Quantitative Susceptibility Mapping (QSM) in Alzheimer's Disease - A Postmortem Study

Andreas Schäfer[1], Solveig Tiepolt[2], Elisabeth Roggenhofer[1], Robert Trampel[1], Carsten Stueber[1], Vilia Zeisig[2], Udo Grossmann[2], Thies H. Jochimsen[2], Osama Sabri[2], Robert Turner[1], and Henryk Barthel[2]

[1]*Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig, Germany,* [2]*Department of Nuclear Medicine, University of Leipzig, Leipzig, Germany*

PURPOSE: It has been shown that positron emission tomography using tracers which target β-amyloid plaques is an excellent tool to diagnose Alzheimer's disease (AD) in an early stage [1]. Furthermore, iron is accumulated in regions with β-amyloid plaques [2-4]. The aim of this study is to investigate whether a difference in quantitative magnetic susceptibility values in gray matter between postmortem tissue samples of AD patients and healthy controls can be detected using magnetic resonance imaging, via the high sensitivity of quantitative susceptibility mapping (QSM) to iron content [5].

METHODS: Two different human brain tissue samples of the frontal lobe from the Netherlands Brain Bank were scanned at a 7Tesla whole body scanner: One sample was obtained from an AD patient in which histopathology was positive for β-amyloid plaques (age: 66 years). The second sample was from a β-amyloid-negative control subject without AD (age: 60 years). These formalin fixed tissue samples were washed in a phosphate buffered solution to increase the transverse relaxation times and then placed in a spherical container containing agar gel. To measure the field perturbation due to the magnetic susceptibility distribution a 3D high-resolution spoiled gradient echo sequence was used (170 µm isotropic voxels; TR/TE=500/23 ms, no averaging). 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 filtered phase images at three different orientations to the main magnetic field (-60, 0, +60 degree) and applying the COSMOS approach to these data [7].

RESULTS: Figure 1 shows a T1-weighted anatomy scan (top row) together with the QSM (bottom row) for both tissue samples. For the healthy control sample the magnetic susceptibility values are smaller (i.e. more diamagnetic) for the GM than for the agar gel, and also smaller than in white matter. In contrast the susceptibility values of GM of the diseased sample are more positive and thus more paramagnetic. Quantitative analysis of QSM values for the entire GM yielded susceptibility values of -0.008±0.003 ppm and 0.011±0.002 ppm compared to agar gel for the healthy and diseased tissue sample, respectively. This is shown in Figure 2.

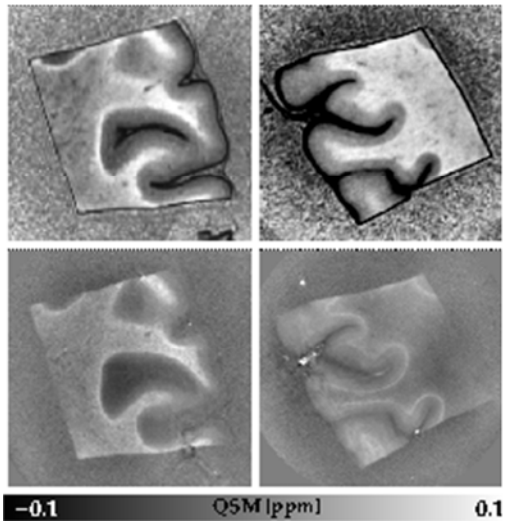

Fig. 1: The T1-weighted anatomy (top row) and the QSM (bottom row) are shown for the healthy control (left column) and the Alzheimer's disease (right column) sample.

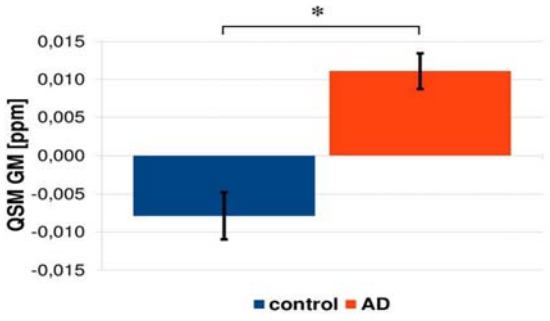

Fig 2: QSM values for the entire GM for both healthy and diseased tissue.

DISCUSSION: Usually the magnetic susceptibility of GM is more paramagnetic than WM. In the frontal lobe of the human brain the QSM GM-WM contrast is reversed. This accords with a recent finding by Deistung et al. [8]. However, our data show that the susceptibility of GM is increased in AD, probably due to increased iron accumulation in regions with β-amyloid plaques. This is important, since the resolution of MRI is insufficient to image β-amyloid plaques directly in vivo, since these usually have a size of 20-50 µm in diameter.

CONCLUSION: We have measured a significant susceptibility difference in the GM between β-amyloid-positive AD and β-amyloid-negative control tissue, with higher values for the AD tissue. Future work will not only correlate the QSM data with histopathological and autoradiographical data on the concentration of beta-amyloid plaques, but also with data on the brain tissue iron concentration.

REFERENCES:

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