Quantitative Diffusion Weighted Imaging Measures in Multiple Sclerosis patients

E. Tavazzi[1], M. G. Dwyer[1], B. Weinstock-Guttman[1], J. M. Lema[1], S. Bastianello[2], R. Bergamaschi[2], V. Cosi[2], R. H. Benedict[1], F. E. Munschauer[1], R. Zivadinov[1]

[1]Buffalo Neuroimaging Analysis Center, Jacobs Neurological Inst, SUNY at Buffalo, Buffalo, New York, United States, [2]Neurological Institute Casimiro Mondino, Pavia, Italy

Objective: 1) To show the validity of a new and fully automated method for the measurement of quantitative diffusion weighted imaging (DWI) parameters; 2) To correlate whole brain (WB)-DWI variables and clinical and MRI measures of disease severity in a large cohort of multiple sclerosis (MS) patients.

Background: Several pieces of evidence in literature indicated DWI as a sensitive measurement of disease burden able to detect subtle changes in white matter (WM) and grey matter (GM) in MS. However, only few studies have applied whole brain DWI indices to the study of MS clinical subtypes.

Design/Methods: We studied 437 MS patients (age=44.3 ± 10.2 years) and 28 normal controls (NC) using 1.5 T brain MRI. Clinical disease subtypes were as follows: 289 relapsing-remitting (RR), 118 secondary-progressive (SP), 15 primary-progressive (PP) and 15 clinically isolated syndrome (CIS). Mean disease duration (DD) was 11.9 ± 8.6 yrs. Mean Expanded Disability Status Scale (EDSS) was 3.2 ± 2. 3D-SPGR-T1 and conventional dual-echo and DWI scans were performed on all subjects. After classification into GM and WM compartments, brain parenchymal fraction (BPF), GM and WM fractions were calculated using fully automated Hybrid SIENAX method. Parenchymal mean diffusivity (PMD) maps were created voxel-by-voxel after fully automated segmentation of the brain parenchyma and CSF using T2-WI. In order to minimize partial volume effects, the PMD map was eroded by one voxel using an automated 3D erosion algorithm. Histogram analysis for each subject was performed on the PMD map, and DWI indices of peak position, peak height, mean diffusivity (MD) and entropy were obtained. The reproducibility of DWI measures was as follows: inter- and intra-rater coefficient of variation (COV) = 0%, scan-rescan COV = 1.08 % for MD and 1.01% for entropy. T2- and T1-lesion volumes (LV) and EDSS were also assessed for all patients. Parametric, correlation and multiple regression analysis have been performed.

Results: In our cohort of subjects, MS patients were significantly different from NC in MD ($p<.0001$) and entropy ($p=0.001$) (Figure 1). RR and SP significantly differ with respect to all DWI indices (peak height and entropy: $p<.0001$; MD $p=.046$). Entropy and peak height were significantly different between SP and CIS patients ($p<.001$). In RR and SP patients, we found stronger correlation between entropy and the following MRI variables than with MD: BPF ($r=-0.67$, $p<.0001$ and $r=-0.39$ $p=.001$), GM fraction ($r=-0.58$, $p<.0001$ and $r=-0.24$, $p<.001$), T1-LV ($r=0.59$, $p<.001$ and $r=0.23$, $p=.001$) and T2-LV ($r=0.54$, $p<0.001$ and $r=0.29$, $p<0.001$). DWI entropy showed also a stronger correlation than MD with EDSS ($r=0.37$, $p<.001$ and $r=0.17$, $p=.001$) (Figure 2) and DD ($r=0.35$, $p<0.001$ and $r=0.12$, $p=.001$). In RR patients entropy was the best predictor of clinical disability ($p<.001$).

Conclusions: This study showed the capability of our fully automated DWI method to distinguish differences between NC and MS patients as well as between MS subtypes, suggesting a higher sensitivity in identifying tissue dysfunction. The observed correlations between entropy and other MRI and clinical measures of disease severity make this automated method a powerful diagnostic and prognostic tool in MS.

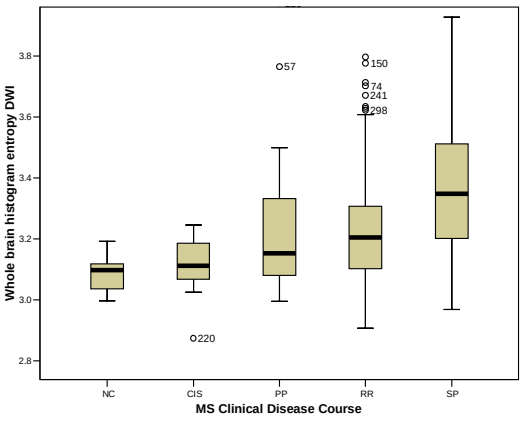

Figure 1

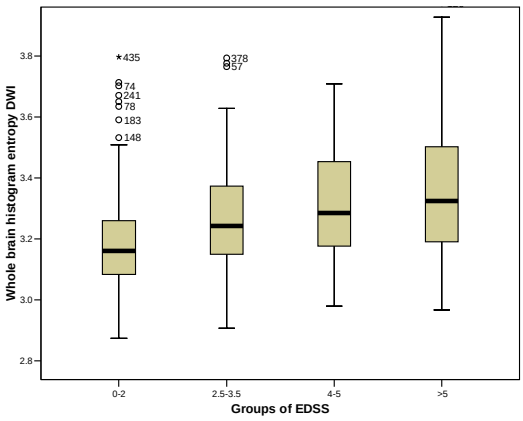

Figure 2