Magnetic Susceptibility Anisotropy and Susceptibility Tensor Imaging

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1. Introduction
Recent advances in processing maps of B_0 field and the availability of high-field magnets have started to reveal some unique contrast and meaningful information of tissue magnetic properties (1-5). We are now able to measure magnetic susceptibility in 3D with MRI in vivo. Studying the magnetic susceptibility has significantly improved our understanding of tissue magnetic property. In the brain in particular, susceptibility has provided a rich source of tissue contrast between gray and white matter. Susceptibility of white matter was also found to be anisotropic (6-7). In other words, the value of the susceptibility depends on the orientation of the underlying white matter fibers with respect to the B_0 field. This anisotropy can be characterized with a susceptibility tensor in a second model (7). A minimum of six non-collinear measurements is necessary for determining a susceptibility tensor. Magnetic susceptibility anisotropy may be a useful tool for studying tissue microstructure, for example, for probing the myelin structure (8) and for fiber tractography (9).

2. Susceptibility tensor imaging
The resonance frequency shift ($\Delta f$) of each voxel is related to the spatially distributed macroscopic susceptibility tensors as (7)

$$\Delta f = FT^{-1}\left[ \frac{1}{3} \hat{H}^T FT (\chi) \hat{H} - k^T \hat{H} \frac{k^T FT (\chi) \hat{H}}{k^2} \right] \gamma \mu_0 H_0. \quad [1]$$

Here, $FT (FT^{-1})$ is the Fourier transform (inverse Fourier transform); $\hat{H}$ is the unit directional vector of the applied magnetic field; $k$ is the spatial frequency vector; $\gamma$ is the gyromagnetic ratio of water proton; $\mu_0$ is the vacuum permeability; $H_0$ is the magnitude of the applied magnetic field; $\chi$ is a second-order (or rank-2) susceptibility tensor.

3. Molecular underpinning of susceptibility anisotropy
At the molecular level, most biomolecules are known to have anisotropic magnetic susceptibility, which has been widely used to elucidate molecular structures using NMR and EPR spectroscopy (10-13). The investigation of the contribution of anisotropic molecular magnetic properties to the MRI-observable macroscopic magnetic susceptibility is of particular importance for the understanding of frequency shift and susceptibility contrast between gray and white matter. In the shiverer mouse brain, the axon structure is intact as demonstrated by the presence of strong diffusion anisotropy (though slightly reduced) and unaltered fiber orientations; however, the amount of myelin sheath surrounding the axon is greatly impaired as visualized in electron micrograph (14). These results demonstrate the importance of myelin in generating susceptibility contrast, and further suggest myelin as the potential source of susceptibility anisotropy.
Nerve axons in the central nervous system are insulated by the multilayered myelin sheath as commonly illustrated by the dense lines in the cross sectional electron micrograph (EM) of axons (Fig. 1A). Myelin is rich in lipids (~70% dry weight) and proteins (~30% dry weight) (15). It is composed of spiraling sheaths of double bilayers separated by aqueous layers of 3-4 nm thickness that alternate between cytoplasmic and extracellular cell membranes (16) (Fig. 1B). In this complex structure, water molecules in myelin experience fast molecular tumbling ($\tau_c \sim 10^{-12}$ sec) and are not expected to contribute to the anisotropy. The abundant lipids in the myelin membranes, on the other hand, are strongly anisotropic at the molecular level and are highly organized around the axons but with limited mobility ($\tau_c \sim 10^{-8}$ sec) (17). Denote $\chi^{\parallel}$ the susceptibility of a myelin lipid molecule in the direction parallel to the long axis of the molecular chain, $\chi_m^{\perp}$ the susceptibility perpendicular to the long axis and $\alpha$ be the fiber angle with respect to the B0 field. It can be shown that the susceptibility of myelinated axons is expressed as (18):

$$\chi = f_{\text{lipid}} \left( \frac{\chi^{\parallel} - \chi_m^{\perp}}{2} \right) \sin^2 \alpha + \chi_0$$  \hspace{1cm} [2]

Notice that, since the longitudinal direction of a lipid molecule is perpendicular to the axon fiber direction, $\chi^{\parallel}$ is in fact perpendicular to the axon fiber direction. Eq. [2] suggests a simple sine-squared relationship between the macroscopic susceptibility and the susceptibility anisotropy of an individual lipid molecule. If the macroscopic susceptibility anisotropy is defined as the susceptibility difference between parallel ($\alpha = 0^\circ$) and perpendicular ($\alpha = 0^\circ$), this equation predicts that magnetic susceptibility anisotropy or the maximum variation of macroscopic susceptibility ($\Delta \chi_{\text{max}}$) is $f_{\text{lipid}} (\chi^{\parallel} - \chi_m^{\perp})/2$.

4. STI fiber tractography

The susceptibility tensor calculated from Eq. [1] can be decomposed into three eigenvalues and corresponding eigenvectors. The three eigenvalues define three principal susceptibilities, $\chi_1$, $\chi_2$ and $\chi_3$, ranked in a descending order. In DTI tractography, the fractional anisotropy (FA) map is used to identify regions of white matter fibers, and to set the threshold for initializing and terminating the fiber tracking procedure. Unlike DTI, the definition of susceptibility anisotropy is challenging, given the difficulties in susceptibility tensor quantification and the relative nature of susceptibility tensor values. Instead of defining a quantitative measure of susceptibility anisotropy, we used a susceptibility index $SI$ to highlight the white matter for fiber tracking, based on the fact that white matter has anisotropic susceptibility and has the smallest susceptibility (9):

$$SI = \left( |\chi_1 - \chi_3| + \gamma \right) / \bar{\chi}$$  \hspace{1cm} [3]

where $|\chi_1 - \chi_3|$ is a direct measurement of susceptibility anisotropy, $\gamma$ is an adjustable parameter and $\bar{\chi}$ is the mean susceptibility. Since the image quality of $|\chi_1 - \chi_3|$ is usually not sufficient for fiber tracking while $\bar{\chi}$ provides excellent contrast between gray and white matter, $\gamma$ and $\bar{\chi}$ are introduced to achieve a balance between characterization of susceptibility anisotropy and sufficient image quality for fiber tracking.

Although more sophisticated tracking algorithms are conceivable to utilize the unique properties of the susceptibility tensor, existing algorithms developed in DTI (19-20) can be readily translated to STI given their common utilization of the tensor field. In the current
implementation, tracking is initiated from a given voxel (or region of interest) when $SI$ is above a certain level (0.35 in this study) and propagated through a continuous vector field defined by the major eigenvector that is associated with the largest principal susceptibility. Tracking is terminated when $SI$ decreases to below a minimum threshold (0.35 in this study). Tracking is also terminated when the angle between two adjacent vectors is larger than a given tolerance ($60^\circ$).

5. References


