Report on QBrain software in comparison automatic and manual segmentation in brain MR images of the Multiple Sclerosis patients and normal volunteers.

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Aims and objectives

Multiple Sclerosis (MS) is a chronic progressive disease of the central nervous system that is characterized by inflammation and neurodegeneration. It is the most common demyelinating disease in the western world and affects mainly young adults in the age between 20 and 40 years old. There is a female predominance with a female to male ratio of about 2:1.

The disease can manifest itself in various ways; symptoms may include motor symptoms like muscle weakness, sensory problems, ataxia, cognitive problems and many others. Quantitative assessment of the changes in the brain magnetic resonance images (MRI) in association with clinical judgment can provide accurate assessment of disease progress. Due to high resolution and good differentiation between soft tissues and other structures, MRI is superior to other imaging techniques in the studies of nervous system diseases. On MRI damaged white matter usually has a prolonged T2 relaxation due to increased tissue water content and degradation of the macromolecular structure of myelin. Therefore, white matter lesions are well depicted with conventional PD and T2-weighted (T2WI) spin echo (SE) or fast SE sequences but are even more conspicuous on fluid-attenuated inversion recovery (FLAIR) images.

MS plaques appear hyperintense on T2W1 images and their perivenular distribution predisposes to the typical ovoid shape. Sometimes they are seen as 'Dawson's fingers' at sagittal images: finger-like hyperintensities surrounding the vessels, and perpendicular to the lateral ventricles.

The traditional interpretation of MR images by a specialist is a difficult and time-consuming task, and the result directly depends on the experience of the specialist. This difficulty reflects the complexity and visually vague edges of anatomical borders. Therefore, it is desirable to have an effective automatic segmentation method. Previous approaches were automatic or semiautomatic procedures for segmentation of brain into different tissues, including MS lesions. Quantitative image analysis and its advantages have been reported in the literature for more than ten years.

Several methods have been proposed for performing quantitative white matter lesion load measurements. These methods vary from fully manual (manual outline techniques) to fully automatic (no user interaction). The fully manual methods are labor intensive and time consuming, requiring well-trained reviewers for moderately accurate results. Nowadays, semi-automated techniques are therefore considered superior to manual contouring or visual scoring in large-scale studies. However, even if they are less time consuming and more reproducible, they still remain labor intensive for trials on large number of subjects. The need for truly automated methods (ultimately fully automatic) is growing as large-scale longitudinal trials in degenerative brain disease are becoming more and more important. Used in this study in order to improve the quantification of white matter lesions, is a new method incorporated in the QBrain software (Medis, Leiden, the
Netherlands). It allows for the analysis, detection and quantification of volumes in MR studies of the brain. Specifically, it offers the possibility to detect and quantify manually and automatically the intracranial volume (IC), lobes of the brain, cerebrospinal fluid (CSF) and also possible lesions in MS patients.
Methods and materials

Materials

MRI data of 27 patients with MS including 19 female and 8 male with aged 40 ± 20 years, were retrospectively reviewed and selected from a cohort of 231 from an ongoing natural history study of patients who were scanned with the MS MRI-protocol. The MS patients in this study were divided into four groups because of the clinical symptoms presented during the diagnostic MR: (1) primary-progressive (PP), (2) relapsing-remitting (RR), (3) secondary-progressive (SP), and (4) stable (ST) (MS patients who at the time of the MR examination did not show symptoms characteristic of MS).

MR Imaging

MRI of the brain was performed on a 1.5 Tesla MR scanner (Magnetom Sonata; Siemens, Erlangen, Germany) of the Radiology Department of University Medical Center Groningen from April 2004 to November 2008. Conventional axial scanning for MS patients with T1WI (T1-weighted imaging), T2WI and FLAIR sequence without contrast administration was performed. Scan parameters of repetition time (TR)/echo time (TE)/inversion time (TI), for FLAIR images were 9999/119/2500 milliseconds, TR/TE for T1WI images were 424/10 milliseconds and TR/TE for T2WI images were 4500/120 milliseconds. Each image volume (patient data) consisted of slice thickness 6mm, average number of slices 19 with a 256 x 256 scan matrix.

Manual and automatic segmentation of MS lesions

In this study our first aim was to compare and to check this novel QBrain software. We wanted to see if the computed brain lesions such as those encountered in Multiple Sclerosis in the brain are correct. Automated results were compared with manual delineation- quantification serving as gold standard. Manual and automatic segmentation of MS lesions was performed simultaneously by DK and PB by means of novel QBrain software. The radiologist in training who was not aware of the automatic results in this research, was asked to perform manual segmentation of MS lesions in FLAIR images with visual inspection of the corresponding T2WI images. Specifically, he measured every visual Multiple Sclerosis lesion in MS patients. In the same time another researcher, who was trained in the QBrain software, performed automatic segmentation. Then the marked MS plaques were compared and analyzed for their three largest volume sizes. We calculated the total volume of MS plaques and number of lesions. We decided only to take into account all
plaques with the volume above 0.1 ml because that volume was obtained by the formula of a ball with a diameter equal to the slice thickness of 6mm ($4/3 \pi R^3 = 113 \text{ mm}^3 = 0.113 \text{ ml};$ image 1.). It has been assumed here that MS lesions have a shape relatively circular in nature. Additionally MS plaques were characterized for lobe locations. One patient was removed because of three times larger plaques than any other volume patients MS plaques. Automatic segmentation was also used to calculate Intracranial Volume (IC) and cerebrospinal fluid (CSF).

**Automatic segmentation of a normal volunteer in three different MR scanners**

Our second aim was to compare the automatic repetitive procedures of QBrain on a normal volunteer (M, 31yo) volumes. So, we made an evaluation on how the system works and some scientific suggestions and results have been obtained in order to see how QBrain performs with the DICOM data. The volunteer was scanned with the same MS sequence on three different MR scanners (Siemens, Erlangen, Germany) of the Radiology Department of University Medical Center Groningen. MRI of the brain was performed first on a 1.0 Tesla MR scanner (Magnetom Impact). Second on a 1.5 Tesla scanner (Magnetom Sonata). Next on a 1.5 Tesla scanner (Magnetom Avanto). Furthermore, the volunteer was scanned in the same MRI system two times with the same sequence values used for the MS patients and segmented in QBrain software program in order to see how it performs on three different scanners. The measurements were performed only automatically and not manually. Some clinical and scientific results were observed which will be presented and described in the following pages.

**Postprocessing software.**

The QBrain software (Medis, Leiden, the Netherlands) allows for the analysis, detection and quantification of volumes in MR studies of the brain, specifically the detection and quantification, manually and automatically, of the intracranial volume (IC), lobes of the brain, cerebrospinal fluid (CSF) and also of white lesions in MS patients. QBrain has been developed in close cooperation with the Division of Image Processing of the Leiden University Medical Center, which has created the detection algorithms used in QBrain.
Fig. 1: Examples of QBrain's application with automatic segmentation; QBrain found 261 MS plaques

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Fig. 2: Examples of QBrain's application with automatic segmentation; red line is showed this border

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Fig. 3: Examples of QBrain's application with automatic segmentation; all small MS plaque below 0.1 ml were removed

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Results

There was a linear relationship between the automatic and manual total and individual lesions volume and also between the automatic and manual total number of lesions. The average difference between the automatic and manual segmentation of the total and individual lesion volumes in the studied group was under 1 ml.
Conclusion

1. In our group the average difference between the automatic and manual segmentation of the total and individual lesion volumes was under 1 ml.

2. There is a need for continual improvement of the automatic segmentation in the algorithms for the evaluation of the plaque volume of MS patients.

3. QBRAIN software is very user-friendly and enables fast measurements of MS plaque.
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