Quantitative Susceptibility Mapping (QSM) of the Motor Cortex as a Potential Biomarker in Amyotrophic Lateral Sclerosis (ALS)

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INTRODUCTION. Amyotrophic lateral sclerosis is a rapidly progressive, invariably fatal neurological disease that attacks both upper and lower motor neurons. Patients with amyotrophic lateral sclerosis (ALS) demonstrate T2 hypointensity in the motor cortex, possibly due to the T2* effect of deposition of paramagnetic species such as iron [1]. However, there currently exists no quantitative laboratory, imaging, or electrophysiological test that correlates with disease severity. Quantitative susceptibility mapping (QSM) is a novel MRI technique whose pixel intensity directly reflects tissue susceptibility [2]. We sought to determine whether ALS patients, when compared to those without the disease, demonstrate a quantifiable increase in tissue susceptibility.

MATERIAL AND METHODS. *Data acquisition*: Six patients with clinically confirmed ALS and 30 age- and sex-matched control patients were retrospectively analyzed. MR examinations were performed on a 3.0T scanner (GE Excite HD) using a 3D multi gradient echo sequence (TE/ΔTE/#TE = 5ms/5ms/11, TR/FA/BW=59ms/20°/±62.50 kHz, voxel size=0.57×0.75×3mm^3). *Data analysis*: Real and imaginary images were saved and the morphology enabled dipole inversion with nonlinear formulation (MEDIN) method [2-5] was used for QSM reconstruction. The motor cortices of each ALS and control patient were outlined on each axial slice in a standardized fashion under the guidance of an experienced neuro-radiologist. A semi-automatic program refined the segmentation between the motor cortex and the surrounding white matter by applying a threshold (Fig. 1a). *Statistical analysis*: The mean susceptibility was calculated in the entire motor cortex volume as well as in the hand lobule on a single slice, respectively. Linear regression was performed between these mean values. Wilcoxon rank sum test was used to evaluate for statistical differences between ALS and control groups.

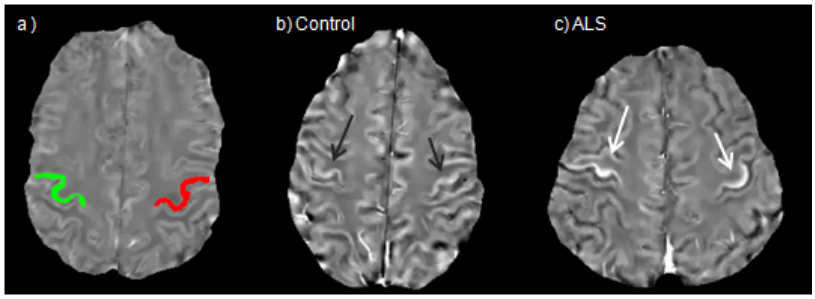

Fig. 1. a) Example of the segmented hand lobules with the characteristic inverted omega shape. b&c) are QSM images of a control and an ALS patient, respectively.

RESULTS. Exemplary QSM from a control (Fig 1b) and an ALS patient with strong hyperintensity (Fig. 1c) in the motor cortex that incorporated the hand lobule are shown in Fig. 1. There was a strong correlation between the mean susceptibility measured in the hand lobule only and the mean susceptibility measured in the entire motor cortex volume (Fig. 2). The difference between the ALS group and the control group was statistically significant using either mean susceptibility measurements (Fig. 3, p=2.7×10^{-4} in hand lobule, p=2.0×10^{-4} in motor cortex volume).

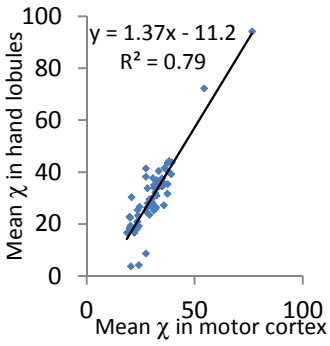

Fig. 2. Linear regression between mean susceptibility in the hand lobule and in the entire motor cortex.

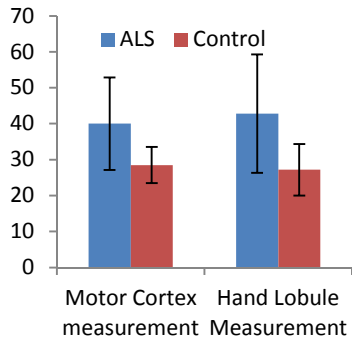

Fig. 3. Mean susceptibility of ALS and control group using volume and hand lobule measurement.

DISCUSSION AND CONCLUSION. The strong linear correlation between susceptibility in motor cortex and in hand lobule is expected because ALS affects all muscles. The correlation supports the use a single slice for disease characterization [1]. This pilot study demonstrates that QSM has the potential to be the first quantitative imaging biomarker for patients with ALS. Further studies are necessary to determine whether QSM signal in the motor cortex correlates with disease severity in ALS.

REFERENCE. [1]Oba et al. Radiology:189:843-6; [2] de Rochefort et al. MRM:63(1):194-206. [3] Liu et al. MRM:66(3):777-83. [4] Liu et al. Neuroimage:59(3):2560-8. [5] Liu et al. MRM: doi: 10.1002/mrm.24272