Whole Brain inhomogeneous MT using an ihMT prepared 3D GRE sequence at 1.5T

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Target audience: Researchers and clinicians interested in novel endogenous contrast and myelin imaging.

PURPOSE: Myelin MR imaging has become a prolific research area because of high clinical relevance of myelin-associated diseases. Inhomogeneous Magnetization Transfer (ihMT) has been proposed as a new technique able to provide specific MR signal from myelinated tissues [1,2]. It is believed that motion restriction of lipid chains within the myelin sheath prevents complete averaging of the dipolar interaction between methylene protons, hence leading to inhomogeneous line broadening. Most of previous ihMT studies have been performed in 2D with limited multi-slice capability, though 3D ihMT has been previously demonstrated at 3T [3,4]. However 3T ihMT has its own challenges, including power deposition limitation and non-uniformity of the resulting contrast [4]. Here we present an implementation of an ihMT prepared 3D gradient-echo (GRE) sequence at 1.5T and we show preliminary assessment of whole brain ihMT ratios in healthy volunteers.

METHODS: MRI: Experiments were performed at 1.5T (Avanto, Siemens, Erlangen, Germany) on two healthy volunteers using a 32-ch head coil. IhMT weighting was introduced in the GRE sequence by applying a short train of off-resonance saturation pulses within each TR. In comparison with previous work using pulse amplitude modulation [3,4], the dual-frequency saturation was achieved by alternating (±Δf) the carrier frequency of short Hann-shaped pulses. Six MT pulses were used every TR (±Δf=±7kHz, 0.5ms pulsewidth, repeated every 1ms, 3.8μT B_{1RMS} over TR, leading to ~75% of the SAR limit). IhMT and MT datasets were reconstructed by simple linear combination of 4 acquired imaging volumes (2×single- and 2×dual-frequency saturated), as described previously [1-4]. 3D GRE readout parameters were: TR/TE=19/4.8ms, FA=10°, BW=100Hz/pixel, FOV=256mm, Mx=My=128, Mz=80 for a 2mm isotropic resolution. Partial Fourier (ky and kz), asymmetric echo and ipat 2 (ky) were used to speed up acquisition and reduce intra-volume motion. For improved SNR, each volume was averaged three times, for a total acquisition time of ~12min (including one unsaturated reference volume for calculation of quantitative ratios - ihMTR and MTR). Post-processing: 3D volumes were registered automatically using the SPM8 toolbox [5] to calculate ihMTR and MTR parametric maps. A whole-brain mask was extracted from the MNI probabilistic atlas [5] to assess the distribution of MTR/ihMTR. 3D masks for cortical grey matter (GM) and white matter (WM) were extracted from T_1-w MP-RAGE data using Freesurfer segmentation [6], and were used to calculate histograms and statistics (mean ± SD). In addition, Thalami (Th), as an example of myelinated GM, as well as Corpus Callosum (CC) and the Pyramidal Tract (PT), segmented from the JHU tract atlas [7], were also considered. These two latter structures differ in the WM track orientation with respect to B_0.

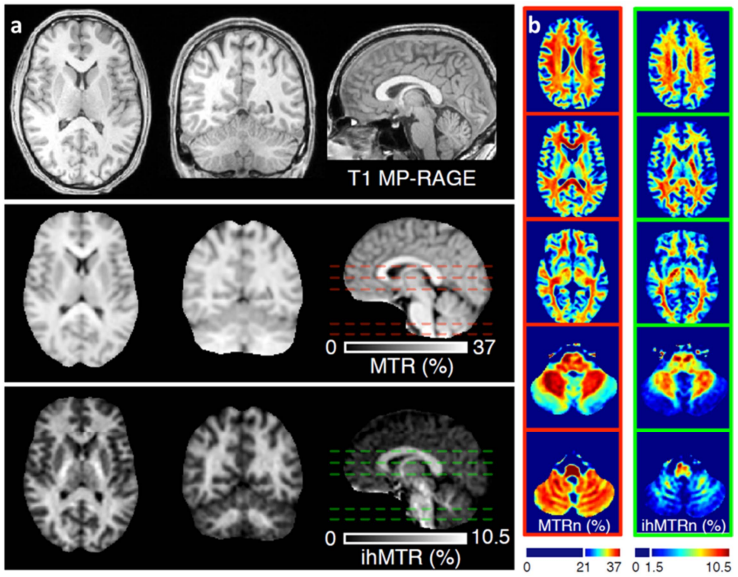

Fig.1 a) Representative 3D ihMTR, MTR and T_1w MP-RAGE datasets. **b)** Normalized ratio images for visual comparison. Display ranges were chosen according to : $min_{MT/ihMT}$=mean(GM)-SD(GM) max_{MT}=mean(CC)+SD(CC) and max_{ihMT}=mean(PT)+SD(PT) (see Table1)

RESULTS AND DISCUSSION: Thanks to higher B_{1RMS} allowed at lower field (3.8μT used here vs. 3μT at 3T [3]), the hereby measured ihMT ratios (Table 1) were higher than those previously reported at 3T using a similar 3D sequence [3], whereas MTR were in fair agreement. In addition, no sign of strong RF inhomogeneity was seen over the whole brain dataset. Fig. 1 shows several representative slices of ihMT, MT and MP-RAGE datasets. One can appreciate the exquisite WM/GM contrast provided by the ihMT technique, in comparison with conventional MT and T_1w scans in Fig. 1a. Display-normalized ihMTR and MTR maps are shown on Fig. 1b for visual comparison. Quantitative ihMT and MT measurements are displayed on Fig. 2. Interestingly, the whole brain ihMT histogram shows two well distinct modes (white curve) corresponding to GM and WM as evidenced by the Freesurfer segmentation. Such modes are more diluted in the whole brain MTR histogram, suggesting less precise tissue characterization (e.g. sensitivity to a variety of macromolecules, including myelin). Thalami gave ihMTR and MTR values in between GM and WM, consistent with mild myelination. Interestingly, CC and PT appear in reversed order in terms of their quantitative values of ihMTR and MTR (see Fig. 2 and Fig. 1b), emphasizing that conventional and inhomogeneous MT do not measure the same tissue structural properties: whereas MT is believed to be sensitive to the whole macromolecular content, ihMT would be more specific for myelin. Noteworthy, the PT (tracts ≈ aligned with B_0) yields the highest ihMTR values within the whole brain, stronger than CC (tracts ≈ ⊥ which B_0). Overall, this suggests significant effect of the WM track orientation on ihMT metrics. This latter finding warrants further study. Finally, since ihMT ratios are semi-quantitative metrics, that vary with power deposition and ihMT sequence parameters [1,2] (e.g. the dual frequency switching time), the hereby reported values and histograms may not be generalized, especially since the SAR limit was not reached during this protocol. Nevertheless they do provide great insight into the relative values across brain regions and compare well with MT data.

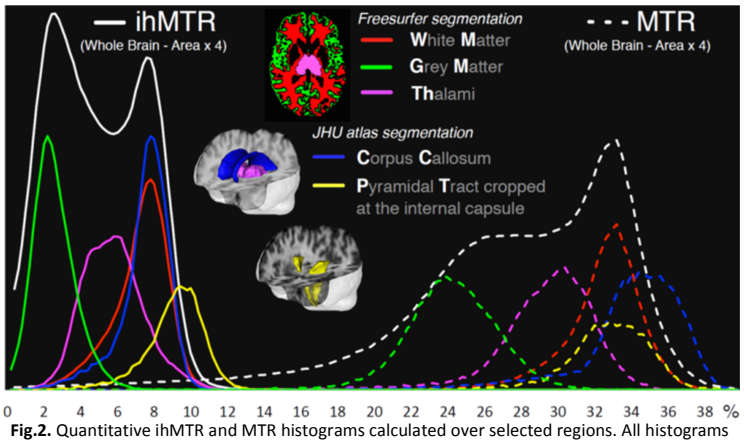

Fig.2. Quantitative ihMTR and MTR histograms calculated over selected regions. All histograms were area-normalized (arbitrary y-axis), except for whole brain (area × 4) for improved display.

Table 1	MTR (%)	ihMTR (%)
WM	32.4 ± 2.2	7.2 ± 1.5
GM	24.5 ± 3.3	2.8 ± 1.4
Th	29.3 ± 2.7	5.7 ± 1.6
CC	33.8 ± 3.3	7.5 ± 1.4
PT	32.8 ± 2.3	9.1 ± 1.6

CONCLUSION: A 3D ihMT prepared GRE sequence has been implemented at 1.5T, allowing for stronger B_1 and better RF uniformity as compared to 3T. Conversely to previous 2D implementations based on single-shot readout approach, the 3D acquisition scheme has great SNR efficiency, allowing for full brain volume coverage (2mm isotropic resolution, 80 reconstructed slices) in around 12 minutes (WM ihMT SNR ~25). Noteworthy, a conventional MT ratio map, similar to product sequences, is delivered within the same sequence at no extra cost. Here, distributions of both ihMTR and MTR across the whole brain were assessed, evidencing notable differences, and providing great insight for WM characterization. This opens new horizons for future work on WM microstructure and to study diffuse WM pathology such as Multiple Sclerosis.

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