EXPLORATION OF ADVANCED MR IMAGING CONTRASTS FOR AUTOMATED DETECTION OF WHITE MATTER AND CORTICAL LESIONS IN EARLY-STAGES OF MULTIPLE SCLEROSIS

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Introduction: Multiple Sclerosis (MS) is a disease characterized by inflammation, demyelination and neurodegeneration, affecting both white matter (WM) and grey matter (GM). MS lesions are a hallmark of the disease and their number and location are important both for diagnosis and patient follow-up. Several research groups have proposed image processing methods to automatically detect and segment MS lesions[1]. Nevertheless, existing methods are exclusively dedicated to WM lesions and are mostly applied to MS patients with long disease duration. Recently, advanced magnetic resonance imaging (MRI) sequences such as double inversion recovery (DIR) and high-resolution magnetization-prepared 2 rapid acquisition gradient echoes (MP2RAGE) have proven to be sensitive to the presence of cortical lesions[2,3]. Moreover, 3D volumetric brain imaging sequences are widely available today and provide high spatial resolution and optimized contrasts supposedly allowing the detection of smaller lesions such as often encountered in early stages of the disease[3,4].

Purpose : The aim of this study was to investigate the contribution of advanced MRI sequences on the performance of an automated lesion detection tool in early-stage MS patients. In addition, more than existing state-of-the-art methods, we targeted both WM and cortical lesions, starting from a small lesion volume of 3.6 µL.

Materials and Methods: Thirty-nine patients (14 males, 25 females, median age 34 years, age range: 20-60) with early relapsing-remitting MS (RRMS, disease duration < 5 years from diagnosis) and Expand Disability Status Scale (EDSS) score between 1 and 2 (median EDSS=1.5), benefitted from a 3T MRI scan (MAGNETOM Trio a TIM System, Siemens AG, Erlangen, Germany) using a 32-channel head coil. The MRI protocol included: (i) high-resolution magnetization-prepared acquisition with gradient echo (MPRAGE, TR/TI= 2300/900 ms, voxel size = 1.0 x 1.0 x 1.2 mm^3) (ii) MP2RAGE (TR / TI1 / TI2=5000/700/2500 ms, voxel size = 1.0 x 1.0 x 1.2 mm^3) (iii) 3D fluid-attenuated inversion recovery (FLAIR, TR/TE/TI=5000/394/1800 ms, voxel size = 1.0 x 1.0 x 1.2 mm^3) and (iv) 3D DIR (TR/TE/TI1/TI2=10000/218/450/3650 ms, voxel size = 1.1 x 1.0 x 1.2 mm^3). All imaging volumes of MPRAGE, FLAIR and DIR were intensity-normalized[5]. Automated lesion detection was performed by a supervised classifier based on k-nearest-neighbor (k-NN) algorithm only for use in this research study. The features used for classification were: i.) image intensity (a combination of MPRAGE, MP2RAGE, FLAIR and/or DIR); ii.) spatial location[6] (coordinates in mm) in Montreal Neurological Institute (MNI) space and iii.) tissue prior probabilities[7] provided by the International Consortium for Brain Mapping (ICBM). Manual detection of lesions from two experts (a neurologist and a radiologist) was used as a ground truth as well as to train the classifier. Lesion detection performance was evaluated for different combinations of the advanced MRI protocol through a "leave-one-out" cross-validation. Detection rate sensitivity (number of detected lesions/total ground truth lesions) was obtained for each combination of the MRI sequences and statistical differences were computed using the Wilcoxon signed-rank test.

Results : The best detection rate of WM lesions as small as 3.6 µL (3 image voxels) in our cohort of early MS patients was obtained using MP2RAGE, FLAIR and DIR intensities, with a median of 77% (Figure 2a). Similar results were obtained excluding the DIR intensity as well as when using both MPRAGE and FLAIR. The best detection sensitivity for the automated detection of cortical lesions was obtained when DIR and MP2RAGE were included, with a median sensitivity of 62% (Figure 2b).

Discussion & Conclusion: 3D FLAIR combined with advanced sequences such as DIR and MP2RAGE provided a very good sensitivity to detect WM lesions in early MS stages, including very small lesions. Considering that the prolonged acquisition time for DIR and MP2RAGE may be not acceptable in a clinical setting, it should be noted that similar results were observed when using only "conventional" clinical product sequences (3D FLAIR and MPRAGE, p=0.10). The automated detection of cortical lesions, however, is more challenging due to the low number of cortical lesion samples in our cohort for training and the fact that cortical lesions are strongly affected by partial volume (small size and location at WM/GM tissue interface). Our results show that using advanced sequences such as MP2RAGE and DIR, the automated detection rate sensitivity of cortical lesions can be significantly increased (p<0.01).

References: [1] Garcia-Lorenzo et al. Med image Anal. 2013; [2] Geurts et al. Radiology. 2005; [3] Kober et al, Invest Radiol. 2012; [4] Bonnier et al., Annals of Clinical and Translational Neurology. 2014; [5] Nyul et al. IEEE 22 Transactions on Medical Imaging. 2000; [6] Anbeek et al. Neuroimage. 2004; [7] Steenwijk et al. Neuroimage Clin. 2013; **Acknowledgements**: This work was supported by the Swiss National Science Foundation under grant PZ00P3_131914/11; The Swiss MS Society and the Societé Académique Vaudoise, the CIBM of the University of Lausanne (UNIL), the Swiss Federal Institute of Technology Lausanne (EPFL), the University of Geneva (UniGe), the Centre Hospitalier Universitaire Vaudois (CHUV), the Hôpitaux Universitaires de Genève (HUG) and the Leenaards and the Jeantet Foundations.

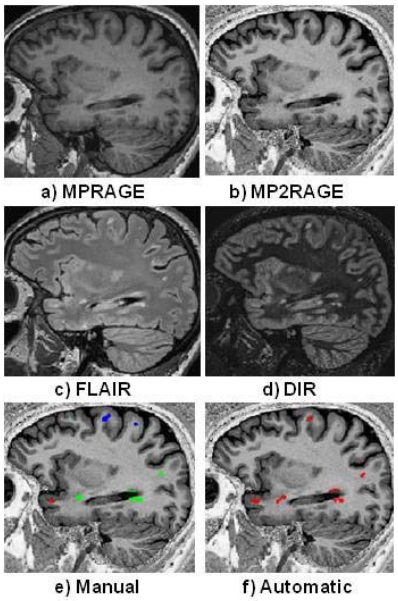

Figure 1 - Slices of different image contrasts (a-d), manual and automated segmentations (e-f). In the manual segmentation, white matter lesions are shown in green and cortical lesions in red and blue.

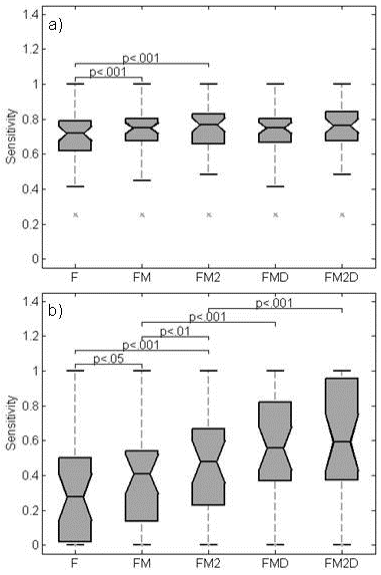

Figure 2 - Boxplot representing the distribution of the detection rate sensitivity in a) WM lesions and b) cortical lesions. The x-axis is labeled with different features configurations where F, M, M2 and D represent FLAIR, MPRAGE, MP2RAGE and DIR respectively. FM means FLAIR+MPRAGE and so on. MNI coordinates and ICBM prior tissue probabilities are included as features.