

Optimization of Susceptibility Weighted Imaging at 7T for Improved Detection of Alzheimer's Amyloid Plaques Associated with Iron in Human Postmortem Brain

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INTRODUCTION:

Amyloid plaques are one of the hallmarks of Alzheimer's disease (AD). Iron component in the immediate vicinity of amyloid plaques has been shown in animal studies of AD and acts as a source of reactive oxygen species for oxidative damage [1,2]. In addition, an interest of microstructural hippocampal imaging has emerged in recent years [3]. Any imaging technique capable of directly visualizing amyloid plaques and fine hippocampal structures is critical for early and accurate diagnosis of AD. This work is to evaluate imaging parameters on 7T MR using SWI without MRI contrast agent to better identify the histopathologic correlate of amyloid plaques containing iron and otherwise invisible subhippocampal structures of human post-mortem brain in patients with AD.

MATERIALS AND METHODS:

Post-mortem brain specimens of the frontal lobe and hippocampus were obtained from 6 patients (with age mean/SD 72.2/4.3 years) with clinically diagnosed AD and 6 age-matched healthy controls (with age mean/SD: 71.4/5.2 years) without AD. Coronal 1~3 cm thick brain slices were preserved and fixed in 2% agar for this study. Imaging was performed on a 7.0T Siemens MAGNETOM with maximum effective gradient strength of 72 mT/m and a slew rate of 200 T/m/s. A 24-element phased array head coil was used. To maximize SNR, the coil array comprises two separate components: a birdcage-like circularly polarized transmit coil and a 24-element phase array coil located on a close fitting helmet-like device. High resolution 3D SWI was obtained with isotropic voxel size 150~320 μ m. For imaging optimization to better visualize amyloid plaques, we varied TR, TE, bandwidth (BW) and flip angle from 30-100ms, 12-36ms, 60-140Hz/pixel and 10-40 $^\circ$, respectively. The SWI filtered phase images were used (multiplication factor of 4 ~ 8) to enhance susceptibility contrast in the SWI images. Regional iron quantification from optimized sequence based on the phase calculation was also computed to compare the iron load in AD and controls. Coronal vibratome sections were then cut stained with Thioflavin-S for amyloid plaques detection, and correlated with slice-matched high resolution SWI.

RESULTS:

Optimal imaging parameters were optimized with improved visualization of amyloid plaques with the best contrast and SNR that were obtained at TR/TE/FA of 80ms/20ms/30 $^\circ$ with phase multiplication factor of 6. Figure 1 shows pre- and post-processed SWI images different phase multiplication factors. Figure 2 shows SWI in AD frontal specimen and its histologic correlates as compared to an age-matched healthy control. Compared to controls, AD brain samples revealed a large increase number of hypointense foci on post processed SWI images along the cortical mantle of the frontal and entorhinal cortex. The average phase value in the cortex region of AD data (2282 \pm 62) is significantly higher than that of control data (2068 \pm 44), which indicates higher iron amount in AD samples. Histological staining of AD samples has also demonstrated an increase in amyloid plaques in these regions that confirms and correlates the imaging findings. In addition to excellent image contrast, 7T SWI also provides high resolution images for subregional hippocampal structures including CA1, CA2, CA3, subiculum, and dentate gyrus with significant atrophy of these structure in AD patient (Figure 3).

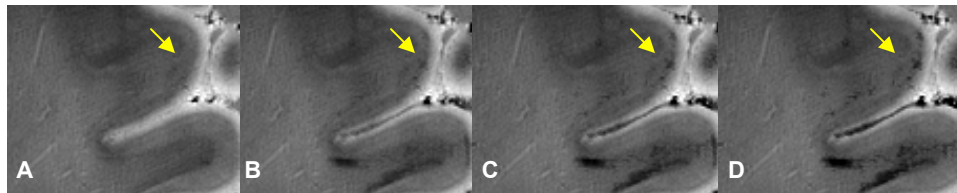


Figure 1. Pre-(A) and post-processed SWI images with phase multiplication factors of 4 (B), 6 (C), and 8 (D) of postmortem slice in AD sample showing various detectability of the iron deposition in the cortex (arrow).

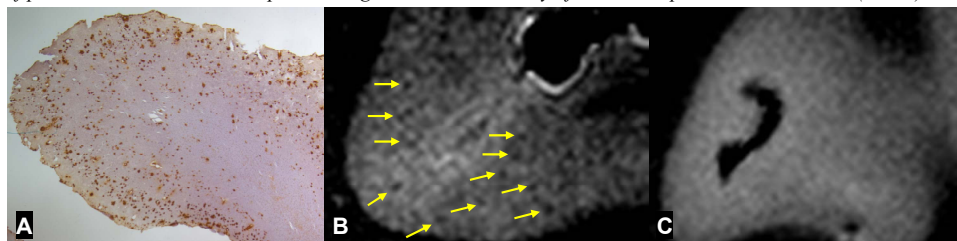


Figure 2. With markedly enhanced susceptibility contrast and superb signal on 7T, amyloid plaques identified with histologic slice (A) are seen on the matched SWI postmortem slice in the frontal cortex (arrows) of a patient with AD (B) as compared to a healthy control.

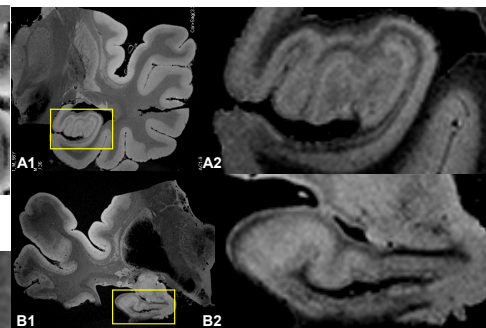


Figure 3. 7T SWI with high resolution of 200 μ m (0.008mm³) demonstrate subregional hippocampal structures including CA1, CA2, CA3, subiculum, and dentate gyrus in a healthy control (A1 and A2) and significant atrophy of these microstructures in a patient with AD. As expected, the amyloid plaques in the hippocampus are not seen as many as in frontal and entorhinal cortex.

CONCLUSION & DISCUSSION:

Our findings suggest that SWI with optimization at ultra-high-field strength MR has exhibited the capability to detect diminutive susceptibility contrast associated with iron deposition and otherwise invisible fine hippocampal structures with near histopathologic resolution. Our data concur with studies of AD transgenic mouse models [1,2] that have previously correlated "susceptibility stains" with iron-containing amyloid plaques. Therefore, SWI has great potential for direct detection and quantification of amyloid plaques in live human brain on ultra-high-field MR, and may become feasible in the near future.

Reference: [1]. Benveniste H et al. Proc Natl Acad Sci U S A. 1999;23;96(24):14079-84. [2]. Lee SP et al. Magn Reson Med 2004;52:538-544. [3]. Chetelat G et al. Neuroimage 2003;18:525-541.