COMPARISON OF SEGMENTATION TECHNIQUES TO MEASURE TISSUE-SPECIFIC ATROPHY IN MULTIPLE SCLEROSIS

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TARGET AUDIENCE: Physicians and scientists interested in brain tissue segmentation in neurological diseases.

PURPOSE: To investigate the performance of SPM12 and a novel brain segmentation technique GIF in a pilot study of people with MS and HC.

INTRODUCTION: Reliable and accurate automated MRI image segmentation techniques are a key goal of current imaging analysis research. Brain atrophy is a well established feature of multiple sclerosis (MS) pathologically and is principally driven by the effects of irreversible neuroaxonal loss. Rates of brain atrophy in MS vary in different tissue compartments, and grey matter (GM) atrophy in particular has been shown to correlate with clinical outcomes at all stages of the disease. There is growing interest in the use of tissue-specific brain atrophy measures in MS clinical trials. Statistical Parametric Mapping (SPM) is an established segmentation method that is based on a mixture of Gaussians[1]. GIF is a novel segmentation technique that uses imaging databases as sources of information[2]. GIF can thus be used to propagate any information from any group of subject to every other subject in a database with great accuracy. This study compares GIF, which has not been previously applied in people with MS, to SPM12 results.

METHODS: ***Subjects:*** Five people with MS and 5 healthy controls (HC). ***MR acquisition:*** Acquisition was performed on a 3 T Philips Achieva system (Philips Medical Systems, Best, The Netherlands) with a 32-channel head coil. The protocol consisted in (i) multi-echo PD/T2 for lesion marking: voxel size 1x1x3mm^3, TE=15/85ms, TR=3500ms (ii) 3-D T1-weighted gradient echo for tissue segmentation: voxel size 1x1x1mm^3, TE=3.1ms, TR=6.8ms, TI=824ms. ***Lesion filling:*** T2 hyperintense lesions were marked by an experienced observer on the PD-weighted images using a semi-automated edge finding tool (JIM v6.0, Xinapse systems, Aldwincle, UK, http://www.xinapse.com). The same observer marked all lesions (WB). The PD-weighted images were co-registered to the 3D-T1 images using an automated technique[3] that relies on a non-local patch match strategy; the transformation matrix was then applied to the lesion mask. The data was corrected for intensity inhomogeneity using a bias field correction[4]. ***Tissue segmentation:*** Tissue volumes were calculated taking into account all the voxels with a probability higher than 25%, and the voxel volume was then added to the tissue class with maximum probability inside each voxel. ***Analysis:*** Total intracranial volume (TIV) was determined by adding the GM, white matter (WM) and CSF volumes. Brain parenchymal fraction (BPF), and grey and white matter fractions (GMF and WMF) were calculated using respectively (WM+GM)/TIV GM/TIV and WM/TIV. The comparison between techniques was performed using linear correlation and paired t-test. Qualitative assessment was performed in a blinded fashion by three experienced neurologists (DC, MP, WB) who qualitatively rated the accuracy (0=poor, 1=fair, 2=good) of tissue segmentation at five anatomical sites (pons, above the globe, the genu of the corpus callosum (CC), top of the CC and 2cm above CC).

RESULTS: Table 1 shows the results for HC and MS applying the proposed analysis. Figure 1 shows axial and coronal segmentation result. Mean and standard deviation of the qualitative accuracy analysis between observers was 0.203±0.292 for SPM12 and 0.740±0.116 for GIF.

HC	SPM12	GIF	r, paired t-test	MS	SPM12	GIF	r, paired t-test
GM	785.92 (60.9)	648.56 (49.8)	0.956,p<0.05	GM	758.18 (116.2)	666.18 (100.5)	0.962,p<0.05
WM	440.60 (63.5)	456.42 (55.8)	0.988,p<0.05	WM	438.19 (101.1)	468.38 (93.1)	0.989,p<0.05
CSF	330.89 (52.9)	325.65 (22.0)	-0.081,p=0.9	CSF	450.63 (112,7)	410.07 (78.0)	0.939,p=0.1
BPF	0.787 (0.032)	0.772 (0.006)	-0.091,p=0.4	BPF	0.726 (0.051)	0.734 (0.029)	0.975,p=0.5
GMF	0.505 (0.024)	0.454 (0.008)	-0.073,p<0.05	GMF	0.461 (0.024)	0.432 (0.007)	0.643,p<0.05
WMF	0.282 (0.019)	0.318 (0.012)	0.891,p<0.05	WMF	0.265 (0.031)	0.302 (0.024)	0.991,p<0.05
Accuracy	1.154 (0.384)	1.585 (0.223)		Accuracy	1.467 (0.353)	1.347 (0.346)	

Table 1: Mean (standard deviation) volume in ml for GM, WM and CSF for each technique. Mean (standard deviation) for GMF, WMF and BPF are also presented for each technique. Last column shows linear correlation and paired t-test between methods. Last row presents the qualitative analysis results.

CONCLUSIONS: We applied a novel brain segmentation technique (GIF) in MS subjects for the first time. Results were compared to those obtained from a technique commonly used to measure brain atrophy (SPM12). Acknowledging the small number of subjects, statistical measures and qualitative assessment showed that GIF provides a relatively significant improvement in segmentation accuracy based on the qualitative analysis when compared to SPM12, with an improved agreement between observers (r=0.740 VS r=0.203). Additionally, GIF was found to be more robust (i.e. lower standard deviations) at estimating brain atrophy (i.e. volume fractions) on both HC and MS subjects. This pilot study is very encouraging as it suggests that GIF can improve the accuracy of brain segmentation and therefore brain atrophy estimation in MS, and therefore further analysis of a larger patient sample will be performed to confirm results.

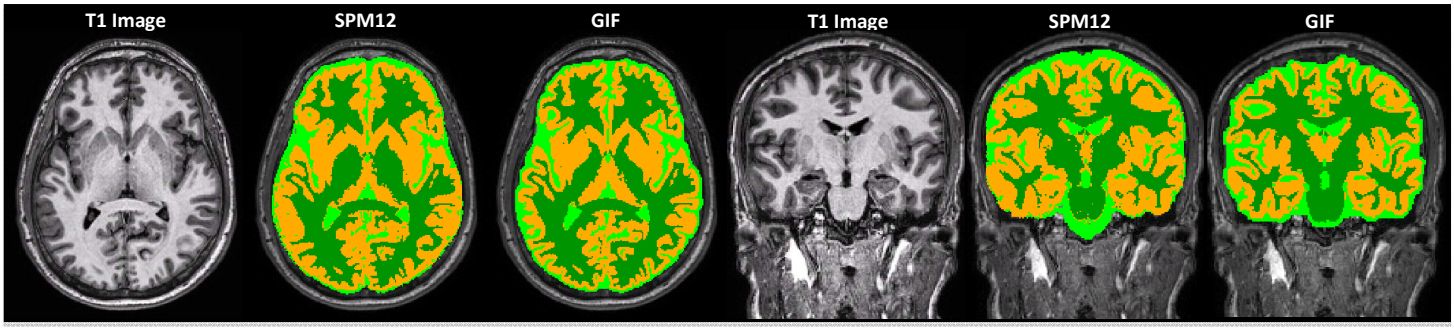

Fig 1: Slices from a HC subject's T1-weighted 3D scan and the corresponding segmentation masks derived from SPM12 and GIF.

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