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Communication

Computerised volumetric analysis of lesions in multiple sclerosis using new semi-automatic segmentation software

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Abstract—*The paper describes the application of new semi-automatic segmentation software to the task of detection of anatomical structures and lesion and their three-dimensional (3D) visualisation in 23 patients with secondary progressive multiple sclerosis (MS). The purpose is to study the correlation between magnetic resonance imaging (MRI) parameters (volumes of plaques and cerebrospinal fluid spaces) and clinical deficits (neurological deficits in the form of EDSS and RFSS scores, and neuropsychological deficits). The software operates in PC/Windows and PC/NeXTstep environments and utilises graphical user interfaces. Quantitative accuracy is measured by performing segmentation of fluid-filled syringes (relative error of 1.5%), and reproducibility is measured by intra- and inter-observer studies (3% and 7% variability, respectively). The mean volumes of MS plaques show significant correlations with the total RFSS scores ($p=0.04$). Relative intracranial cerebrospinal fluid (CSF) volumes show statistically significant correlation with EDSS scores ($p=0.01$). The mean volume of MS plaques shows a significant correlation with the overall neuropsychological deficits ($p=0.03$). 3D visualisation helps to understand the relationship of lesions to the surrounding brain structures.*

Keywords—*Multiple sclerosis, Magnetic resonance, Image processing, Volume measurement, Segmentation, 3D visualisation*

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1 Introduction

MULTIPLE SCLEROSIS (MS) is the most common demyelinating disorder of the central nervous system. Magnetic resonance imaging (MRI) is the single most important paraclinical investigation in the diagnosis of MS and has become increasingly important in describing the natural history of the disease and in monitoring therapy. Its sensitivity surpasses that of cerebrospinal fluid (CSF) examination and trimodal evoked potentials (TRUYEN, 1994).

The quantification of MS plaques and associated atrophy on magnetic resonance (MR) images provides objective measures that are continuous and on a linear scale and that are sensitive to disease changes (FILIPPI *et al.*, 1997). The different issues that need to be considered for MS lesion quantification with computerised methods are recognition (the process of determining and distinguishing a specific object from other structures), delineation (defining the extent of the object) and efficacy (representing how practical the method is) (MILLER *et al.*, 1998). Developments in MRI and digital image processing have made possible accurate volumetric estimation, which requires accurate and reproducible segmentation (PECK *et al.*, 1996).

This work describes the application of a new, fast semi-automatic segmentation software, called Anatomatic (HEINONEN *et al.*,1997; 1998*a*), to study the correlations between the MRI parameters and neurological and neuropsychological deficits in patients with secondary progressive MS disease.

2 Materials and methods

2.1 *Patients*

Twenty-three patients suffering from secondary progressive MS disease were studied at the Tampere University Hospital during the year 1996–1997. Detailed neurological examinations were carried out using the expanded disability status scale (EDSS) (KURTZKE, 1983) and regional functional scoring scale (RFSS) (LYCKE *et al.*, 1996) scores. Neuropsycho-

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logical examinations included analysis for frontal function impairment, long-term verbal memory, visuo-spatial short- and long-term memory and visuo-perceptive disorders.

2.2 *MRI protocol*

MRI was performed at the Department of Diagnostic Radiology on a GE 0.5 Tesla MRI machine*, using a standard head coil. In addition to routinely used axial T2 weighted images, proton density weighted images, fluid attenuated inversion recovery (FLAIR) images and gadolinium DTPA enhanced T1 images for diagnosis, the imaging protocol also included axial T1 weighted images (TR 300 ms; TE 20 ms; matrix size 160 × 256; NEX 5; FOV 22 cm; slice thickness 5 mm and gap 2 mm) and axial 3D fast spin echo (FSE) images (TR 2000 ms; TE 150 ms; matrix size 192 × 224; NEX 1; FOV 22 cm; ETL 16; slice thickness 2 mm with no interleaving gaps) for segmentation.

2.3 *Segmentation and volumetric analysis*

Segmentation and volumetric analysis were performed on axial T1 weighted images, covering the whole brain, and axial 3D T2 FSE images, covering a range of 42 mm from the floor of the fourth ventricle to the level of corona radiata. 3D T2 FSE images were used for segmentation of MS plaques. The reason for restricting the region of imaging in the 3D T2 FSE sequence was to obtain satisfactory resolution with our MRI device (the plaques are mostly located in that region). A very thin spoiled grass (SPGR) gradient echo sequence could not be performed owing to the same limitation.

Segmentation was carried out using the IARD segmentation algorithm (HEINONEN *et al.*, 1997; 1998*a*) applying, consecutively, image enhancement (Fig. 1, step 1); amplitude segmentation (step 2); region growing (step 3); and decision trees (step 4). Amplitude segmentation was applied three times using different threshold coefficients, and the results were stored as three separate bit-maps. This enables the segmentation of different intracranial tissues and also detects plaques of different intensities simultaneously. Decision trees help in determining that a particular tissue covers another in a definite order, to achieve a reasonable final image.

Intracranial cerebrospinal fluid volume (a measure of brain atrophy) was estimated from 2D T2 weighted images using the same methods as in MS plaque segmentation, with several exceptions concerning the removal of subcutaneous fat tissues located extracranially. This was resolved by multiple thresholds and decision trees.

2.4 *Segmentation software*

The graphical user interface of the Anatomatic software (HEINONEN *et al.*, 1998*a*) is presented in Fig. 2. The software operates in PC/Windows95 and PC/NeXTstep environments. Various buttons help in achieving the final results. After an image has been selected from the MRI stack, amplitude segmentation is performed either by increasing or decreasing the intensities. Images are then modified manually, unnecessary pixels are deleted, and the plaques and CSF spaces are enhanced with specific colours. The final results are stored, and the program reports the number and the volume of the MS plaque voxels. The segmented data can be stored on a hard disk and presented three-dimensionally (Fig. 3). 3D rendering of images is made in any plane using Medimag software (HEINONEN *et al.*, 1998*c*).

2.5 *Validation and reproducibility of the method*

The validation of the method has been performed earlier, in our previous study, using phantom tests. The studies demonstrated an error ranging from 0.3% to 4%. A test on the variability of the MS plaque and CSF volumes was performed as an intra- and inter-observer study in six randomly selected MR image sets of MS patients. The inter-observer test demonstrated a variability of 7%, and the intra-observer test demonstrated a variability of 3% (HEINONEN *et al.*, 1998b).

3 Results

The whole procedure, including the MRI examination, image segmentation and volumetric estimations, took on average 40 min. Segmentation of images took 5–20 min, depending on the number of plaques. The time used for manual interaction was 2–5 min. A good discrimination was obtained between the white matter, cortical and deep grey matter and the cerebrospinal fluid spaces in the brain. The margins of the MS plaques were accurately delineated, and thus MS plaques were readily separated from normal brain tissue. Accurate 3D reconstruction images were acquired.

The median total lesion volumes obtained in our patient group for T1 and T2 weighted plaques were 0.5 cm^3 and 3.8 cm^3, respectively. The median volume for total intracranial cerebrospinal fluid spaces was 11.3 cm^3. The mean volumes of MS plaques showed significant correlations with the total RFSS scores ($p = 0.04$). No significant correlation was found between the mean plaque volumes and the total EDSS scores. Relative intracranial CSF volumes showed significant

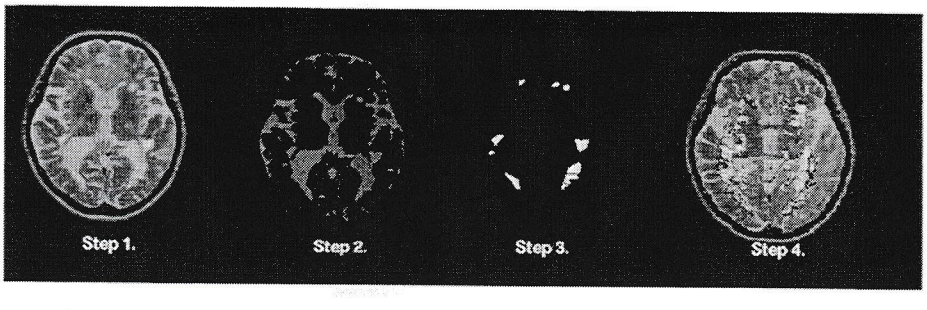


Fig. 1 *Segmentation algorithm: segmentation of MS plaques from raw MR images consists of several stages, including plaque highlighting using amplitude segmentation (step 2), lesion detection using region growing and manual editing (step 3), and image integration (step 4)*

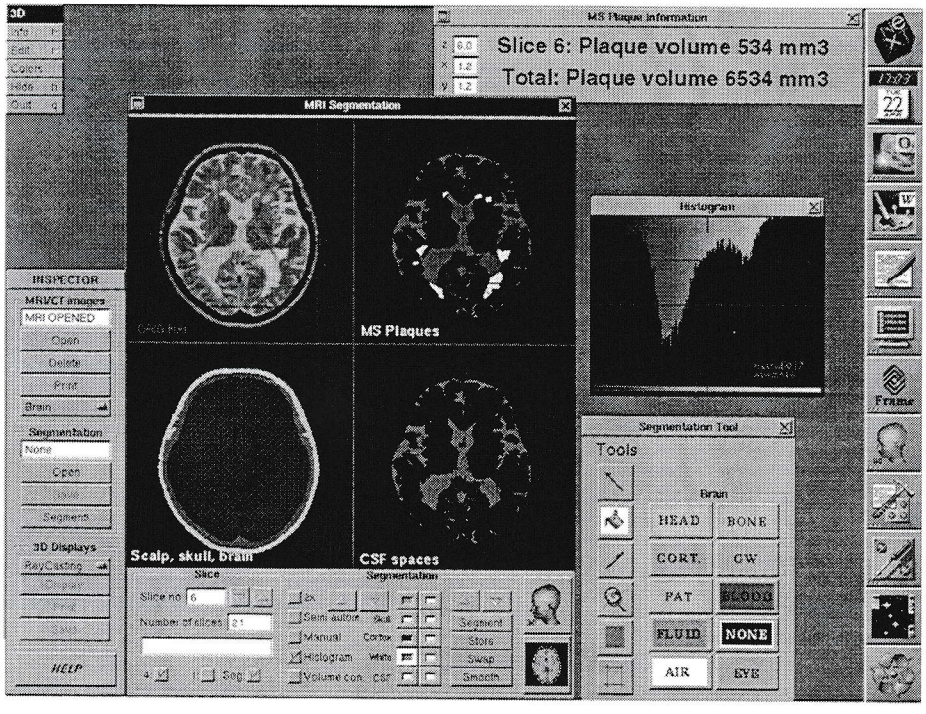
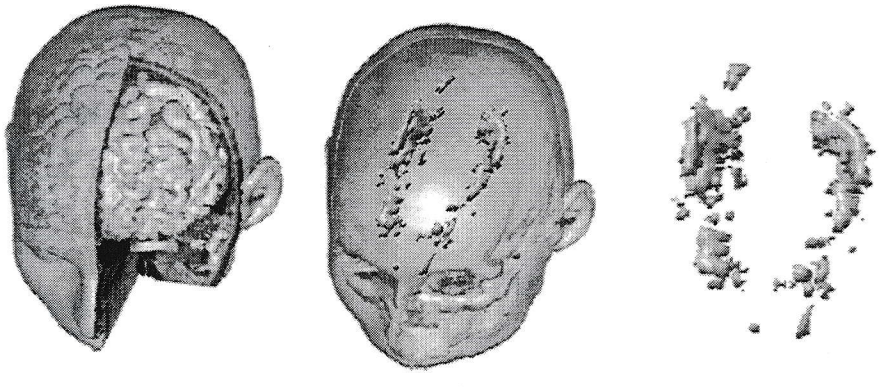


Fig. 2 *Anatomatic software running in PC/NeXTstep environment. Software also operates in PC/Windows95 environment. Segmentation procedure is controlled using 'MRI segmentation' window, in which original MR image and amplitude-segmented and manually modified images are presented. Segmented data can be stored and new MR images can be opened using 'inspector' panel on left. Segmentation tools and colours representing different tissues can be selected from 'segmentation tool' window. Individual volumes from axial slices and total plaque and CSF volumes can be identified at top*



a *b* *c*

Fig. 3 *3D images reconstructed from segmented MR images using Medimag software (a) surface of cortex is visible through transparent scalp and skull. (b) Scalp, skull and MS plaques are displayed simultaneously, applying transparency. (c) 3D rendering of MS plaques in axial plane*

correlation with EDSS scores ($p = 0.01$). The mean volume of MS plaques showed a significant correlation with the overall neuropsychological deficits ($p = 0.03$).

4 Discussion

This study shows the successful use of semi-automatic segmentation in the detection of MS plaques and brain atrophy, and studies their correlations with neurological and neuropsychological dysfunctions. The reasonably good inter- and intra-observer variations and the comparable validation errors achieved in our study prove the reproducibility and reliability of this segmentation technique. In this prospective study, the MS plaques from T1 and T2 weighted images and CSF spaces from T2 images have been studied as a package analysis for volumetric estimation.

Manual methods of segmentation are prone to operator variability and can be very time-consuming (GIBBS *et al.*, 1996) when a trained operator outlines the lesion. Intra-observer variability has varied in different studies, from as low as 6% in experienced hands to as high as 14–20% in less

experienced hands (GONSALEZ *et al.*, 1994). Automatic segmentation methods, although fast, are prone to mistakes owing to variable degrees of differentiation between normal and pathological tissue. We believe that the reasonably fast computational and interaction times achieved with this segmentation software are comparable with those of an earlier study (UDUPA *et al.*, 1997), where the computational time for segmentation was 5–40 min, and interaction time was 1–15 min.

Threshold-based semi-automatic lesion methods do require different degrees of operator assistance but improve the variability for volume determination when compared with manual tracing (GRIMAUD *et al.*, 1996). Although small threshold changes result in significant changes in lesion load (FILIPPI *et al.*, 1996) and in false positives, false negatives and wrongly delineated lesions, the technique ignores these problems or requires operator assistance (MILLER *et al.*,1998). Anatomatic being a segmentation procedure based on partially interactive morphological region detection and region growing, it has the advantage of partially automated, interactive supervision of lesion detection, and being accurate and reasonably fast compared with the manual and automatic techniques.

Important factors for correlation studies are patient selection, clinical scoring systems, field strength of MRI and the choice of pulse sequences and orientation (TRUYEN *et al.*, 1990). In this study, to optimise the situation, we selected a homogenous group of MS patients (secondary progressive MS), used a conventional neurological disability marker (EDSS), the less-used new RFSS scoring system, and a range of neuropsychological tests, examined all patients on the same 0.5 machine and selected modern 3D imaging sequences, such as 3D fast spin echo and T1 images for lesion quantification.

The reported correlations of the lesions with the clinical parameters have varied widely from weak to moderate (KAPPOS *et al.*, 1987). Also, several correlations between the quantified MS lesions and cognitive abnormalities have been reported (FEINSTEIN *et al.*, 1992). In this study, the analysis was performed under optimum MRI conditions, and, hence, significantly positive correlations were observed between the EDSS, new RFSS, cognitive dysfunctions and selected MRI deduced parameters. To our knowledge, in this study, for the first time in literature, RFSS has been correlated with MRI parameters.

The ability to obtain very thin plane intervals enables the reconstruction of 3D images in any plane. Images acquired in axial planes can be reformatted in the sagittal and coronal planes to achieve an accurate analysis of the location of the MS lesions and their correlations with surrounding structures.

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