Magnetization transfer fMRI in humans at 7T

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INTRODUCTION: Recently a magnetization transfer (MT)-varied fMRI technique [1] was proposed to simultaneously measure stimulus-induced arterial CBV (CBVa) change and BOLD response. This idea is based on differential MT effect of tissue and arterial blood. MT RF pulses can significantly reduce extravascular signals by magnetization transfer from tissue macromolecule protons to tissue water protons, while intravascular (arterial and venous) signals are much less affected due to low macromolecule concentration in blood. Additionally, MT-affected arterial spins are replenished by fresh inflowing blood (enhancing signal), while venous intravascular signal is reduced by its short T_2* at high magnetic field. Thus, the MT-independent signal is considered mostly from arterial blood, while MT-dependent signal originates from tissue. In this condition, the percentage signal change is expected to increase with MT (i.e., decreased MTR) if the relative contribution of arterial blood signal increases. In previous anesthetized cat studies [2], the percentage change was increased with MT, and the CBVa change obtained from MT-varied fMRI was ~0.4% in the visual cortex during visual stimulation. However, this 9.4-T animal MT fMRI contradicts to previous 1.5-T human MT studies [3], in which MT reduced the percentage signal change (i.e., increased MTR). This discrepancy can be due to different magnetic field (9.4 T vs. 1.5 T), different spatial resolution (0.3 mm vs. 3.7 mm), different MT pulse scheme (long CW vs. one short pulse), or different species. Thus, in order to investigate the source of discrepancy, we performed MT fMRI with high spatial resolution in humans at 7 T. If MT-varied fMRI observation is similar to animal studies, then arterial blood volume change can be estimated [2].

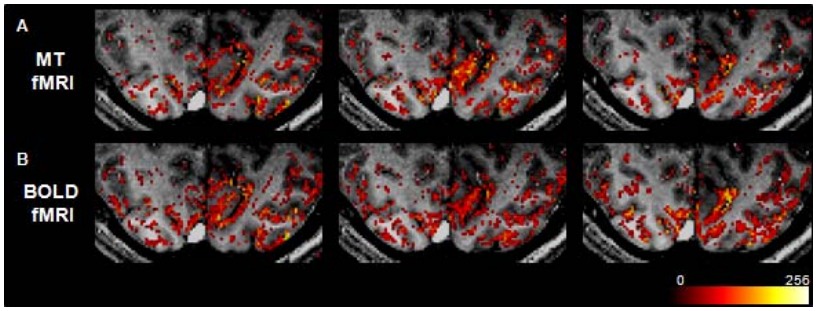
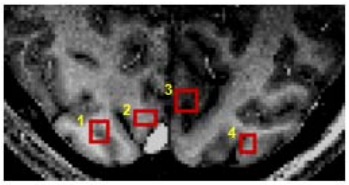


Fig.1. Results of (A) MT fMRI map compared with (B) conventional BOLD fMRI map. Zoom on the visual areas of three different slices from the SPM activation maps calculated with the high resolution data sets.



MATERIALS and METHODS:

***MRI acquisition*:** All MRI data were obtained on a 7.0T scanner (Siemens). Two-channel Tx/Rx home-built surface coil was used for enhancing inflow effects of arterial blood and for obtaining high-resolution images with high sensitivity. Since motion artifacts severely affect the results, a bite-bar system was used for some subjects to minimize head motions. Two fMRI runs with or without MT were separately performed with single-shot GE EPI (TE/TR=30/2000ms, 1.0mm isotropic resolution, 96 measurements and 10 slices). Offset frequency and power level of a MT-inducing (sinc shaped) RF pulse was optimized (within SAR limit) to be 1.5 kHz, and 400°. In order to reduce eddy current, we used sinusoidal readout gradient for EPI. ***Stimulation Scheme*:** For stimulus, we used an alternating black and white checker board pattern of 32x32 patches (8 Hz frequency). Each fMRI run had 16 blocks, in which each block consisted of 12 s cross fixation as a control and 12 s checkerboard stimulation. ***General data analysis*:** We performed data analysis using SPM8 and MarsBaR (marsbar.sourceforge.net), a graphical user interface-based fMRI analysis software package and in-house Matlab (Mathworks, Natick, MA) routines. fMRI maps in each MT level were generated from the baseline and the stimulation images. For pixels with P-values<0.05, percentage signal changes at each MT level ($\Delta S_{MT}/S_{MT}$) were calculated as the stimulus-induced signal changes divided by the baseline signals. Quantitative analysis was performed on each ROI, which was chosen in the visual cortical area, based on high-resolution T_1-weighted anatomical image.

ROI	voxels	MT value	std	CBVa	std
1	30	0.8766	0.0897	0.0784	0.5714
2	24	0.8896	0.0411	0.1638	0.3115
3	36	0.878	0.1137	0.3553	1.8136
4	20	0.9024	0.0525	0.0013	1.4359

	MT	BOLD
ROI	signal change, %	signal change, %
1	5.12	3.171
2	5.925	5.157
3	8.668	6.585
4	5.711	4.646

Fig.2. Results of quantitative ROI analysis

RESULTS and DISCUSSION: We successfully obtained high-resolution functional maps with and without MT effect at 7 T (Fig. 1). Generally both MT fMRI and BOLD fMRI show similar activation patterns, mostly in gray matter. To determine the difference between MT fMRI maps and BOLD maps, ROIs were selected in the visual cortex (Fig. 2, red ROIs). In all four ROIs, percentage change of MT fMRI with MTR value of ~0.9 was higher than the corresponding value of BOLD fMRI. Both time courses (see Fig. 3) show rapid response during stimulation and small post-stimulus undershoot. When we determined arterial blood volume changes from two fMRI data with and without MT, it ranged between negligible (ROI 4) and ~0.4% (ROI 2). The similar observations were also detected in other subjects. Our findings are similar to previous animal studies, but differ from 1.5-T human data. Differences between our 7-T and previous 1.5-T human fMRI studies may be explained by different magnetic field, and different spatial resolution, since the MT pulse used for both studies is similar. At 1.5 T, MT-less-sensitive intravascular venous blood change can contribute significantly to fMRI signals, while it will be minimal at 7 T. Since larger intravascular signal contribution will result in a higher percentage change with MT, different magnetic fields cannot explain the discrepancy. Alternatively, different spatial resolution is likely to be a main reason. High spatial resolution (1 mm isotropic resolution) minimizes the contribution of MT-insensitive cerebrospinal fluid (CSF) contribution within voxels. If voxels contain significant CSF contribution, those may not pass statistical thresholds due to low baseline sensitivity at 7T (see dark pixels between two hemispheres in Fig. 1), but not at 1.5 T. When the CSF volume fraction with a voxel is reduced during stimulation, then the percentage signal change with MT effect is reduced, which can explain 1.5-T MT data. Our value of arterial blood volume change (0-0.4%) in human is consistent with animal data obtained during visual stimulation (~0.4%), indicating that our human data is quite reasonable. In conclusion, we have demonstrated that MT fMRI can be obtained in humans at 7 T, and arterial CBV changes can be obtained *in vivo*.

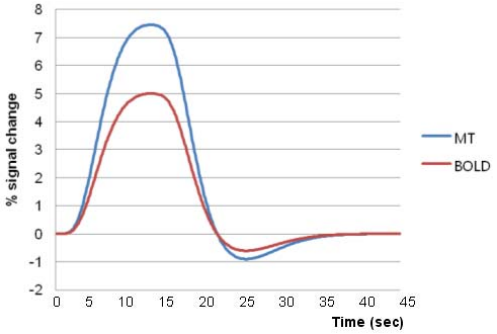


Fig.3. Results of time course analysis. (case ROI 1)

REFERENCES: [1] Ogawa et al. *Proc.Natl.Acad.Sci*,1990;87:9868-9872. [2] Kim et al. *Neuroimage*,2010;49:1340-1349 [3] Zhang et al. *MRM*,1997;38:187-192

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