MR Microscopy of Brain Cytoarchitecture by Quantitative Mapping of Magnetic Susceptibility

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INTRODUCTION: Traditionally, image phase has been largely discarded due to the lack of contrast and the perceived lack of meaningful information. Recently, following the increasing availability of high and ultra-high field strength, contrast existing in the phase image itself has generated a significant amount of interest. At these high field strengths, phase images showed excellent image contrast and revealed anatomic structures that were not visible on the corresponding magnitude images (1, 2). Here, we demonstrate that phase images and, more importantly, the corresponding susceptibility maps provide a novel contrast mechanism to visualize the microstructure of brain anatomy at the exquisite resolution offered by MR microscopy. In particular, we believe the described technique may provide a powerful tool to visualize brain cytoarchitecture and detect potential abnormalities at high speed and with ultra-high spatial resolution.

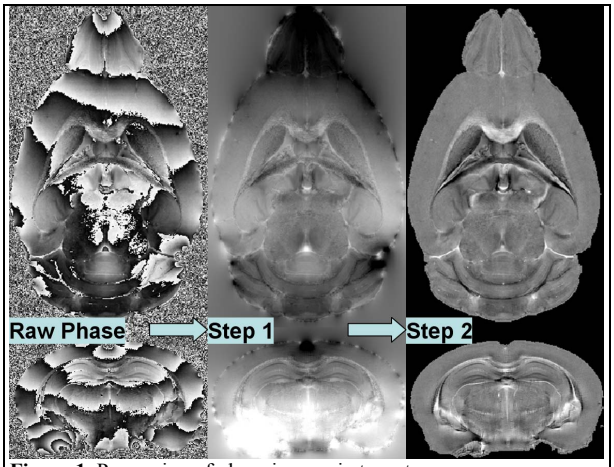

Figure 1. Processing of phase images in two steps.

METHODS: Ex vivo imaging of mouse brain was approved by Institutional Animal Care & Use Committee (IACUC) of our institution. Animals (9–12 weeks old C57BL/6 mice [The Jackson Laboratory, Charles River, NC]) were anesthetized with Nembutal. A catheter was inserted into the left ventricle of the mouse heart. The animal was perfused with a peristaltic pump first with a mixture of 0.9% saline and ProHance (10:1, v:v) (Bracco Diagnostics, Princeton, NJ), then followed by a mixture of 10% buffered formalin and ProHance (10:1, v:v) (3). The perfused mouse brain is kept within the skull to reduce artifact damage to the brain. Ultra-high resolution 3D SPGR images were acquired using a 9.4 T vertical bore Oxford magnet with shielded coil providing gradients of 95 G/cm. The imaging parameters are: matrix = 512x256x256, FOV = 22x11x11 mm^3, TE = 9 ms, and TR = 50 ms.

Raw phase images were reconstructed from the complex SPGR data. These raw phase images contain strong background phase and are typically corrupted by phase wraps. As a result, tissue contrast and structural details are also corrupted. To reveal the structural details, we use a two-step algorithm to eliminate the background phase and phase wraps. Although phase provides a unique tissue contrast, phase is not an intrinsic tissue property. To obtain the intrinsic magnetic susceptibility, we further compute the underlying magnetic susceptibility from the measured phase maps using the LSQR algorithm (4).

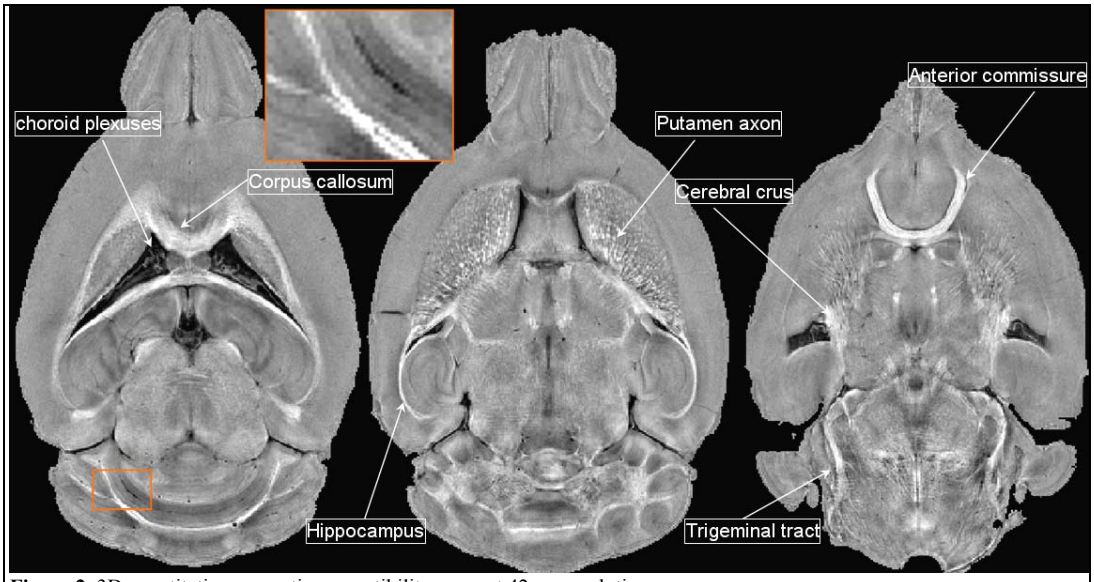

Figure 2. 3D quantitative magnetic susceptibility maps at 42μm resolution.

RESULTS: Figure 1 illustrates the two-step procedure of removing background phase. The removal of background phase is achieved by relying on the harmonic property of Laplacian equation that background phase satisfies. The resulting phase is free of phase wraps and shows excellent contrast between gray and white matter.

Figure 2 shows three representative slices of computed magnetic susceptibility at ultra-high spatial resolution. The computed magnetic susceptibility offers a strong contrast between gray and white matter. It allows us to identify major white matter structures such as the corpus callosum, the commissure and the hippocampus. It also allows visualization of small axons in the putamen. Interestingly, the susceptibility map shows a sharp delineation of the choroid plexuses that is responsible for producing cerebral spinal fluid. The multilayered cortical structures are clearly identifiable, e.g. in the cerebellum (orange boxes).

DISCUSSIONS & CONCLUSIONS: We show that quantitative mapping of magnetic susceptibility at microscopic resolution provide an exquisite delineation of brain microstructures. The calculation of susceptibility was made possible by the combination of a novel method of removing background phase and an accurate algorithm of solving an ill-posed inverse problem. In the phase map, white matter may appear bright or dark depending on its location. In the intrinsic susceptibility map, white matter appears bright (diamagnetic). The contrast resembles to that of diffusion fractional anisotropy in which the axons show high contrast against surrounding gray matter. Importantly, the susceptibility contrast can be generated at high speed with a single 3D SPGR acquisition. Given the robustness of the SPGR sequence (robust against motion, eddy current and B1 inhomogeneity), imaging magnetic susceptibility can become a useful tool for brain microscopy.

The particular high contrast of white matter axons indicates that the source of this phenomenon may originate from the myelinated axonal structures. It is known that proteins are diamagnetic which is consistent with our findings. We thus further anticipate that imaging magnetic susceptibility may provide a powerful tool for studying animal models of white matter diseases.

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