Quantitative Susceptibility Mapping (QSM) in β-amyloid-PET-confirmed Alzheimers Disease at 7T

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PURPOSE: One of the key features of Alzheimer's disease (AD) is the accumulation of β-amyloid plaques in the brain [1]. Using tracers which target such plaques, positron emission tomography (PET) can diagnose AD at an early stage [2]. A recent mouse model study suggests that iron might also be an effective biomarker for this purpose [3]. Quantitative susceptibility mapping (QSM) has been shown to detect paramagnetic concentrations of iron in brain tissue [4]. The aim of this study is to examine whether magnetic susceptibility measured by QSM is increased in β-amyloid-PET-positive AD patients, compared to β-amyloid-PET-negative healthy controls, in regions typically affected by the disorder.

METHODS: We examined 6 AD patients (72±7 years, 2 female) and 10 age-matched healthy controls (67±4 years, 6 female). The PET data were acquired either at an EXACT HR+ scanner (Siemens, Erlangen, Germany) using 300 MBq (± 20%) of [^{18}F]-Florbetaben or at a Biograph mMR (Siemens, Erlangen, Germany) using 370 MBq (± 20%) [^{11}C]PiB. Both the AD patients and the healthy controls underwent an MRI scan (7T Siemens Magnetom). All measurements were approved by the local ethics committee. T1-weighted images as well as T1 maps were acquired using the MP2RAGE sequence [5]. To measure the field perturbation due to the magnetic susceptibility distribution a 3D high-resolution spoiled gradient echo (GRE) sequence was used (0.7 mm isotropic voxels; TR/TE=31/10 ms, acq. time 13 min). To remove the bias field due to B0 inhomogeneities, the phase images were high-pass filtered using the SHARP algorithm [6]. Quantitative susceptibility maps were calculated using the superfast dipole inversion approach to these data [7]. To coregister the QSM to the T1-weighted anatomy, the magnitude image of the GRE sequence was coregistered to the MP2RAGE image of the second inversion time. The resulting coregistration matrix was applied to the susceptibility maps. To analyze the same ROI's in both the QSM and β-amyloid-PET the PET data were coregistered to the T1-weighted anatomy as well.

RESULTS: Figure 1 shows a T1-weighted anatomical scan together with the thresholded and color-coded QSM (left column) and the β-amyloid-PET scan fused with the 7T MRI (right column) for one healthy control (top row) and one AD patient (bottom row). There is a striking difference in magnetic susceptibility distribution between this AD patient and the control subject. Across the group, QSM values in the AD patients were significantly increased compared to healthy controls ($p=0.017$). The regional analysis showed a significant ($p<0.05$) increase of QSM values in regions typically affected in AD, e.g., bilateral superior frontal cortex and bilateral parietal cortex, right temporal cortex as well as left precuneus.

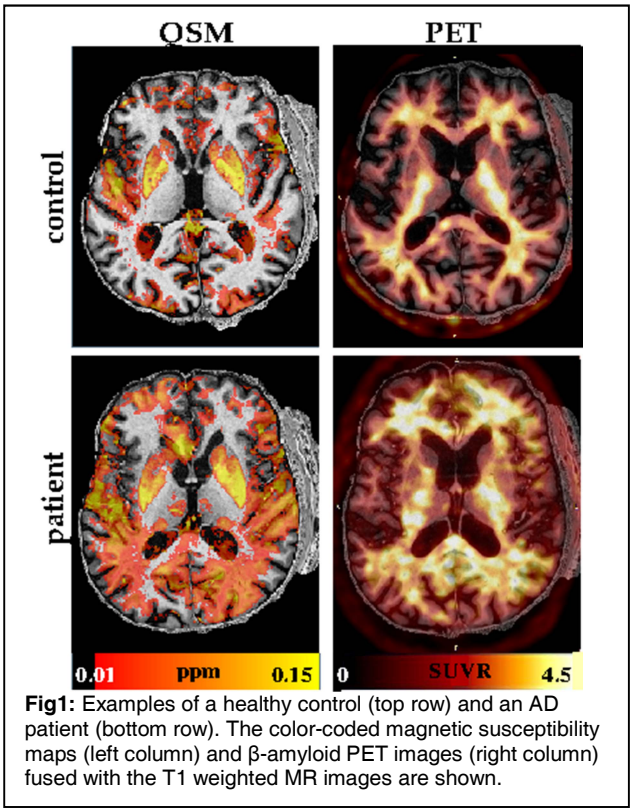

Fig1: Examples of a healthy control (top row) and an AD patient (bottom row). The color-coded magnetic susceptibility maps (left column) and β-amyloid PET images (right column) fused with the T1 weighted MR images are shown.

DISCUSSION: Our 7Tesla data show for the first time that the susceptibility of GM is increased in β-amyloid-PET-positive AD patients as compared to β-amyloid-negative healthy controls in-vivo. This more paramagnetic behavior could be due to an increased iron accumulation in brain regions in Alzheimer disease [8], which may coincide already with early plaque formation [3]. Whether the iron is increased within or around the β-amyloid plaques is a question that can be addressed only with histological studies [3]. Future studies will also include QSM at 3 Tesla using simultaneous PET/MR, to determine whether 3T QSM is sensitive enough to detect differences in magnetic susceptibility in Alzheimer patients compared to healthy controls.

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