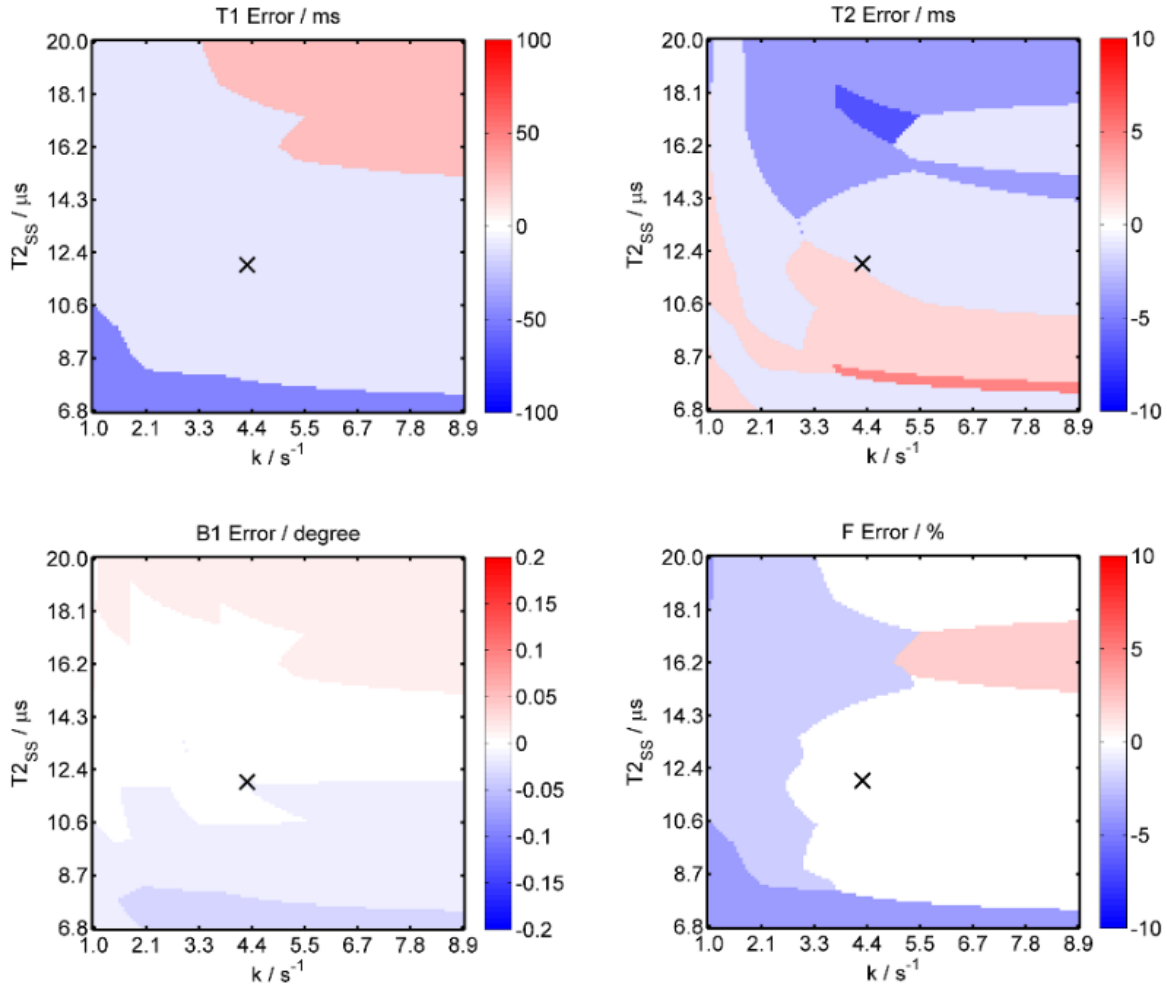
Supporting Information Figure S1

Introduction: In the main manuscript, two parameters that govern magnetization transfer ($T_{2,SS}$ and k) were held constant in the EPG-X simulations to reduce the dimensionality of the dictionary ($T_{2,ss}$ = 12 µs, k = 4.3 s^{-1}). Fixing these parameters will introduce errors, since these parameters have a direct impact on the strength of the MT effect. Goal of this supporting information is to use simulations to evaluate the impact of these errors, and to determine which estimates (T_1, T_2, B_1^+, or F) are affected the most.

Methods: A synthetic dataset of fingerprints was generated for an image size of 128 x 128, where each voxel represents a different combination of $T_{2,SS}$ and k. The remaining parameters were fixed (T_1 = 800 ms, T_2 = 60 ms, B_1^+ = 1, and F = 10 %). For all simulations, the two-pool model of the IRFF-MT sequence was used. Afterwards, the dictionary with fixed parameters (same as in the in-vivo experiments) was used to estimate T_1, T_2, B_1^+, and F. The absolute error relative to the ground truth was calculated.

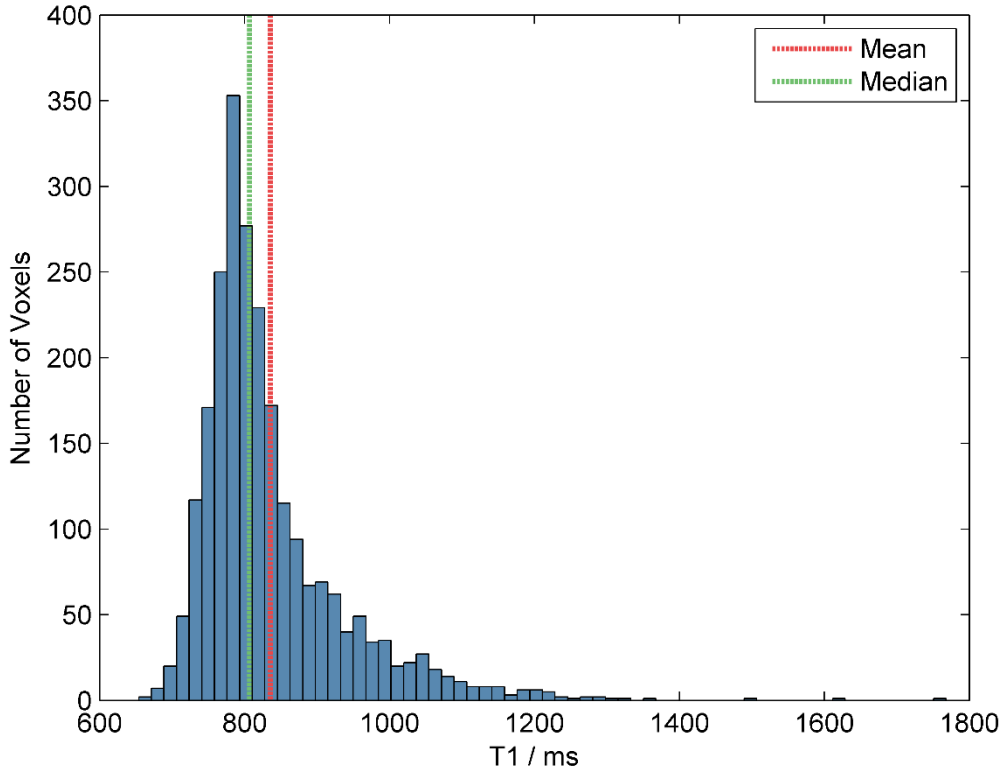
Results: The error maps are shown in the figure below. A cross indicates the location corresponding to the correct assumed parameters. The T_1 error ranges from -50 to 27 ms at the edges of the tested range where mostly the extremes of $T_{2,SS}$ result in a bias of T_1 values. On the other hand, the error in T_2 (ranging from -7 to 5 ms) is more complex and mostly depends on which dictionary entry fits best with regards to T_1, B_1^+, and F. Notably, a small error in T_1 and T_2 is observed even when the assumed values of $T_{2,SS}$ and k are correct (at the cross in the figure) because of the discrete step size in the dictionary, i.e. there is no entry that exactly matches values of T_1 = 800 ms and T_2 = 60 ms. The estimation of B_1^+ is only affected by variations in $T_{2,SS}$, resulting in errors ranging from -0.03 to 0.02 in nominal flip angle. The estimation of the fractional pool size F is relatively robust to the assumptions, with errors between -4 % and 2% with respect to the gold standard.

Discussion and Conclusion: The error caused by assuming fixed values in the dictionary results in moderate biases of all estimated parameters. The estimation error is highly interdependent between the parameters due to the discrete solution space of the dictionary. In general, within the tested range, $T_{2,SS}$ seems to have a larger impact on estimation errors in comparison to the exchange rate k. These errors should be considered when interpreting the quantitative results obtained with the proposed method.



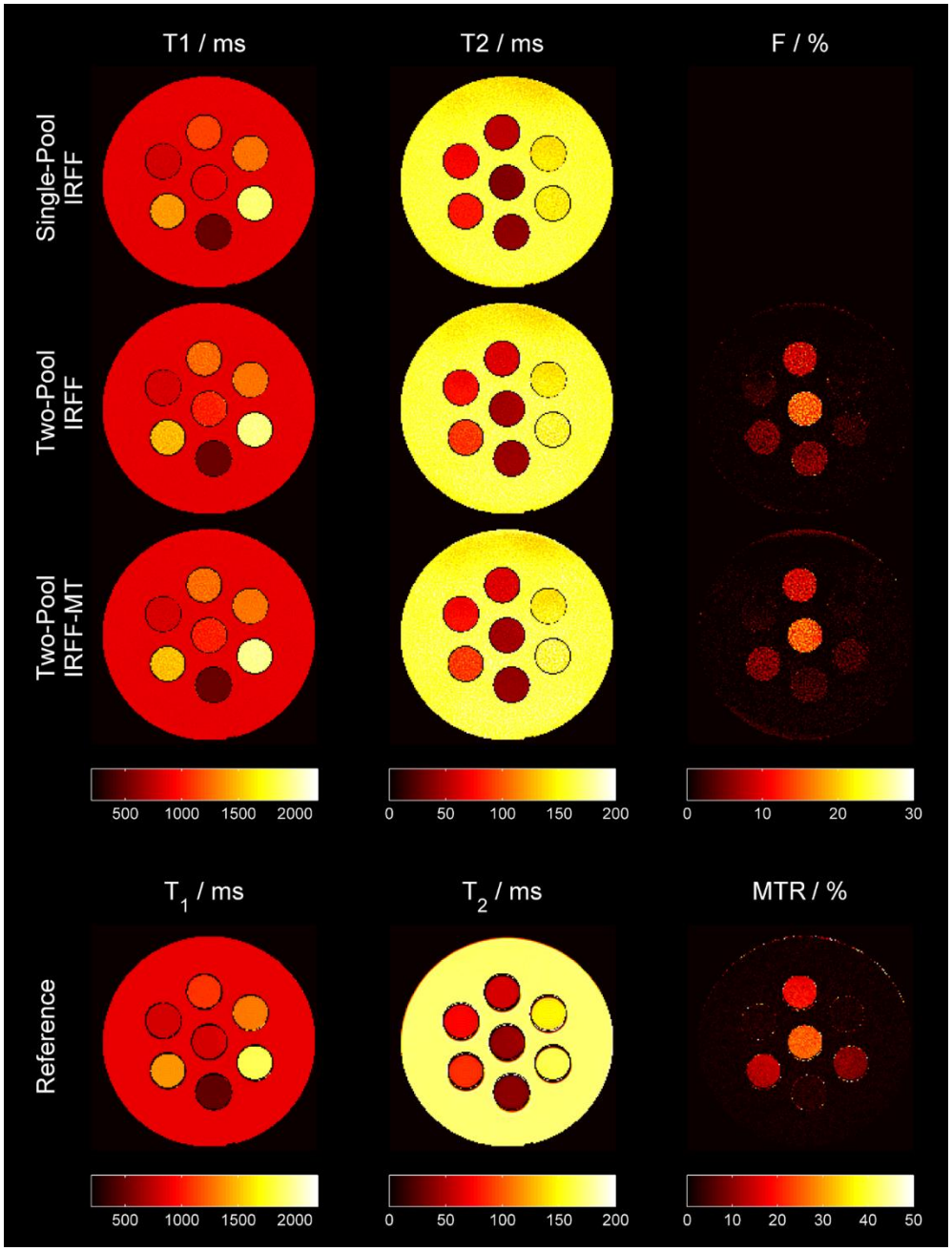
Supporting Information Figure S1: Absolute estimation errors in T1, T2, B1⁺, and fractional pool size F if the assumption of the fixed T2 of the semisolid pool ($T2_{SS}$) and exchange rate (k) is not met. The cross indicates the location where the assumption is true.

Supporting Information Figure S2



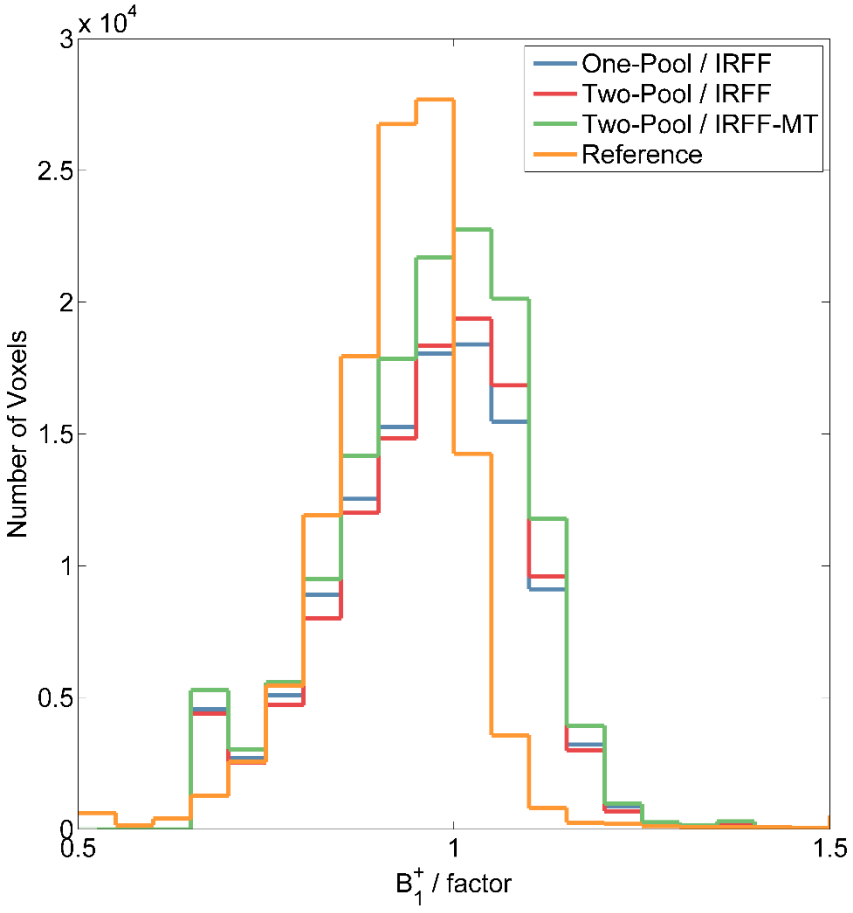
Supporting Information Figure S2: Distribution of T1 values obtained from the MP2RAGE in the frontal white matter of one example subject. The green and red lines indicate the median and mean of the distribution respectively.

Supporting Information Figure S3



Supporting Information Figure S3: Quantitative maps obtained from the phantom experiment with different compartments, which were used to compare the values of the different models/sequences to the reference values.

Supporting Information Figure S4



Supporting Information Figure S4: Histograms of B_1^+ values for the different methods from all voxels within the brain of all subjects. The MRF methods appear to agree well with each other whereas the GRE based mapping resulted in lower values.

Supporting Information Figure S5

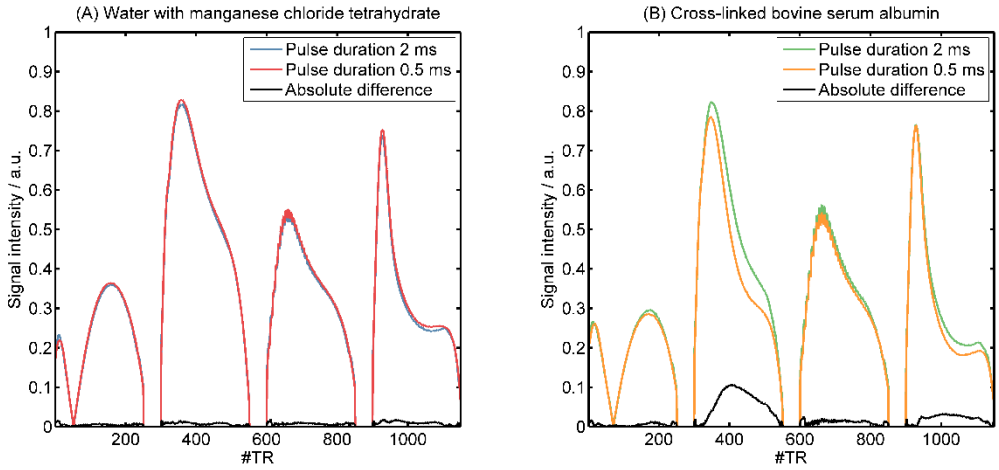
Introduction: To improve the encoding of magnetization transfer (MT) in the fingerprint, it was proposed to introduce off-resonance MT pulses in the first two gaps of the sequence. Alternatively, the MT effect can be varied by changing the applied pulse power during the acquisition of the fingerprint. This was tested in an early version of this work[1] by varying the pulse duration. In this supporting information, we provide some of the early results that demonstrated that varying the pulse power may be confounded by other effects and may not be ideal for encoding MT in the fingerprint.

Methods: The same IRRF sequence design was used to acquire MR signals from two samples (as in the main manuscript: doped water and xl-BSA). For both samples, the MR signal was acquired twice, each time with a different pulse duration (2 ms and 0.5 ms). The assumption is that the MR signals acquired with different pulse durations in the water are supposed to be identical since there is no MT expected. However, a difference in NMR signals is expected for the xl-BSA sample because the different pulse durations (and associated pulse powers) will result in different MT effects.

Results: For the xl-BSA sample, changing the pulse duration results in larger differences throughout the fingerprint but especially in segments with larger flip angles (see figure B below). The shorter pulse duration (i.e. larger pulse power) results in a lower signal intensity. However, the water sample also shows differences between MR signals with different pulse duration (see figure A below). These differences are smaller in comparison to the xl-BSA sample, but the shorter pulse duration resulted in higher signal intensities in water.

Discussion and Conclusion: The differences that were observed in the water sample may be caused by relaxation during the pulse. These effects may be confounding since they will overlap with the MT effect that the method is intended to encode. Currently, the simulation used to create the dictionary assumes an instantaneous application of the pulse. Therefore, no differences can be observed when simulating the signals with different pulse durations, although we can observe effects experimentally.

In conclusion, if it is desired to measure MT by varying pulse durations, it will also be necessary to simulate potential confounding effects such as relaxation during the pulse application.



Supporting Information Figure S5: Acquired MR signals (fingerprints) from the water and xl-BSA samples using the IRFF sequence with two different pulse durations of 2 ms and 0.5 ms.

1. Hilbert T, Kober T, Zhao T, et al. Mitigating the Effect of Magnetization Transfer in Magnetic Resonance Fingerprinting. In: *International Society for Magnetic Resonance in Medicine*. ; 2017:0074.