High Resolution Magnetization Transfer Imaging at 3T VS. 1.5T

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INTRODUCTION: While most clinical studies using magnetization transfer (MT) imaging have been performed at 1.5T, high resolution-MT imaging (hr-MT) is feasible at 3T. Higher field enables efficient acquisition with improved conspicuity of brain structures (1). Hr-MT has considerable potential for investigating neurological disorders affecting small brain structures such as early stage Alzheimer's disease. Before implementing hr-MT in a patient population, it is critical to optimize scan parameters, assess the reliability and establish a quality assurance procedure at 3T. This investigation takes a two-fold approach to systematically optimize and compare scan parameters at 1.5 and 3T. First, phantom experiments optimize signal-to-noise ratio (SNR), MT ratio (MTR) and repeatability. Second, human studies evaluate acquisition parameters to study regions of clinical interest, such as the hippocampus, and support findings with simulations to maximize MTR contrast between brain tissue types.

METHOD AND MATERIALS:

Image Acquisition:
All hr-MT scans were performed on 1.5 and 3T scanners (MAGNETOM Avanto and Verio, Siemens Healthcare, Erlangen, Germany).

Phantom Scans: An agar phantom was constructed of six tubes with varying concentrations of homogeneous agar gel (0.5%, 1%, 1.5%, 2%, 2.5%, 5%) submerged in a sealed water-filled cylinder and used to optimize the hr-MT protocol using a range of flip angles (FA), voxel sizes and correction for pulsation artifacts. To assess reliability, hr-MT measurements were obtained at three different times at both 3T and 1.5T. MT parameters were: MT-1 (TR/TE/FA of 37 ms/4ms/10°; spatial saturation, 10 mm inferior to the 50 mm 3D acquisition slab); MT-2 (TR/TE/FA 30 ms/4 ms/10°); MT-3 (TR/TE/FA 30 ms/5.45 ms/5°). All scans used MT FA of 500 degrees. MT-1 and MT-2 both used a fast GRE pulse, while MT-3 used normal a GRE pulse. The spatial resolution was 1x1x1.2 mm for MT-1 and MT-2, and 1.3x1x2 mm for MT-3. MT preparation consisted of a Gaussian shape saturation pulse (with and without MT) at 1200 Hz and 1500 Hz offset from water resonance for 3T and 1.5 T, respectively.

Human Scans: Eight healthy volunteers (7 male, 1 female. Age: Mean ± SD: 37 ±17.22; range 22 to 60) were scanned twice one week apart at 3T (90 axial slices with whole brain coverage using MT-1 and MT-2). These images were compared to MT images obtained with 3D GRE human scans at 1.5T (TR/TE/FA 19 ms/4 ms/25°, spatial resolution = 1x1x1.3 mm).

Image Analysis:
MTR values were estimated using standard equations on a Linux workstation for the human brain images and phantom data were analyzed on a LEONARDO workstation (Siemens, Germany). On brain images, an operator manually placed regions of interest (ROIs) to obtain the Mean and SD of signal intensity in genu, splenium, hippocampus (R, L), caudate (R,L), putamen (R, L) and thalamus (R, L). An operator obtained MTR for different concentrations of agar gel tubes on the phantom images.

Quantitative Evaluation:
Apparent SNR was estimated for data collected at 1.5T and 3T. To simulate relative white matter / gray matter ratio, relative contrast ratio based on the mean signal intensity of the 5% ($SI_{5\%}$) and 2.5% ($SI_{2.5\%}$) was computed using the following equation: Relative contrast ratio $_{5\%/2.5\%} = (SI_{5\%} - SI_{2.5\%}) / SI_{2.5\%}$.

Statistical Analysis: Statistical methods included analysis of variance for repeated measures, independent *t*-tests, paired *t*-tests and Spearman intra-class correlation coefficients (ICC). All statistical tests were executed with SAS 9.1 by using a significance level of 0.05.

RESULTS: The apparent SNR at 3T was 1.44 ~ 3.44 fold that of 1.5T (Table 1), while maintaining similar MTR values (Figure 2) and relative contrast ratios (data not shown). MT-2 had the highest apparent SNR in the phantom study (Table 1); however, MT-2 brain images showed hippocampal pulsation artifacts. MT-1 compensated for pulsation artifacts, but apparent SNR in the phantom study was significantly lower than that of MT-2 ($p<.0001$) likely caused by image degradation from the saturation band. While MTR is negatively correlated with FA (r_s: -0.667, $p<.0001$), SNR is positively correlated with FA (r_s: 0.454, $p=0.0003$). Therefore, MT-3 offers the best balance of SNR with minimized artifacts. Figure 2 shows that repeated measurements at 3T generated similar or more consistent MTR values over time relative to 1.5T for phantom scans (Table 2). For the human scans at 3T, much higher reproducibility of MTR was obtained for MT-2 compared with MT-1 (Table 3). Excellent reproducibility of MTR in hippocampus were obtained (ICC: 0.86 ~ 0.91).

CONCLUSION: Phantom scans were effective in sequence optimization and served as the foundation for human studies and comparison across field strengths. At 3T the increased field strength significantly improved image quality, as indicated by the increase in apparent SNR compared with 1.5T. While potentially increased scan variation at higher field is a concern, this investigation suggests that 3T studies provide more consistent MTR measurement over time relative to 1.5T, overall the reproducibility were very high for both 1.5T and 3T. This study combines phantom and human data to optimize parameters and improve reliability at 3T relative to 1.5T. These findings serve as a precursor to transition for 3T clinical studies requiring high spatial resolution and repeated measurements over time. Importantly, our findings in the human study indicate excellent reproducibility in regions such as the hippocampus that are critical regions for detecting early changes in Alzheimer's disease and other neurological disorders. Our results demonstrate the promising potential of high resolution MT for clinical application.

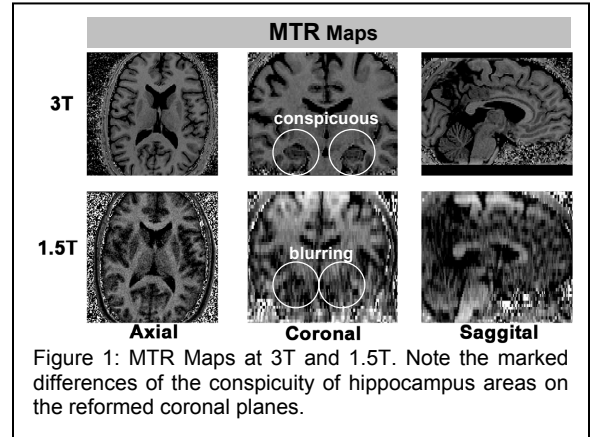**REFERENCES:** 1. Gringel et al. JRMI. 2009 Jun;29(6):1285-92.

Figure 1: MTR Maps at 3T and 1.5T. Note the marked differences of the conspicuity of hippocampus areas on the reformed coronal planes.

Table 1. Apparent SNR

	1.5T	3T	3T/1.5T
MT-1	20.03	28.90	1.44
MT0-1	19.94	32.83	1.65
MT-2	14.22	51.28	3.61
MT0-2	13.81	50.34	3.65
MT-3	8.62	29.62	3.44
MT0-3	11.72	41.13	3.51

Table 2. hr-MT Reproducibility - Human Brain

	ICC		COV (%)	
	MTR-1	MTR-2	MTR-1	MTR-2
Genu	0.0	0.8	4.1	2.0
Splen	0.1	0.6	5.7	2.4
R Hippa	0.5	0.9	9.2	2.2
R Caudate	0.0	0.9	9.1	2.1
R Putaman	0.0	0.6	11.3	3.0
R Thalamus	0.2	0.6	6.6	2.5
L Hippa	0.0	0.9	17.7	2.8
L Caudate	0.0	0.9	12.4	2.3
L Putaman	0.4	0.9	7.8	2.1
L Thalamus	0.0	0.7	10.6	2.7

Table3. hr-MT reproducibility - Phantom

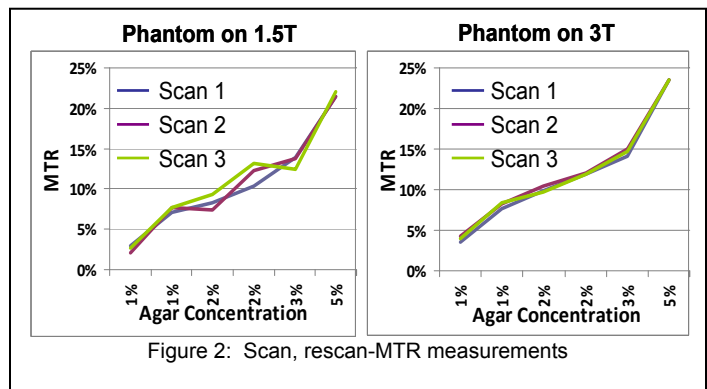|	1.5T	3T
MTR-1	0.993	0.994
MTR-2	0.982	0.999
MTR-3	0.992	0.999

Figure 2: Scan, rescan-MTR measurements