Assessment of cortical phase changes in Alzheimer's disease patients at 3T using T2*-weighted imaging.

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Purpose: High resolution T_2^*-weighted MRI at 7T has recently been used to highlight cortical changes due to differences in iron accumulation related to amyloid deposition in vivo [1,2]. Recent findings suggested that the level of iron accumulation, which may reflect AD pathology and more specifically amyloid deposition, is reflected by phase information on T_2*-weighted MRI at 7T. Measurement of the relative phase in regions of interest demonstrated a high specificity with respect to AD detection [1]. Moreover, these phase shifts correlated significantly with global cognitive functioning. However, since 7T MRI systems are not widely available, the aim of this study was to translate the imaging methods from 7T to 3T MRI to investigate whether these differences could be detected using T_2*-weighted 3T MRI data.

Methods: In total 12 AD patients (6 male/ 6 female) with a mean age of 70.9 years and 12 matched control subjects (7 male/ 5 female) with a mean age of 67.8 years were included. All patients underwent a complete battery of neuropsychological tests measuring global cognitive function (Mini mental state examination (MMSE) and Cambridge Cognitive Examination (CAMCOG)), memory (Wechsler Memory Scale (WMS)), and executive function ((Trailmaking test (TMT) part A and B). MRI was performed on a whole body human 3T MR system. Participants were scanned using a 3D T_2*-weighted gradient-echo scan with a total imaging duration of approximately 6 minutes. Imaging parameters were: repetition time (TR)/echo time (TE) 45/31 ms, flip angle 13°, FOV (AP/RL/FH) 250/175/112 mm, acquisition matrix 320 x 222 x 140 mm, resulting in a nominal voxel size of 0.78 x 0.79 x 0.80 mm, SENSE factor 2, one signal average. Scan parameters used for 7T imaging were described in our previous work [1].The phase images were subsequently unwrapped by highpass filtering with a 64 x 64 kernel [3]. Phase shifts in the cortex were determined in the transverse plane. The phase values of the cortical gray matter (GM) were determined on the unwrapped phase images in regions of interest (ROIs) in four areas of the brain: frontal, temporal, parietal, and occipital. The overall peak-to-peak phase shift (expressed in radians) between cortical gray and subcortical white matter (WM) (lobar cortical phase shift) was calculated for each region in each subject. Mann–Whitney *U* tests were used to assess differences in age, phase measurements, and different neuropsychological tests between groups. To evaluate differences in gender, chi-square tests were performed. To determine the association between the different neuropsychological tests and phase shift in the cortex, univariate general linear modeling was used adjusted for age and gender.

Results: No difference in age or gender was found between patient and control groups. Figure 1 shows an example of a 3T (a) and 7T (b) unwrapped phase image of an AD patient, showing much higher GM/WM contrast on the 7T scan as expected. Table 1 shows the lobar phase shifts for the different regions and the whole brain (the average of all sub-regions). No significant differences in phase shift between subjects with AD and controls were found in any of the regions. AD subjects demonstrated a lower cognitive performance on all cognitive tests compared to control subjects ($p<0.05$). Furthermore, no significant association was found between the measured phase shift and any of the individual neuropsychological tests.

Conclusion: Our 3T MRI data show no phase differences between AD patients and controls as opposed to our previous 7T MRI data which showed an increased cortical phase shifts in AD patients, and an association with cognitive performance. This indicates that 3T MRI in comparison to 7T MRI is not sufficiently sensitive to reflect amyloid pathology. Therefore, translation of the methodology to 3T is not straightforward. In addition to differences in field strength, differences in scan parameters may have contributed to our findings.

Table 1: Mean phase shifts and SDs of the cortical regions in AD patients and control subjects.

	AD (rad) (n = 12)	Control (rad) (n = 12)	p-value
Frontal	0.19 ± 0.04	0.18 ± 0.02	0.89
Temporal	0.24 ± 0.04	0.23 ± 0.02	0.91
Parietal	0.20 ± 0.03	0.20 ± 0.03	0.52
Occipital	0.23 ± 0.04	0.22 ± 0.03	0.62
Whole brain	0.21 ± 0.03	0.21 ± 0.01	0.84

References:

1.Van Rooden et al., Alzheimers Dement 2013, in print.

2.Nakada et al., J Neuroimaging 2008;18:125-129.

3.Haacke et al., Magn Reson Med 2004;52:612-618.

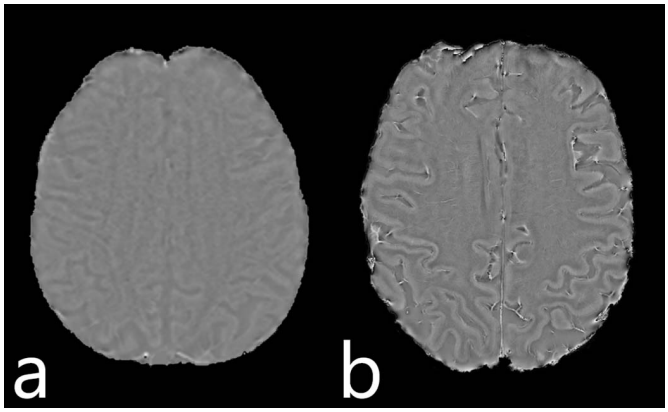

Figure 1: (a) 3T and (b) 7T T_2*- weighted gradient echo phase image of an AD patient.

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