

## A Quantitative Susceptibility Mapping (QSM) Analysis in Subjects with Alzheimer's Diseases and Mild Cognitive Impairment

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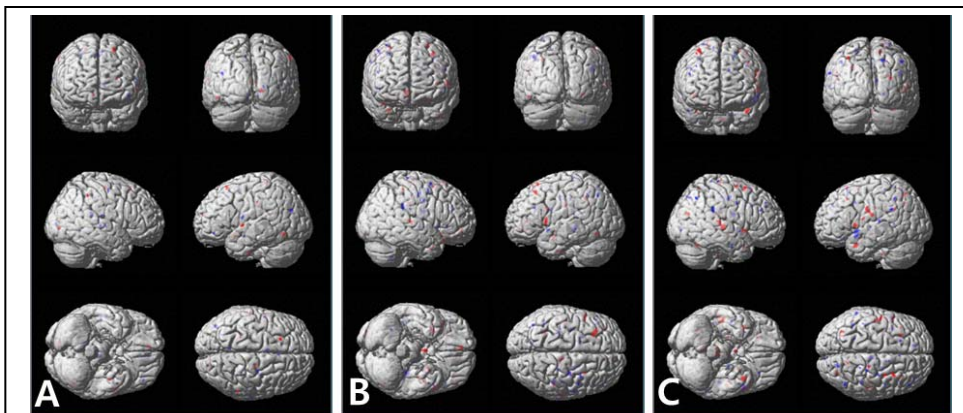
**Introduction:** Although susceptibility weighted imaging (SWI) has been widely used to reinforce susceptibility effects by combining magnitude images with phase images [1], the exact quantification of the iron contents could not be achieved due to its strong dependency on the shape and orientation of the structures; therefore, the final SWIs is not only affected by susceptibility effects but also by geometric factors such as voxel size and by acquisition parameters such as field strengths and echo time [2]. Alternatively, the quantitative susceptibility mapping (QSM) technique proposes a new way to estimate the amounts of irons. Being the new method to quantify susceptibility effects, QSM has much potential in clinical researches to elucidate physiological roles and variations of iron concentration relative to a number of neurological disorders. Therefore, the objective of this study was to differentiate quantitative susceptibility effects in subjects with cognitive normal (CN), mild cognitive impairments (MCI) and Alzheimer's diseases (AD).

**Methods and Materials:** Twenty CN subjects (mean age = 66.0, 18 females and 3 males), 21 MCI subjects (mean age = 65.7, 12 females and 9 males), and 21 AD subjects participated after informed consent. The MR imaging was performed on a 3T MR system (Achieva, Philips), and a fully first-order flow-compensated 3D gradient echo sequence ran to obtain magnitude and phase images, which were later used to produce final QSM. Furthermore, sagittal structural three-dimensional T1-weighted (3DT1W) images were acquired with the magnetization-prepared rapid acquisition of gradient echo (MPRAGE) sequence for the brain segmentation and image registration. The RDF (Removal Dipole Field) and QSM images for each group were produced by implementing the Morphology Enabled Dipole Inversion (MEDI) method, which aims to minimize differences between acquired phase images and real susceptibility effects [3]. The phase, RDF, and QSM images were co-registered with 3DT1W images and normalized to a Korean standard structural brain template for the elderly [4] using a Statistical Parametric Mapping Version 8 (SPM8) program. The QSM images were smoothed using a 4 x 4 x 4mm Gaussian kernel. The differences of phase, RDF, and QSM among the three groups were investigated by performing a voxel-based statistical analysis using a one-way analysis of variance (ANOVA) test. The gender and age information were included as covariates.

**Results:** Fig.1 demonstrates the differences of QSM values emerged among three different groups. Compared with MCI subjects, QSM values in CN subjects were high in the left superior frontal gyrus and the left superior temporal gyrus. The lower signals were also found in the left superior frontal gyrus and the left superior temporal gyrus. Compared with the AD group, the QSM values in CN subjects were high in the left parahippocampal gyrus and the left inferior frontal gyrus but low in the right cingulate gyrus. Compared with AD patients, QSM values in MCI subjects were high in the right superior temporal and the left superior temporal but low in the left middle frontal gyrus.

**Discussion:** Quantifying iron concentrations in vivo is instrumental for understanding the role of irons in many neurological diseases. The QSM technique has been proposed to accurately estimate the amounts of irons, which advanced the previous SWI technique. The objective of this study was to utilize a QSM technique to investigate different susceptibility effects among three different groups, CN, MCI and AD, through a direct voxel-by-voxel comparison of the whole brains. QSM values would decrease from CN to MCI and to AD, since iron is a paramagnetic substance and contributes to dephasing of the signals. Because AD is expected to have the most iron plaques, we expected that the AD brains would produce the

least signals in comparison to the CN and MCI brains; however, some higher QSM signals in AD were also found when MCI and CN groups were compared with an AD group. We assumed that these higher signals in AD may be attributed to the presence of the diamagnetic substances such as calcium, which needs further investigations on possible presence of these materials in AD subjects. Our statistical analysis also illustrates that more differences were found when CN and AD groups were compared than when CN and MCI groups were compared. Also, the most differences were found between the signals between the MCI group and the AD group. Although MCI is known to be an intermediate stage moving from CN to AD, our result suggests that some severe changes might occur in a MCI stage that produces the opposite effect of AD. However, what the change is and how it occurs are



**FIG.1.** The results of difference of QSM data between three subject groups. A: Red: CN>MCI, Blue: CN<MCI, B: Red:CN>AD, Blue :CN<AD, and C: Red: MCI>AD, Blue:MCI<AD.

unknown and are subject to further investigations.

**Conclusion:** Throughout the study, we were able to conduct a voxel-based analysis of QSM images among CN, MCI and AD groups. We were able to identify the brain regions in which the susceptibility changes occurred among the different groups. We therefore suggest the voxel-based analyses to investigate susceptibility effects using QSM images.

**Acknowledges:** This research was supported by a grant of the Korean Health Technology R&D Project, Ministry for Health, Welfare & Family Affairs, Republic of Korea (A111282).

**References:** : 1. Haacke, E.M., AJNR Am J Neuroradiol, 2009, 30:19-30, 2. de Rochefort, Magn Reson Med 2010, 63:194-206, 3. Liu T, Magn Reson Med, 2011, 66:777-783, 4. Kim, M.J., J Korean Soc Magn Reson Med, 2010, 14:103-114.