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Multiple sclerosis exploration based on automatic MRI modalities segmentation approach with advanced volumetric evaluations for essential feature extraction

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ABSTRACT

Multiple Sclerosis (MS) could be considered as one of the most serious neurological diseases that can cause damage to the central nervous system. Such pathology has increased dramatically during the past few years. Hence, MS exploration has captivated the interest of various research studies in clinical as well as technological fields such as medical imaging.

In this context, this paper introduced a new MS exploration approach based on cerebral segmentation and MS lesion identification using the fusion of magnetic resonance (MRI) modalities sequences.

The proposed segmentation approach is based on extracted volumetric features that could be deduced from the gray-level co-occurrence matrix (GLCM) and the gray-level run length (GLRLM) matrix. Volumetric features extraction would be performed by using new voxel wise techniques while preserving connectivity, spatial and shape information.

In addition, our segmentation approach includes an optimized feature selection process combining the genetic algorithm (GA) and the support vector machine (SVM) tool in order to preserve only the essential features that could distinguish the main brain tissues and the MS lesions within both white matter and gray matter.

The evaluation was carried out on four clinical databases. The results revealed an acceptable conformity with the ground truths compared to those of the usual methods Besides, our approach has proved its ability to select the most discriminative features, ensuring an acceptable cerebral segmentation (averages: Dice = 0.62 ± 0.11, true positive rate 'TPR' = 0.64 ± 0.12 and positive predictive value 'PPV' = 0.64 ± 0.14) and MS lesions identification with an acceptable accuracy rate (averages: Dice = 0.66 ± 0.07, TPR = 0.70 ± 0.12 and PPV = 0.67 ± 0.03).

Based on these promising results, a computer aided diagnosis (CAD) system was henceforth conceived and could be useful for clinicians in order to carefully facilitate MS exploration. Such a helpful CAD system was really highly needed for clinical explorations and could be extended to other neurological pathologies such as Alzheimer's and Parkinson's diseases.

1. Introduction

Severe neurological pathologies threatening people lives such as Multiple Sclerosis (MS), Alzheimer's disease, Parkinson's disease and brain tumors are increasing relentlessly. Thus, scientists, clinicians and technologists are investing considerable efforts to explore and study these pathologies more carefully in order to provide a better control and efficiency in the diagnosis process. Thanks to the actual technological progress, advanced biomedical tools are actu-

Abbreviations: MRI, magnetic resonance imaging; MS, multiple sclerosis; GLCM, gray-level co-occurrence matrix; GLRL, gray-level run length matrix; SVM, support vector machine; GA, genetic algorithm; FLAIR, fluid attenuated inversion recovery; T1w, T1-weighted; T2w, T2-weighted; T1Gado, T1w enhanced by Gadolinium; T1BravoGado, T1wBravo enhanced by Gadolinium; CHU-HB, CHU Habib-Bourguiba, Sfax-Tunisia; UNC, University of North Carolina; CHB, Children's Hospital Boston; TLL (ml), total lesion load; CAD, computer aided diagnosis.

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ally needed for processing the various medical image modalities facilitating henceforth their diagnosis and control.

Magnetic resonance imaging (MRI) modalities are in fact essential imaging tools largely used during these diseases diagnosis and exploration. In particular, the MRI image segmentation is considered as an effective and needed tool for precise lesions identification as well as a subsequent quantitative exploration of brain components. Such modalities segmentation has been highly needed for its practicality during clinical routines and for further clinical research applications. For example, precise lesion segmentation helps considerably during surgery, the identification of the brain disorders mechanisms and the evaluation of the effect of administered drugs.

MS lesion segmentation was consequently the focus of various research groups [12,34,48]. However, the MS manual segmentation requires not only special and efficient skills but also a great deal of time, effort and money. This would also increase inter- and intra-expert variability with probable errors. To face these problems, several automatic and semi-automatic methods have been introduced. Some methods have used supervised algorithms such as the support vector machine (SVM) tool [8,50], while others have used unsupervised algorithms like the expectation-maximization (EM) tool [6,13], k-means criterion [36,19], threshold constraints [31], active contour tool [35] and fuzzy C-means tool [3].

In addition, some lesion segmentation processes consider spatial and textural information via Markov random fields (MRF) [50], fuzzy connectedness methods [22] and probabilistic atlases [4]. Furthermore, most existing lesion segmentation approaches used only one MRI modality [11]. For example, Abdullah et al. [8] proposed an automated SVM based on fluid attenuated inversion recover sequence (FLAIR) analysis, whereas some other authors used different MRI modalities in order to extend and reinforce the lesion segmentation process. García-Lorenzo et al. [11] proposed one multimodal graph cut based on T1-weighted (T1w), T2-weighted (T2w) and proton density weighted (PDw) sequences. Moreover, Sweeney et al. [15] proposed a multimodal approach based on sequences subtraction.

Over the past two years, the majority of authors have proposed supervised techniques for the segmentation of MS lesions. For instance, Jesson et al. [1] proposed a method based on MRF model built from anterior spatial information derived from multi-atlas fusion (MALF). The refinement of the lesions was then carried out by a random forest classifier. Prados et al. [1] proposed an optimized PatchMatch label fusion approach to classify the lesions as a function of the local multimodal intensity similarity. Deshpande et al. [1] proposed a sparse representation of data and learning dictionaries derived from various information related to lesions and healthy brain tissues. Other proposed supervised techniques used the convolutional neural networks (CNN). Jain et al. [1] for instance proposed a 3D CNN to classify voxels. Birenbaum et al. [2] used the CNN to refine the lesions detected on the basis of MR intensities and a set of white matter (WM) priors. Moreover, Brosch et al. [44,45] used a 3D CNN based on shortcuts for multiscale feature mixing. As for Yoo et al. [49], they used the CNN and lesion masks to reveal hidden MS lesion features describing the early disease activity.

The most recent unsupervised methods for MS lesion segmentation include the study by Sudre et al. [1] in which the authors built, for each clinical case, a Gaussian mixture model (GMM) able to distinguish healthy tissues from lesions based on a variety of MRI images. This model was, then, used to estimate the lesions in each MRI examination (time-point) corresponding to the clinical case. In addition, Catanese et al. [1] used a graph-cut algorithm initiated by an EM algorithm. Furthermore, Iheme et al. [1] used a method based on intensity thresholding and 3D voxel connectivity analysis. Tomas-Fernandez et al. [1], however, proposed a technique for both brain segmentation and lesion detection based on the model of population and subject (MOPS) intensities which is a tissue mixture model mixing two other models. The first is a global tissue intensity model related to the patient in consideration. The second is a population local tissue intensity model constructed from a reference database made up of MRI scans related to healthy subjects. The MOPS model identifies lesions as the sites in the brain with aberrant levels of intensity compared to their expected values in the reference model of healthy subjects.

In this paper, we proposed a novel automatic segmentation approach that could be applied for cerebral zones differentiation first, and then for MS lesions localization and characterization. This approach suggested, on the other hand, the MRI modalities fusion using wavelet technique. This fusion would involve one unique image summarizing all the needed information related to the existing lesions present in both gray and white matters. Moreover, the proposed method takes into account spatial, statistical and textural features, which have been extracted using the volumetric gray-level co-occurrence matrix (GLCM) and gray-level run length matrix (GLRL), in addition to certain shape features (skewness and kurtosis). From the set of all the extracted features, the proposed approach aimed to preserve the optimal ones, including the most discriminative, giving therefore an adequate segmentation. This optimization was performed using a genetic algorithm (GA) combined with an SVM tool. All the segmentation results allowed henceforth performing other volumetric evaluations that were pretty useful and complementary for improving MS lesions exploration. These promising segmentation results would consequently be synthesized and reassembled to conceive a clinical helpful environment referred to as a computer aided diagnosis (CAD) system that could be useful in satisfying the various clinical needs.

2. Materials and methods

In this section, we first described the MRI data used for the evaluation of the proposed segmentation approach. Next, the different stages of the proposed segmentation process were detailed: Preprocessing stage, Feature extraction, Feature selection and segmentation. The proposed approach could be summarized according to the following organizational chart (Fig. 1):

2.1. Databases

The evaluation of the proposed segmentation approach was carried out using four real databases (Table 1), including various MS phases: relapsing-remitting, clinical isolated syndrome, secondary progressive and primary progressive. Each clinical case data were segmented manually by two highly qualified radiologists except for the CHB database in which there was only one expert manual segmentation.

- **CHU-HB:** It is a cross-sectional database which was collected at Habib-Bourguiba University Hospital (CHU-HB Sfax-Tunisia). It consists of 70 pathological cases and 50 healthy subjects obtained on a 1.5T General Electric MRI scanner. The various MRI sequences were rigidly registered to the MNI152 atlas and resliced via a spline interpolation to a $1 \times 1 \times 1$ mm resolution.
- **MICCAI2008:** It is a cross-sectional database related to the MS lesion segmentation challenge MICCAI in 2008 [32,55]. It includes 10 subjects with manual segmentations and 10 others without manual segmentations gathered at the University of North Carolina (UNC). Besides 10 subjects with manual segmentations and 15 others without manual segmentations gathered at the Children's Hospital Boston (CHB). The subjects were obtained on a 3T Siemens Allegra scanner at UNC and a Siemens 3T scanner

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