Validation of T_1 Mapping Techniques: Are Phantom Studies Sufficient?

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INTRODUCTION: T_1 mapping is critical for most quantitative MRI [1], yet there is a large variation of reported T_1 values *in vivo*, an inconsistency that highlights the issues of reproducibility and accuracy. Literature values of T_1 in white matter (WM) at 3T vary from 690ms to 1150ms, a variation much greater than the reported biological range [2-8]. In this work we compare two of the most commonly used T_1 mapping methods, Look-Locker (LL) [9, 10] and Variable Flip Angle (VFA) [11, 12], against the gold standard for T_1 mapping (Inversion Recovery, IR). While there is reasonable agreement between the different methods in phantoms, such an agreement is not found *in vivo*.

METHODS: The IR T_1 maps were acquired at 3T (Siemens Trio, 32-channel receive-only head coil, 2x2x5mm^3) with four IR spin-echo scans (TI = 30, 530, 1030, 1530ms, and TE/TR = 11ms/1550ms) in accordance with [13]. The Look-Locker (LL) scans [14] were acquired with the same inversion times using a four-shot sequence (TE/TR = 12ms/1550ms) employing a non-selective composite inversion pulse. VFA data were acquired with a 3D spoiled gradient echo sequence (TE/TR = 3.5ms/15ms, α = 3°, 10°, 20°, 30°), using optimal spoiling [15] and analyzed using 2pt/4pt linear/nonlinear fitting with and without B_1 correction. The VFA slice was picked to match the single-slice IR and LL scans. The LL and VFA protocols employed the same B_1 measurement using a double-angle method with a non-selective preparation pulse (α = 33° and 66°) followed by a fast spin-echo readout (ETL=7) [14]. We first computed the IR, LL, and VFA T_1 maps at 3T of two aqueous $MnCl_2$/NaCl phantoms (111/65µM $MnCl_2$ + 85.5mM NaCl) whose T_1 and T_2 values were matched to human grey and white matter. We then applied the same protocol to 10 healthy subjects (5 male, 5 female, age range 22-32). CSF was masked out. We computed the individual T_1 histograms, and the pooled T_1 histogram summed over 10 subjects, clipping the values at 1300ms and labeling the WM peaks in the brain to facilitate comparisons. In the brain, we report the VFA values obtained with B_1-corrected 4pt nonlinear fits, as they are closest to the IR values.

RESULTS: Fig. 1 shows example T_1 maps of a single slice through phantoms and a brain acquired using IR, LL, and VFA. Fig. 2 shows that, depending on the method used, the measured T_1 peaks varied from 807ms to 863ms in the WM phantom, and from 724ms to 906ms in a single subject. The variation across 10 subjects is even greater, and while the pooled histograms are broader, there are still distinct WM peaks at 735ms (LL), 825ms (IR) and 1037ms (VFA).

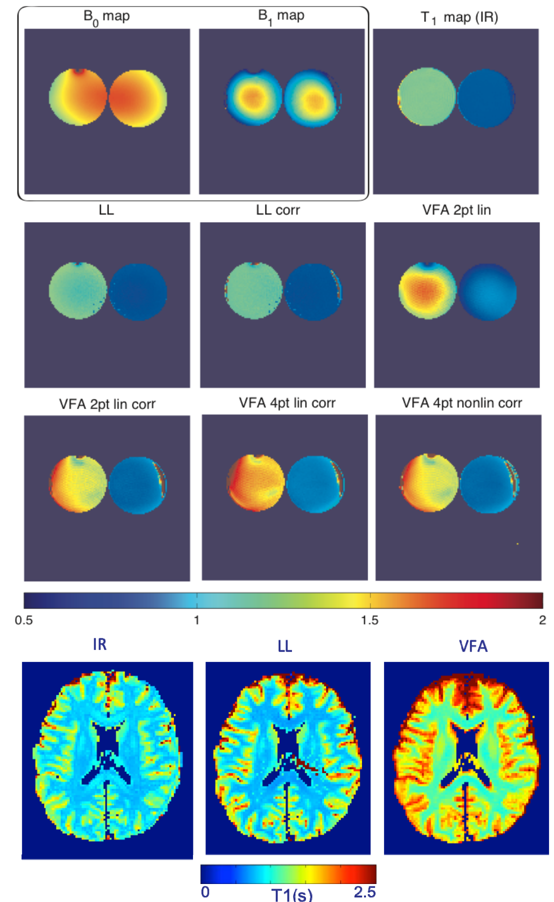

***Figure 1:** Single slice T_1 maps (IR, LL, VFA) in phantoms (top) and in a single subject (bottom).*

DISCUSSION: The histograms in Fig. 2 show that the WM peak *in vivo* varies considerably more than in phantoms, and the pooled histogram shows that the sequence-dependent bias is greater than the intersubject variability. The observed variations follow a similar trend as the values reported in literature, with LL underestimating the T_1 values in WM, and VFA overestimating them [2-8]. This discrepancy cannot be explained by differences in the imaging parameters, because they were kept constant, and the same B_1 map was used for the LL and the VFA protocol. We have accounted for overestimation due to incomplete spoiling [15], and accounting for magnetization transfer effects in VFA would only further overestimate the WM peak [16]. It is possible that there is a difference in the flip angle calibration for different media [17], even though the phantoms were matched for brain tissue conductivity. Further study is needed to understand this discrepancy, but in the meantime we have shown that phantom validation of T_1 mapping does not necessarily hold *in vivo*.

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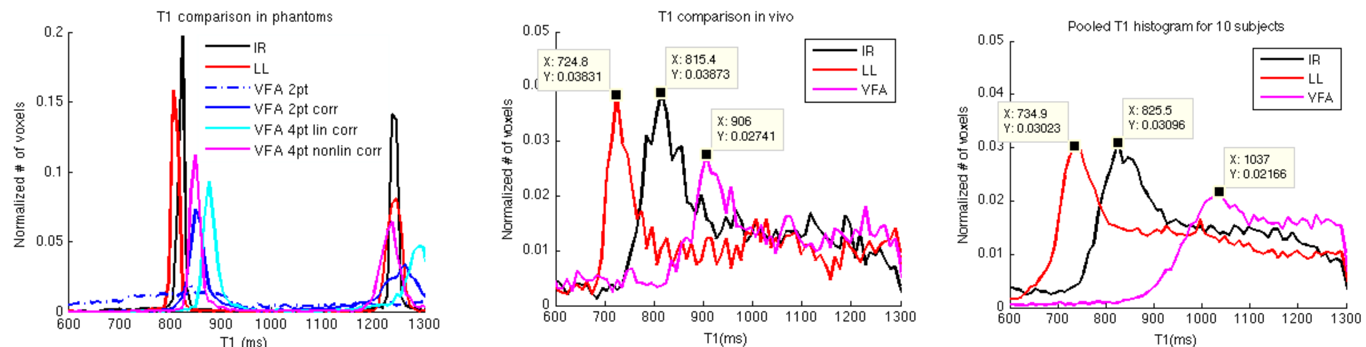

***Figure 2:** Histograms of T_1 maps computed using IR, LL and VFA in (a) WM/GM phantoms, (b) single subject (c) pooled over 10 subjects. The labels mark the WM peaks.*