Tract-based Atlas for Automatic Analysis of Magnetic Susceptibility in Human Brain White Matter

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AUDIANCE: Researchers interested in applying automatic methods for analysis of QSM data

PURPOSE: Quantitative susceptibility mapping (QSM) provides a quantitative measure of tissue magnetic susceptibility. In the brain, magnetic susceptibility is influenced mainly by myelin in the white matter and by iron deposits in the gray matter [1]. QSM atlas of gray matter has been previously explored. The analysis of gray matter is straightforward due to its linear relationship with iron deposition. In contrast, white matter is heterogeneous due to different fiber orientation which significantly complicated the quantitative analysis. Previous studies showed that the magnetic susceptibility of white matter is linearly related with the susceptibility of myelin lipids and it following a sine-squared relationship with the fiber orientation as measured with respect to the main magnetic field [1]. This study aims to develop an atlas for automatic analysis of magnetic susceptibility of white matter and use it to investigate magnetic susceptibility anisotropy.

METHOD: **1) calculation of mean susceptibility map** Brain imaging of 155 adult subjects (age 25.0~83.2 years) was acquired on a Siemens 3T scanner using a multi-gradient-echo sequence with TE1 = 4.92ms, echo spacing = 4.92ms, 6 echoes, TR = 35ms, and a spatial resolution of 0.9×0.9×4 mm^3. The phase maps were unwrapped using Laplacian-based phase unwrapping [3] and then combined to calculate the frequency shift. Background frequency was removed by a modified SHARP method, and the susceptibility mapping was derived by using LSQR method [4]. Images of all subjects were registered to the MNI152 template in FSL and then averaged to obtain the mean susceptibility map of the adult group. **2) QSM atlas** To construct a QSM atlas, we combined the fiber tracking-based white matter atlas (JHU-MNI-GA, contains twenty of the major fiber bundles) [4] with the previously established gray matter parcellation map, which was obtained from the JHU-MNI-SS "EvePM" atlas template [5]. Creation of the new atlas was performed by warping the white matter atlas and gray matter map into the MNI152 standard space via FIRNT and FNRT of FSL (threshold = 0.6 for each ROI). White matter pathways were segmented based on fiber bundles rather than the anatomical regions. The resulting atlas was utilized to parcellate the mean susceptibility image and further to investigate susceptibility anisotropy in each bundle. Orientation of fiber bundles can be determined by Diffusion Tensor Imaging (DTI) and the main field orientation. The largest diffusion eigenvector was considered to show the principal diffusion direction, or the direction of the fiber. The angle map was calculated from the 1st eigenvector of a mean DTI template (http://www.nitrc.org /frs/?group_id= 432). The transformation used to coregister the susceptibility image to the DTI data was applied to the fiber-based percellation map. **3) white matter analysis** For white matter analysis, the mean susceptibility values across all voxels were plotted against the sin-square of fiber angles in 50 angle steps between 0^o-90^o. In calculating the mean susceptibility for each step, the probability of a voxel belonging to a fiber (probabilistic atlas of the fiber) and belonging to the white matter (white matter probability map) was employed as a weighting factor. The resulting data was fit to the following equation using least squares optimization: $\chi(\theta) = \chi_a \sin^2\theta + \chi_0$, where χ is the apparent magnetic susceptibility (averaged across angle bins), θ is the angle between the primary diffusion direction and B_0, χ_a is the anisotropy of the magnetic susceptibility, and χ_0 is the baseline magnetic susceptibility of the tissue. ROIs were ensured to be sufficiently large to include enough angle bins. The curve fitting parameters (χ_a and R^2) were analyzed and compared between ROIs. Similarly, analysis on JHU-MNI-SS fiber-tracking atlas (consist of 108 fibers) and JHU-MNI-GA-WMPM atlas (not fiber-tracking) was performed to test the fiber-based method.

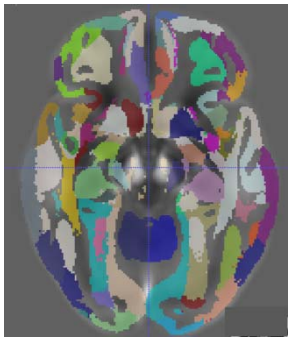

Fig. 1 QSM brain atlas.

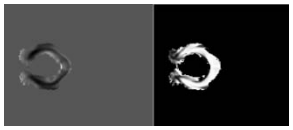

Fig. 2 Susceptibility and sin-square data of Fmajor. (left: susceptibility; right: sin-square of angle)

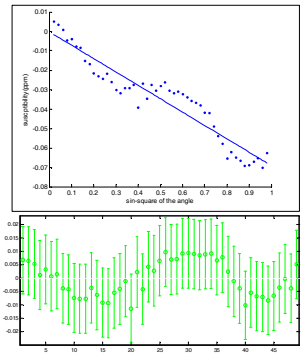

Fig. 3 Curve fitting for Fmajor (top) and the residual (bottom).

RESULTS AND CONCLUSION: The QSM atlas where white matter was segmented based on fiber bundles was shown in Fig. 1. Analysis of more than half of the twenty main fibers indicated a negative χ_a with the $R^2 > 0.5$. Six of them, including Fmajor, Fminor, IFOL, IFOR, IFLR and IFLL, showed $R^2 > 0.7$. These results were consistent with the generally acknowledged fact that an increasing contribution of myelin is associated with a decrease of susceptibility. Seven of the regions showed a positive χ_a, however, $R^2 < 0.3$ in four regions and $R^2 < 0.5$ in the other three. Analysis of the Fmajor fiber was shown as an example (Fig. 2, 3). Anisotropy of the magnetic susceptibility χ_a was around -0.01 ppm for each region. In comparison between the fiber tracking-based atlas and region-based atlas, the former showed more data that were considered to be reliable (results with a negative correlation and $R^2 > 0.5$), and the difference in number of reliable regions was 20.83%. Thus, the fiber-track-based atlas is more useful for anisotropy analysis of the white matter.

DISCUSSION: Previous studies have suggested that susceptibility imaging may provide complementary and sometimes potentially more sensitive information for helping understand disease mechanisms such as cerebral palsy. To utilize QSM in population based imaging analysis, a normalized brain atlas of QSM is needed. Here we developed such an atlas for QSM and proposed a novel method for white matter analysis of the whole brain. In the future, it will be worthwhile to explore how the susceptibility anisotropy is affected by white matter fiber angle distribution.

References: [1] Li W, et al. Human Brain Mapping, 2013. [2] Li W et al. Neuroimage, 2012, 59(3): 2088-2097 [3] Li W, et al, Neuroimage 2011;55:1645-1656 [4] Wakana S et al. Radiology, 2004, 230(1): 77-87. [5] Lim I A L et al. NeuroImage, 2013.