Regional Analysis of Automated Magnetization Transfer in Multiple Sclerosis

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Background. Magnetization transfer imaging (MTI) has been extensively studied in patients with multiple sclerosis (MS). While a bulk of studies have shown differences in magnetization transfer ratio (MTR) between MS and normal controls (NC), the most localized MTR data reflects only whole brain white matter (WM) and gray matter (GM) subdivisions.

Objective. To develop and validate a method for automated generation of regional MTR maps and apply this method to study of regional specific MTR changes in MS patients versus NC.

Design/Methods. We examined 24 patients with MS (age 47.5 +/- 8.4) and 8 healthy controls (age 32.9 +/- 13.9). All patients underwent 1.5 Tesla MRI scan. Patient disease status was as follows: relapsing remitting (RR) = 11 and secondary progressive (SP) = 13. Mean disease duration was 12.13 +/ 8.6. Mean EDSS was 3.7 +/ 2.2. Regions of the brain were determined using our semiautomated brain region extraction (SABRE) process. Briefly, 14 landmarks were manually identified on 3D T1-SPGR images to provide regional boundaries and coordinates for an individualized Tailarach mask. The algorithm automatically generated 26 regions (13 left, 13 right): frontal (medial and lateral superior and inferior, medial and lateral orbitofrontal), temporal (anterior and posterior), parietal (superior and inferior), occipital, basal ganglia (BG)/thalamus (anterior and posterior). These regional masks were automatically applied to MTR maps. MTR maps were further split into cerebrospinal fluid (CSF), GM and WM compartments. In order to minimize partial volume effects, the CSF mask was radially grown by one voxel and then subtracted from GM and WM masks, minimizing CSF inclusion in a parenchymal mask. Peak height (PH), peak position (PP) and mean MTR in each of the 26 regions were automatically calculated. The overall regional MTR showed an excellent level of reproducibility across 26 regions with intra- and inter-rater coefficient of variation (COV) = 0%, scan-rescan COV =0.77%, and inter-scanner COV =1.46%. Parametric and non-parametric statistics and a multivariate generalized linear model were used for group comparisons when age may have been a confounder. A conservative alpha level of $p<.01$ was considered significant due to the exploratory nature of the study.

Results. Mean MTR was lower in MS patients than NC in all regions. MTR characteristics of MS patients that differed significantly at alpha level of .01 from NC were as follows: left inferior frontal ($p=.009$), left medial inferior frontal ($p=.005$), and left posterior basal ganglia/thalamus ($p=.004$). After adjustment for age, only the mean MTR of left posterior basal ganglia/thalamus ($p=.003$) remained significantly different between MS patients and NC. Mean GM MTR of that region differed significantly ($p=.003$) between MS patients and NC. This region showed a trend of lower mean MTR in SP vs. RR patients ($p=.03$).

Conclusions. To the best of our knowledge this is the first study using regional MTR to reveal MTR changes in number of specific brain regions. The study results showed that our automated regional MTR approach is highly reproducible, accurate, reliable, and clinically relevant. MTI is sensitive to regionalized changes in MS, these changes occur selectively in specific subregions, and further postprocessing advancements can increase the sensitivity and utility of this modality.