Anatomically dependent variations in magnetic susceptibility produces spectral asymmetries in high spectral and spatial resolution MRI of post-mortem mouse brain

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Purpose: Widely used MRI techniques show brain morphology both *in vivo* and *ex vivo* at very high resolution. Commonly employed methods such as T_2^*-weighted imaging[1], phase-sensitive imaging[2], and susceptibility-weighted imaging[3] are sensitive to local magnetic susceptibility gradients produced by subtle variations in tissue composition. However, the spectral resolution of these protocols is limited to maintain reasonable run-time combined with very high spatial resolution and this limits sensitivity to susceptibility gradients. In this work we report data acquired with increased spectral resolution using 3-dimensional high spatial *and spectral* resolution MRI[4], in order to analyze subtle variations in water proton resonance frequency and lineshape that reflect local anatomy[5]. Particular attention is paid to cerebellum and deep white matter structures where susceptibility driven variations between anatomical regions produce multiple, anatomy specific resonances in the water spectrum[6,7]. These results provide empirical evidence of the breadth of information contained in the water spectrum that reflect susceptibility differences between anatomical structures and are consistent with recently published modeling techniques[8-10].

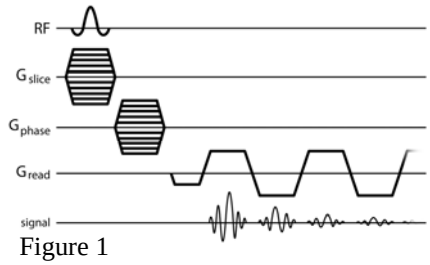


Figure 1

Methods: Excised, perfusion fixed mouse brains (n=3) were imaged at 9.4T (Bruker). Brains were rinsed in PBS and submerged in Fomblin for susceptibility matching. Data were acquired over 18-24 hours using a 3D multi-gradient echo pulse sequence (Fig. 1) with spatial and spectral resolutions of 50x50x70μm^3 and 3.5 Hz, respectively. This approach facilitated for voxel-wise sampling of the FID (TE_1 = 5ms, echo spacing = 9ms, 32 echoes). Fourier transform applied along time produced a high-resolution water spectrum for each image voxel (Fig. 2). Data were analyzed in the spectral domain and images were produced from the various Fourier components of the water resonance (Fourier component images, or FCI's), allowing precise measurements of local variations in resonance frequency and lineshape within a voxel.

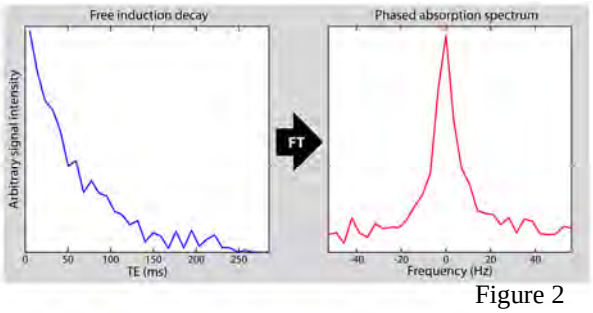


Figure 2

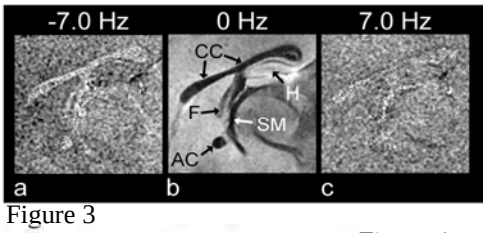
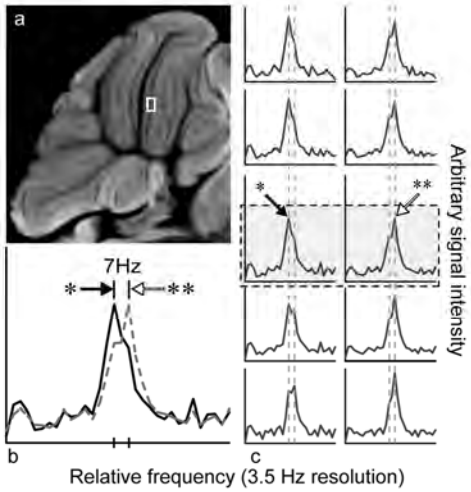


Figure 3

Figure 4



Results: High contrast T_2^*-weighted images were produced from the peak of the water resonance, revealing a high degree of anatomical detail (Figs. 3b and 4a). In FCI's at -7.0 Hz from the peak (Fig. 3a), the contrast between deep white matter tracts (CC-corpus callosum, F-fornix, AC-anterior commissure, SM- stria medullaris) and the surrounding tissue (H-hippocampus) is the reverse of the contrast in water peak height images (Fig. 3b). This indicates the presence of a shoulder in the water resonance that is not present at +7.0 Hz (Fig 3c) and may be specific to white matter microstructure driven variations in susceptibility. Moreover, a frequency shift of 6.76 ± 0.55 Hz was measured between the molecular and granular layers of the cerebellum (Fig. 4b). This shift is demonstrated in spectra (Fig. 4c) signified by the white box in figure 4a; water peaks from voxels in the molecular and granular layers are consistently 2 bins apart (7.0 Hz, as dictated by the spectral resolution) from one another.

Conclusions: High spectral and spatial resolution MR imaging has the potential to accurately measure changes in the water resonance in small voxels. This information can guide optimization and interpretation of more rapid, commonly used imaging methods that depend on local susceptibility gradient driven image contrast. In addition, with improved sampling methods, high spectral and spatial resolution data could be acquired in reasonable run times, and used for *in vivo* scans to increase sensitivity to variations in local susceptibility.

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