Increased Detectability of Alzheimer Plaques at 7T vs. 3T using High Resolution bSSFP

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Introduction: β-amyloid plaques are thought to have an important role in the development and progression of Alzheimer's disease (AD). Amyloid plaques are detectable at high-field as small hypointense regions in animal models [1] and *ex vivo* in human specimens [2], though in the latter case, clear separation of plaques from blood vessels remains an ongoing challenge. The underlying cause of the signal change is unknown, although the iron that is known to co-localize with β-amyloid plaques is suspected. Iron sensitivity is theoretically improved at high field strengths [3]. To investigate the relationship between plaque conspicuity and field strength, we imaged human AD brain specimens at 3T and 7T, and compared experimental measurements of signal-to-noise ratio (SNR), contrast, and contrast-to-noise ratio (CNR) to theoretical predictions of SNR.

Methods: Based on previously demonstrated advantages of 3T high-resolution balanced steady state free precession (bSSFP) imaging for detecting iron-loaded cells in mouse brain [4], we evaluated this methodology for direct detection of β-amyloid plaques in human AD specimens. We designed simulations and experiments to predict image quality and test the hypothesis that plaque detection would be enhanced at 7T compared to 3T.

For purposes of theoretical simulations of SNR, we measured T_1 and T_2 in white and grey matter from a single formalin-fixed AD brain specimen, at 3T and 7T. For T_1 measurement, we used an inversion-prepared fast spin echo sequence, repeated 8 times with different inversion times (TI=50-4000). For T_2 measurement, a spin echo sequence was repeated 6 times with different echo times (TE=8-150). These calculated T1s and T2s were used along with other sequence parameters in the bSSFP signal equation to estimate the relative SNR benefit of scanning at 7T compared to 3T.

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 through 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 size-matched transmit/receive solenoid coils at 3T and at 7T using a modified bSSFP sequence (TR 21, TE 10.5, FA 20, 8 phase cycles, 0.1mm isotropic voxels, FOV 3cm, 256 0.1mm slices, BW 9kHz for 3T and 8kHz for 7T, total scan time 3h38m for 3T and 3h35m for 7T. Image analysis was performed with MRIcro, Microsoft Excel, and MATLAB. SNR was computed by ROI selection of gray matter/hippocampus/white matter/background from matched AD image slices at 3T and 7T. To quantify presumed plaque contrast, approximately 20 focal signal voids were identified in each specimen on the 7T images and corresponding voids were found on matched 3T images. Presumed plaque contrast (ΔS/S) was computed as the difference between minimal presumed plaque SI and mean SI of surrounding gray matter in the same slab, divided by this surrounding gray matter mean SI. Contrast-to-noise ratio was defined as the product of ΔS/S and SNR.

Results: Table 1 reports that T_1s increased by roughly 70% in moving from 3T to 7T, while T_2s decrease by 10-30%. Subsequent predictions of 7T bSSFP SNR are 79-92% higher than that at 3T, depending on the tissue type. Table 2 reports the predicted and measured SNR, as well as the measured contrast and CNR, for hippocampal tissue. Predicted and measured HC SNR were 79% and 70% higher at 7T compared to 3T, respectively. Importantly, presumed plaque CNR was approximately 3 times higher at 7T compared to 3T, which reflects the combined effects of increased SNR and plaque contrast, and this is emphasized in Figure 2. Figure 1 demonstrates the visual appearance of presumed plaques in a single slice through the hippocampus of one specimen at 3T (left) and 7T (right), demonstrated the enhanced detectability at 7T.

Table 1: Measured T1 and T2

	HC	Cortex	WM
3T T1	342	314	203
7T T1	572	520	348
ratio	1.67	1.66	1.71
3T T2	49.8	43.6	21.6
7T T2	34.7	31.1	19.3
ratio	0.70	0.71	0.90
3T SI estimate	0.35	0.34	0.24
7T SI estimate	0.59	0.57	0.43
ratio	1.79	1.79	1.92

Figure 1: 3T and 7T specimens. Corresponding plaques are marked.

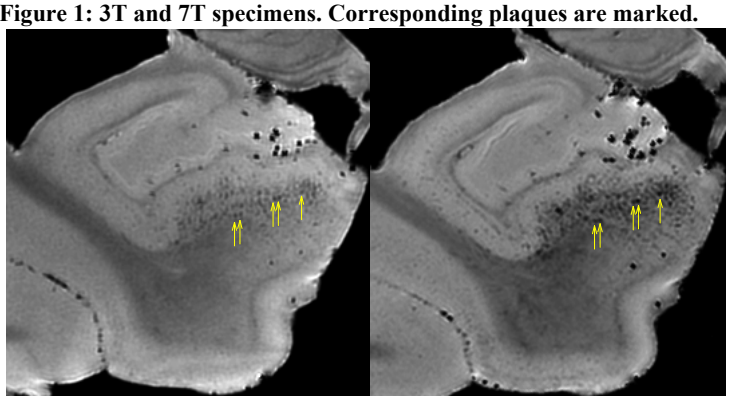

Figure 2

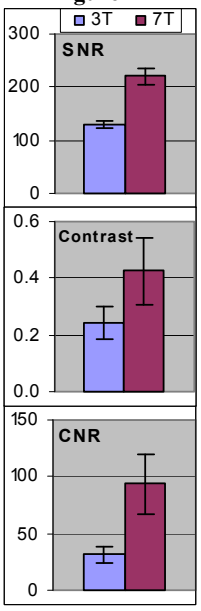

Table 2: Computed SNR and Plaque Contrast

	Predicted HC SNR	Measured HC SNR	Measured HC Contrast	Measured HC CNR
3T	0.35	129.46 +/- 6.18	0.242 +/- 0.057	31.49 +/- 7.47
7T	0.63	220.30 +/- 15.09	0.425 +/- 0.116	93.92 +/- 26.36
ratio	1.79	1.70 +/- 0.14	1.759 +/- 0.632	2.98 +/- 1.10

Conclusions: For the bSSFP pulse sequence, SNR per unit imaging time increases less than linearly with field strength from 3T to 7T, and experimental measurements of SNR closely match theoretical predictions. This less-than-linear increase is explained by the increasing T1 and decreasing T2 of the tissue. Despite this less-than-linear increase, CNR of signal voids which presumably representing β-amyloid plaques increases more than linearly with field strength, but less than quadratically. This contrast behavior is likely the result of the iron content of the β-amyloid plaques. Future studies will include correlation with pathological analysis of these specimens to confirm this hypothesis. We conclude that 7T MRI offers striking benefits for potential β-amyloid plaque detection compared to 3T MRI using the balanced SSFP pulse sequence.

References: [1] Chamberlain R et al. MRM 2009;61:1158-64. [2] Benveniste H et al. PNAS 1999;96(24):14079-84. [3] Yao B et al. Neuroimage 2009; 44(4):11259-66. [4] Bernas L MRM 2009, in press.
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