Effects of tissue structure on magnetic susceptibility contrast

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Magnetic susceptibility contrast has been used in various studies of the brain, including mapping of its vasculature, BOLD fMRI, detection of iron accumulation and hemorrhages, cell tracking, and the visualization of grey and white matter anatomy (for reviews see (1-3)). It originates from magnetic field shifts that occur in tissues when placed in the strong magnetic field of an MRI scanner (4); the resulting changes in NMR Larmor frequency can be sensitively detected with gradient-echo (GRE) techniques where they can result in changes in signal amplitude and phase (5). For example, the paramagnetic properties of hemosiderin and deoxyhemoglobin in hemorrhagic lesions lead to field shifts that change the GRE signal, and this provides an opportunity to assess lesion extent and severity (6).

It should be realized however that magnetic susceptibility contrast not only depends on tissue composition (e.g. the concentration of paramagnetic compounds), but also its sub-voxel structure (7). This is because this structure affects both the pattern and strength of tissue magnetization, and furthermore influences its effect on phase and amplitude of the GRE signal. Although this complicates interpretation, it also may provide valuable opportunities to study tissue structure.

For example, in WM fiber bundles, there is structural organization at various spatial scales (3). At sub-voxel scales, structural anisotropy exists because of the ordered alignment of axons, and a diamagnetic susceptibility of the myelin sheath leads to an anisotropic distribution of the susceptibility. As a result, the phase and magnitude of the voxel-averaged GRE signal become dependent on fiber orientation in the applied magnetic field. In addition, there are significant effects of the structural, molecular-level organization within the myelin sheath, where the particular alignment of phospholipid molecules results in the WM susceptibility itself becoming orientation dependent. Combined, these effects of structural organization in WM not only render GRE signal orientation dependent but also make its evolution with echo time deviate from the simple mono-exponential, single frequency decay typical of tissue structure that can be approximated by randomized distribution of diamagnetic (or paramagnetic) inclusions (8-10).

Because of these phenomena, extraction of compositional and structural information from susceptibility contrast requires sophisticated analysis and modeling approaches, and the development of these is an active area of research. Examples include quantitative susceptibility mapping (QSM (11)) and susceptibility tensor imaging (STI (12)). In addition, recent work has suggested that detailed analysis of the GRE signal may ultimately allow extracting cellular compartment-specific information (e.g. discriminating between water in myelin and in axonal and interstitial spaces), currently not possible or very difficult with other methods (8, 9).

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