widely recognized, and the increase of this influence at ultra-high field has not been reported. Here we characterize this biexponential behavior at 7T, show evidence that it can introduce a dependence on scan parameters into the T_1 estimate, and provide recommendations for reducing the influence of this effect on methods such as inversion recovery fast spin echo (IR-FSE),

Theory: In the presence of two-pool exchange, the apparent T_1 relaxation of water magnetization (normalized to its thermal equilibrium value) is a biexponential function of the inversion time TI[4]:

$$M_Z(TI) = 1 - w_S \exp(-TI/T_{1S}) - w_L \exp(-TI/T_{1L}) \quad [1]$$

Here T_{1S} and T_{1L} denote the short and long T_1 components respectively, and $w_{S,L}$ are their relative weights. However, most T_1 mapping analysis assumes single exponential relaxation, of the general form

$$M_Z = c_1 - c_2 \exp(-TI/T_1^*) \quad [2]$$

with complex coefficients to account for finite TR and imperfect RF pulses[5]. Attempts to fit this model to data described by [1] will result in an apparent relaxation time T_1^* that is a mixture of the two components and that depends on $T_{1S,L}$, $w_{S,L}$ and the chosen TI values. If all TIs are long enough that the short component is fully relaxed, it will be subsumed into c_1, and $T_1^* = T_{1L}$, i.e. T_1^* will estimate the long component T_{1L}, free of any bias toward T_{1S}. However, this will also increase variance, so a careful selection of minimum TI is necessary.

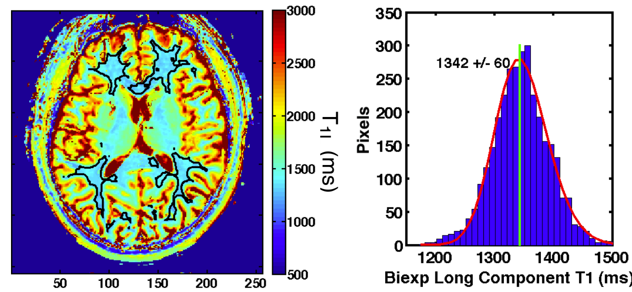

Figure 1. (a) Map of biexponential long T_1 component in one volunteer at 7T, with white matter ROI outlined in black. (b) Histogram of T_{1L} throughout the ROI, with Gaussian fit (red) used to report mean (green line) and standard deviation.

Methods: Images were obtained using a GE Discovery MR950 7T scanner (GE Healthcare, Waukesha, WI) with a Nova 2chTx / 32chRx head coil (Nova Medical, Wilmington, MA). Four volunteers (3M, 31+/-1 years) were scanned after informed consent was obtained. Relaxation was characterized using a 1.5mm thick 2D IR-FSE slice, centered on the thalamus and basal ganglia. This slice was acquired with 13 inversion times (TI=10, 20, 35, 55, 85, 125, 200, 350, 600, 1000, 1600, 2500, 4000 ms), using 128x128 matrix, 19.2cm FOV, ETL=8, TR=6s, scan time 1:42 per TI.

For each volunteer, a region-of-interest (ROI) was defined that included most of the cortical white matter (Fig.1a). At each pixel in this ROI, the biexponential relaxation times $T_{1S,L}$ and weights $w_{S,L}$ were determined by a non-linear least-squares fit of [1], and the apparent single-exponential T_1^* was determined by a reduced-dimension non-linear least-squares fit[5] of [2]. Parameter values are reported as the mean (+/- st.dev.) of a Gaussian fit to the histogram of that parameter within the ROI (Fig.1b). The percent difference was calculated as ($T_1^*/T_{1L} - 1$) using the mean T_1 values.

Based on these results, simulations were performed in Matlab 2013a (The Mathworks, Natick, MA) in which a biexponential recovery was fitted with a single-exponential model using various minimum TI (10-600ms) and four geometrically-spaced inversion times to determine the extent of bias toward the short T_1 component. 5000 repetitions were performed at each combination with 2% noise added to assess variance.

	T_{1L} (ms)	T_{1S} (ms)	wS	T_1^* (ms)	%diff
#1	1342 (60)	53 (12)	11% (2)	1161 (60)	-13%
#2	1347 (64)	51 (19)	10% (2)	1173 (39)	-13%
#3	1331 (77)	61 (12)	11% (2)	1106 (95)	-17%
#4	1374 (46)	64 (14)	12 %(2)	1162 (38)	-18%
Avg	1349 (18)	57 (6)	11% (1)	1151 (30)	-15% (3)

Table 1. Relaxation parameters measured in 4 volunteers at 7T (mean over ROI or across volunteers with standard deviation in brackets).

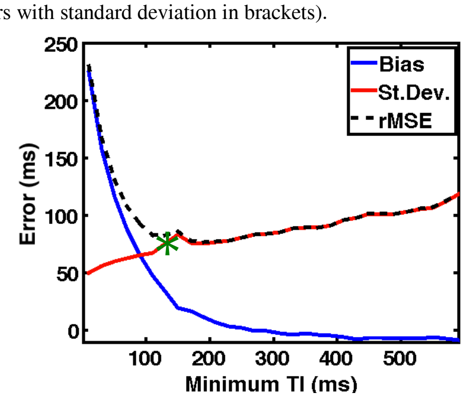

Figure 2. Bias (blue), standard deviation (red) and RMS error (black) as a function of minimum TI. RMSE is minimized at TI=150ms (asterisk).

Results and Discussion: Fits to IR-FSE data show evidence of biexponential behavior in all volunteers, with long and short components having relaxation times of 1349ms and 57ms respectively (Table 1). These values are consistent with reports from quantitative MT experiments[6], as is the short component weight of 11%. The apparent T_1^* with TI_{min}=10ms, 1151ms, underestimates T_{1L} by an average of 15% or 200ms. This value of T_1^* is consistent with simulations, and is also consistent with several literature values of white matter T_1 at 7T[2,7].

Based on simulations, as shown in Figure 2, the root mean square error, sqrt(bias^2 + variance) at 2% noise is minimized at TI=150ms. This represents an optimal trade-off between reduced bias and increased variance; if desired, TI can be increased to 200ms to reduce bias below ~10ms at the cost of slightly increased variance.

While T_{1L} alone is not necessarily an ideal indicator of changes in physiology (which might have a larger impact on T_{1S} or w_S), our analysis indicates that T_1^* is not a reliable estimate of either T_{1S} or T_{1L}, and will depend sensitively on the chosen minimum TI, which is not standardized in the literature. T_{1L} provides a measurement that is reproducible across sites, and a basis for further investigation into efficient measurement of T_{1S}.

Conclusions: The impact of MT-associated biexponential relaxation on T_1 mapping is significant at high field, introducing bias of up to 15% depending on the chosen inversion times. For IR-FSE and similar sequences, careful selection of minimum TI can reduce or remove this bias without introducing much additional variance.

References: [1] Stikov, *MRM* 2014;10.1002/mrm.25135 [2] Wright, *Proc ISMRM* 14 #921 (2006). [3] Dieringer, *PLOS ONE* 2014;9(3) e91318. [4] Henkelman, *MRM* 1993;29:759-766. [5] Barral, *MRM* 2010;**64**:1057-1067. [6] Dortch, *NeuroImage* 2013;64:640–649 [7] Wright, *Magn Reson Mater Phy* 2008;21:121-130.

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