Longitudinal analysis of advanced and conventional magnetic resonance imaging measures of disease impact in multiple sclerosis

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Target audience: *Clinicians interested in multiple sclerosis, quantitative mapping and longitudinal analysis*

Purpose: Conventional magnetic resonance imaging (MRI) of patients with multiple sclerosis (MS) provides only limited insights into the nature of brain tissue damage with modest clinical-radiological correlations. In a previous work [1], we explored the potential of combining non-conventional MRI relaxometry (T1, T2 and T2*) and magnetization transfer imaging to identify brain tissue alteration processes and provided new biomarkers of disease impact. In this study, we evaluated the 2 years longitudinal evolution of conventional and non-conventional markers of MS disease, in a cohort of patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: Twenty-three RRMS patients characterized by: age range, 20-60 years; gender ratio: 14/9 women/men; disease duration: 31 ± 23 months (mean ± std-dev.); Expanded Disability Status Scale-EDSS at enrolment: 1.6 ± 0.3 (mean ± std-dev); at follow-up: 1.7 ± 0.2 as well as 8 age-matched healthy controls were examined at enrolment and at 2 years follow-up. All patients were under effective immunomodulatory treatment (high dosage interferon beta or fingolimod) and had no evolution in disability score (EDSS) over 2 years. T1, T2, T2* relaxometry and magnetisation transfer ratio (MTR) were performed at 3T (MAGNETOM Tim Trio , Siemens AG, Erlangen, Germany). The protocol included : high-resolution 3D fluid attenuated inversion recovery (FLAIR) (TR/TE/TI = 5000/394/1800 ms, voxel size = 1.0×1.0×1.2 mm^3, FoV = 256×240×223.2 mm^3); 3D double inversion recovery (DIR) (TR/TE/TI = 10000/218/3650 ms, voxel size = 1.1×1.0×1.2 mm^3, FoV = 256×240×192 mm^3), MPRAGE (TR/TE = 2300/2.98 ms, voxel size = 1×1×1.2 mm^3, FoV = 256×240×160), MP2RAGE (TR/TE = 5000/3 ms, TI1/TI2=700/2500 ms, FA1/FA2 = 4°/5°, voxel size = 1×1×1.2 mm^3, FoV = 256×240×160), T2 relaxometry (TR/TE = 5850/9-189 ms, 21 echoes, voxel size = 1×1×4 mm^3, FoV = 30×192×160), T2* relaxometry (TR = 47ms, 32 echoes, voxel size = 1.6×1.6×1.6 mm^3, FoV = 217×217×179 mm^3) with and without magnetization transfer (MT) pulse. T2* maps were obtained using a correction method based on an estimated B1 field map. MTR were computed from the T2* data. T2 maps were estimated from the multi spin-echo data using a model-based reconstruction [2]. T1 maps were derived from the MP2RAGE volume [3]. MPRAGE, T2* echoes and T2 maps were linearly registered to respectively MP2RAGE volumes and T1 maps using ELASTIX [4]. In order to evaluate normal-appearing tissue properties, regions of interest (ROIs) were then automatically extracted from the MPRAGE images using an automated morphometry package [5]. The following ROIs were obtained: white and cortical gray matter, thalamus and basal ganglia, cerebellar WM and GM. In addition, we computed lobar WM and GM (temporal, occipital, frontal, parietal). WM and cortical lesions (plaques) in patients were automatically detected and segmented using an inhouse k-nearest neighbourhood algorithm applied to FLAIR, DIR and MP2RAGE images. Lesions masks were subtracted from the 8 ROIs in order to obtain regions of NA tissue. The mean T1, T2, T2* and MTR difference between 2 time points was computed for MS patients and HC. This difference was reported as % parametric variation at 2 years follow-up compared to the first time point. A two-sample permutation t-test corrected for family-wise error rate was performed to assess parametric differences in NA tissue in all ROIs between the two time points. Lesion count and lesion volume differences between time points were also computed for all patients. Last, Spearman correlation coefficients were computed between lesions properties changes (number and volumes) in each single patient and longitudinal parametric changes in his/her NA parametric properties in the 8 ROIs.

Results: The analysis of longitudinal changes of T1, T2, T2* and MTR mean values in the 8 NA ROIs showed no significant differences between HC and RRMS patients. Although patients showed individual variations, the overall number and volume of lesions in our cohort of patients decreased slightly over 2 years (Fig. 1). In addition, no significant correlation was found between parametric properties in NA ROIs in each patient and the longitudinal variation in lesion number and volume.

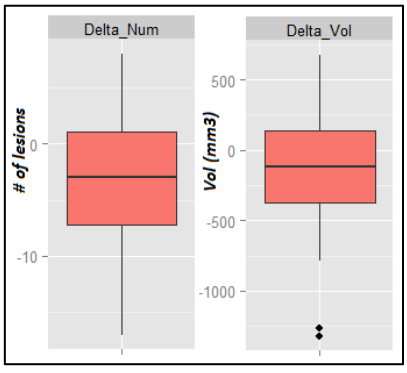

Figure 1. Boxplot of difference of lesion number (left) and volume (right) for MS patient between time point 1 and time point 2.

Conclusion: Our cohort of RRMS patients, under effective therapy and with stable disability scores for 2 years, did not show any longitudinal evolution of microstructural properties in NA brain tissue. In addition, local signs of inflammation and degeneration (MS plaques) appeared to decrease slightly over a 2 years follow-up period. Nevertheless, no correlation was found between individual plaques changes (number and volumes) and microstructural properties of brain and cerebellar ROIs, pointing at the complementarity of conventional and advanced MRI measures for appropriate patient follow-up. Patient enrolment is ongoing in order to extend current results to a larger cohort of MS patients and establish the predictive value of conventional and unconventional disease biomarkers.

References: *1.Bonnier G. et al. 2014 2. Sumpf et al Magn Reson Imaging 2011, 34(2):420-428; 3. Marques JP et al. NeuroImage 2010, 49:1271-1281; 4. Klein et al. IEEE 2010, 29:196-205; 5. Schmitter et al. , 2014, NeuroImage : Clinical*

Acknowlegment : *This study is supported by the UNIL, UNIGE, HUG, CHUV, EPFL and the Leenaards and Jeantet Foundations.*