INTRODUCTION: Gradient-echo MRI has revealed anisotropic magnetic susceptibility in the brain white matter (1, 2). This magnetic susceptibility anisotropy can be measured and characterized with susceptibility tensor imaging (STI) (1). In this study, a method of fiber tractography based on STI is proposed and demonstrated in the mouse brain. STI experiments of perfusion-fixed mouse brains were conducted at 7.0 T. The magnetic susceptibility tensor was calculated for each voxel with a regularization and decomposed into its eigensystem. The major eigenvector is found to be aligned with the underlying fiber orientation. Following the orientation of the major eigenvector, we are able to map distinctive fiber pathways in 3D. As a comparison, diffusion tensor imaging (DTI) (3) and DTI fiber tractography were also conducted on the same specimens. The relationship between STI and DTI fiber tracts was explored with similarities and differences identified. It is anticipated that the proposed method of STI tractography may provide a new way to study white matter fiber architecture. As STI tractography is based on physical principles that are fundamentally different from DTI, it may also be valuable for the ongoing validation of DTI tractography.

METHODS: Proton MRI experiments on perfused fixed mouse brains (C57BL/6) were conducted as described previously (1). The perfused mouse brain was surgically separated from the body, but was kept within the cranium to prevent any potential damage to the brain caused by surgical removal. The specimen was sealed tightly inside a cylindrical tube (length 30 mm and diameter 11 mm). To allow free rotation, the tube was contained within and taped to a hollow sphere (diameter 30 mm). The sphere containing the specimen was placed inside a dual-channel mouse probe (coil diameter 30 mm, MZM imaging Corp, Cleveland OH) and scanned using a 3D spoiled-gradient-recalled-echo (SPGR) sequence with the following parameters: FOV = 22x22x22 mm³, matrix = 256x256x256, TE = 8.0 ms, TR = 50 ms, flip angle = 60° and NEX = 1. After each acquisition, the sphere was rotated to a different orientation and the acquisition was repeated. A total of 15 to 19 orientations were sampled that roughly cover the spherical surface evenly. Magnetic susceptibility tensors were determined voxel-by-voxel in the k-space in the subject’s frame of reference. To reduce registration errors, we constrained the spatial variation of susceptibility anisotropy to be characterized by low spatial frequencies, while the susceptibility of high spatial frequencies components (i.e. at the outer k-space) is relatively isotropic. The resulting tensors were decomposed with eigenvalue decomposition. The large eigenvector was used to identify the fiber orientation. STI-based fiber tracking was realized with the DtiStudio by substituting the diffusion tensor with the susceptibility tensor. As a comparison, DTI-based fiber tracking was also conducted in DtiStudio (4).

RESULTS: Figure 1 compares color-coded susceptibility anisotropy index (SI) maps of STI to FA maps of DTI. Examples of SI are shown in Fig. 1A, demonstrating that the overall contrast exhibited in the SI is similar to that in the FA (Fig. 1B). Color coding was based on the direction of the major eigenvector with the following color scheme: red representing anterior-posterior, green representing left-right and blue representing dorsal-ventral. Although there are discrepancies in the color-coded anisotropy maps between STI and DTI, especially in regions of small fiber bundles, the fiber orientation are mostly consistent in major fiber bundles (arrows).

Figure 2 compares fiber tracts reconstructed using STI and DTI in the anterior commissure, the hippocampal commissure and the posterior corpus callosum. In all three cases, the tube was rotationally constrained by a yellow circle in Figure 6 to initialize the tracking procedure and the same starting and terminating criteria were used. The resulting STI fiber tracts share striking similarities with DTI in all three cases. Particularly, the smooth U-shaped anterior commissure tracks further confirm the long-range coherence of the vector field determined by STI. In general, the two methods of fiber tracking yield comparable results for large fiber bundles with STI fibers being generally shorter. In particular, for smaller and more complicated fiber structures, DTI results longer and smoother pathways than STI.

DISCUSSIONS AND CONCLUSIONS: We have proposed and demonstrated a method of fiber tractography using STI. The tractography relies on the recently discovered anisotropic magnetic susceptibility in the white matter. High-quality susceptibility tensors were calculated with a regularized numerical algorithm. 3D fiber pathways were reconstructed by navigating through the vector field defined by the major eigenvector (corresponding to the least diamagnetic susceptibility eigenvalue) of the susceptibility tensor. The STI-based fiber tracking is compared to DTI for large white matter fiber bundles with both similarities and differences identified. While there is a high level of agreement in most large fiber bundles, STI tracking in small fiber bundles, and also some larger fiber bundles, such as the superior regions of corpus callosum, have shown more pronounced differences. The differences may be attributed to a number of factors. First, small fiber bundles are susceptible to imperfect linear image registration which results in inaccurate estimation of the susceptibility tensor. This is consistent with the fact that the discrepancy also is more likely to occur at the boundaries of larger fiber bundle. Second, STI-based tractography underlies a physical principle that differs fundamentally from diffusion anisotropy. It is possible that this fundamental difference may translate to different fiber tracks. We have assumed that the least diamagnetic susceptibility lies in the direction of white matter fibers. Though this assumption appears to be fully supported in the major fiber bundles, it needs to be further validated in other whiter matter regions and also in vivo. Clearly, more work is needed to completely understand the phenomenon of anisotropic susceptibility and to further develop the proposed tracking method. As STI tractography is based on physical principles that are fundamentally different from DTI, it may also be valuable for the ongoing validation of DTI tractography.


![Figure 1. Comparison of color-coded STI and DTI FA. Overall, the colors in major fiber bundles (arrows) show good consistency while differences are also present. Similar to DTI, STI color maps demonstrate the striking capability of separating fiber bundles in close contact such as the corpus callosum (green) and the cingulum bundle (red) shown in the third column (arrows). Abbreviations: hc – hippocampal commissure; cc – corpus callosum; ac – anterior commissure; cg – cingulum.](image1)

![Figure 2. Comparison of STI and DTI fiber tracts in selected fiber bundles. (A) The anterior commissure; (B) the hippocampal commissure; (C) the posterior corpus callosum.](image2)