

Susceptibility Mapping of Alzheimer Plaques at 7T

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Introduction: Alzheimer's pathology is characterized largely by the presence and distribution of beta-amyloid plaques and tau-containing neurofibrillary tangles. By the time Alzheimer's disease (AD) is clinically diagnosed, there has been extensive neuronal loss, and there is no effective treatment. Because any prevention or treatment may need to occur before this neuronal loss, there is a great need for preclinical diagnosis of patients who will develop AD. β -amyloid plaques may be such a target because they are thought to have an important role in the earliest stages of AD. *Ex vivo* high-field 7.0 Tesla MR studies of human AD specimens have demonstrated that plaques may be visualized as small hypointense foci, but this claim has been the subject of some controversy. The precise etiology of the signal changes is unclear, though it is suspected that microscopic iron, known to be within the plaques, partially contributes to this low signal intensity. One way of potentially ascertaining the role of iron is quantitative susceptibility mapping, an MRI processing technique that deconvolves phase information to deliver quantitative maps of magnetic susceptibility. We have applied susceptibility mapping to human AD brain specimens imaged at 7T with GRE imaging to investigate the relationship between plaques and iron.

Methods: Five AD and five normal formalin-fixed human brain specimens were obtained. Each specimen consisted of five 3cm square slabs that were 4mm in thickness, dissected from the frontal, parietal, medial temporal, temporal, and occipital lobes. These were immersed in Fluorinert (3M, USA) in a 4cm diameter sealed container, and scanned with a closely-coupled transmit/receive solenoid coil at 7T using a GRE sequence (TR 21, TE 10.5, FA 20, 8 NEX, 0.1mm isotropic voxels, FOV 3cm, 256 0.1mm slices, BW 8kHz, total scan time 3h35m. Susceptibility processing was performed using MATLAB using a truncation method. To quantify presumed plaque susceptibility, approximately 20 focal signal voids were identified in each specimen on the GRE magnitude images and the maximum local (3 x 3 x 3 pixel) plaque susceptibility was computed. Background susceptibility was computed for a region of interest (ROI) within hippocampal gray matter that was not plaque-laden.

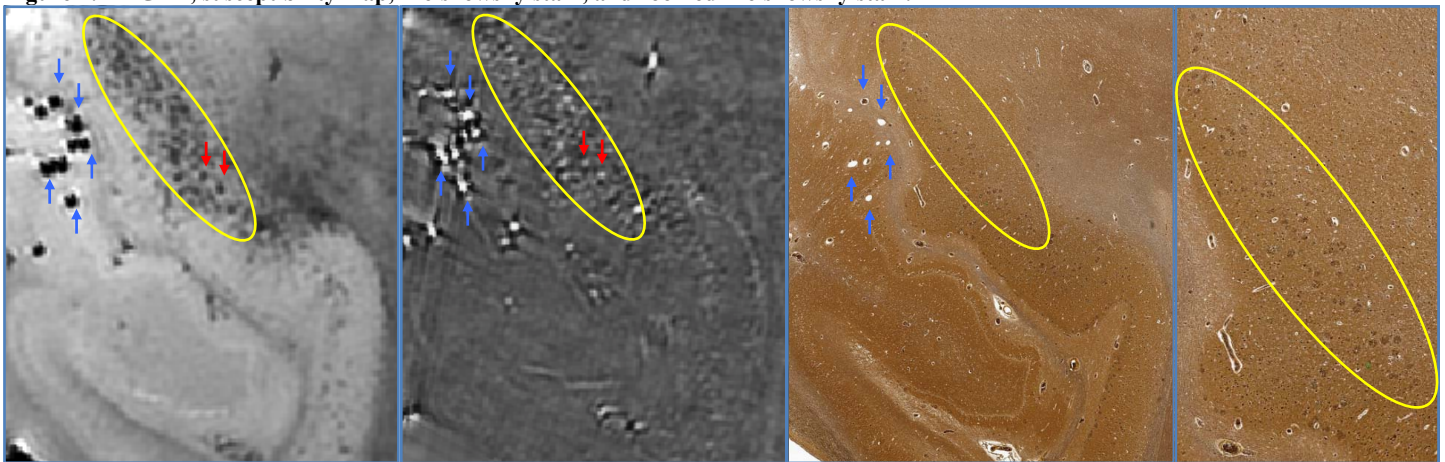
One AD and one normal specimen were then prepared for histologic analysis by slicing with a microtome at 5 μ m slice thickness and staining with a Bielschowsky stain, which identifies neuritic amyloid plaques.

Results: Presumed plaques were identified as tiny round signal voids on the GRE images. An example image is illustrated in Figure 1. These signal voids corresponded to tiny round foci of bright signal on the susceptibility maps (red arrows). Table 1 reports that magnetic susceptibility was significantly greater for the presumed plaques than from background ROIs in relatively plaque free medial temporal gray matter. The histology stain below illustrates a close registration between blood vessels in the GRE image, susceptibility map, and histology stain (blue arrows). There is the suggestion of plaques in a similar distribution (yellow oval). The normal specimens demonstrated no signal voids, no bright foci on the susceptibility maps except for obvious blood vessels, and no plaques on the histology stain.

Table 1: Plaque Magnetic Susceptibility

	Susceptibility (ppm)
Plaques	0.0200 +/- 0.0106
Background	-0.0004 +/- 0.0005

Figure 1: 7T GRE, susceptibility map, Bielschowsky stain, and zoomed Bielschowsky stain.



Conclusions: This initial data offers further evidence that amyloid plaques may be visualized by 3D imaging *ex vivo*. Moreover, it demonstrates that quantitative susceptibility mapping can be achieved at 7T at a spatial resolution level that permits measurements to be made potentially at the level of single plaques, and that this capability will allow a much greater understanding and prediction of future MRI capabilities for plaque detection. The same foci of low signal on magnitude imaging for corresponds closely with high magnetic susceptibility on the susceptibility maps, as would be expected for iron, implying a role of microscopic iron within the plaques.

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