An SPM12 extension for multiple sclerosis lesion segmentation

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Abstract

Purpose: Magnetic resonance imaging is nowadays the hallmark to diagnose multiple sclerosis (MS), characterized by white matter lesions. Several approaches have been recently presented to tackle the lesion segmentation problem, but none of them have been accepted as a standard tool in the daily clinical practice. In this work we present yet another tool able to automatically segment white matter lesions outperforming the current-state-of-the-art approaches.

Methods: This work is an extension of Roura et al. [1], where external and platform dependent pre-processing libraries (brain extraction, noise reduction and intensity normalization) were required to achieve an optimal performance. Here we have updated and included all these required pre-processing steps into a single framework (SPM software). Therefore, there is no need of external tools to achieve the desired segmentation results. Besides, we have changed the working space from T1w to FLAIR, reducing interpolation errors produced in the registration process from FLAIR to T1w space. Finally a post-processing constraint based on shape and location has been added to reduce false positive detections.

Results: The evaluation of the tool has been done on 24 MS patients. Qualitative and quantitative results are shown with both approaches in terms of lesion detection and segmentation.

Conclusion: We have simplified both installation and implementation of the approach, providing a multiplatform tool[1] integrated into the SPM software, which relies only on using T1w and FLAIR images. We have reduced with this new version the computation time of the previous approach while maintaining the performance.

Keywords: Magnetic Resonance Imaging, Multiple Sclerosis, Image Analysis, White Matter Lesion, Automatic lesion detection and segmentation.

1. Introduction

Magnetic resonance imaging (MRI) is a powerful and essential tool for understanding brain anatomic abnormalities. For instance, multiple sclerosis (MS) is characterized by demyelination presenting white matter lesions (WML). Detecting these WML is crucial for the MS diagnosis [2]. However, performing this task manually is tedious and very time consuming and may lead to inaccuracies due to evident human errors, inter- and intra-rater variability.

Automatic and semiautomatic tools to perform this task are numerous [3], but none of them have emerged as a standard on the daily clinical practice. The literature includes both supervised approaches [4,5,6], which require a training step, and unsupervised strategies [1,7]. The work presented here is an extension of a previous unsupervised approach

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[1] http://atc.udg.edu/salem/slsToolbox

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introduced in Roura et al. [1]. The novelty here is that all the steps required for the WML segmentation are integrated into a single framework, which works in the SPM software[2].

2. Methods

2.1. Data

A dataset containing 24 patients with Clinically Isolated Syndrome (CIS) was used to evaluate the performance. The dataset is challenging since lesion volume per patient was very small. The scanner used was the 3T magnet with a 12-channel phased-array head coil (Trio Tim; Siemens, Germany). The following pulse sequences were obtained: 1) transverse proton density and T2w fast spin-echo (TR=2500ms, TE=16-91ms, voxel size=0.78x0.78x3mm^3); 2) transverse fast T2-FLAIR (TR=9000ms, TE=93ms, TI=2500ms, flip angle=120º, voxel size=0.49x0.49x3mm^3); and 3) sagittal 3D T1 magnetization-prepared rapid gradient echo (MPRAGE) (TR=2300ms, TE=2ms; flip angle=9º; voxel size=1x1x1.2mm^3). Lesions were annotated by experts on FLAIR images with a lesion volume variation (mean ± standard deviation) and range (min-max) of 4.1±4.7 [0.18− 18] ml.

2.2. Pre-processing

To deal with brain MRI analysis several factors must be considered depending on the final application. Since we focus on MS WML segmentation, non-brain tissues may affect the intensity distribution of our region of interest. Moreover, during the acquisition the scanner also introduces noise and undesired artifacts leading to the well-known intensity inhomogeneities. In addition and due to the acquisition time, different sequences may present slightly patient movements, which may be appreciated between modalities. Hence, as stated in previous approaches [1,4,5,6], several pre-processing steps should be applied to deal with these issues:

1) **Skull stripping and tissue segmentation,** obtained here by means of the SPM tissue segmentation algorithm [8]. As the result is a probability map (see Figure 1), we performed a maximum likelihood between the three main tissue classes: white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF). To obtain the brain mask we apply a probability threshold set at 0.5 [9,10].
2) **Image denoising** is applied in order to enhance and restore the MRI image. We smooth the image histogram by using the 3D Matlab implementation[3] of the anisotropic diffusion filter of Perona and Malik [11].
3) **Bias correction** is applied to correct the inhomogeneities. For this purpose, we use a Matlab implementation of the bias field correction proposed by Thode et al. [12], which implements the well-known non-parametric, non-uniform intensity normalization (N3) method [13] as a Bayesian modeling method.
4) **Intra-subject registration** to correct spacing and misalignments is solved by using SPM spatial co-registration, estimate and re-slice [14].

2.3. Lesion segmentation

Following the unsupervised strategy presented in Roura et al. [1], we look for the hyperintensity regions as the outliers in the GM tissue of the FLAIR image. First of all, we need to distinguish among the three main brain tissues. This is already obtained when performing the skull stripping process via the SPM tissue segmentation on T1w images. Afterwards, the hyperintensities are detected by a thresholding in FLAIR images and refinement step which is performed twice, where the first iteration takes into account larger and brighter lesions and the second is performed at a lower threshold to look for small lesions. The outliers are computed using a threshold defined as:

$$Thr = \mu + \alpha\sigma \quad (1)$$

where μ and σ are the mean intensity and the standard deviation of the GM histogram (computed by the full width at half maximum) respectively. Candidate lesions are adjusted by the parameter α. As stated in Roura et al. [1], this alpha parameter has a strong impact on the results obtained with this approach. However, assuming the GM histogram as normal distribution and according to the three-sigma rule, a good trade off of the tool has been observed when considering outliers beyond the 99th percentile for the first iteration and 92% for the second.

[2] http://www.fil.ion.ucl.ac.uk/spm/

[3] http://www.mathworks.com/matlabcentral/fileexchange/14995-anisotropic-diffusion--perona---malik-

Originally, three post-processing parameters were used to reduce the false positive (FP) lesions: lesion size, percentage of lesion voxels belonging to either WM or GM, and percentage of neighbor lesion voxels belonging to WM. The effect of this parameter setting was evaluated in Roura et al. [1], where the authors determined as default values a 60% for each ratio and a minimum lesion size of 3mm. However, depending on the α, these values might need to be readapted, especially for the second iteration where those ratios must be increased since the threshold is reduced to detect darker lesions which are usually smaller.

In this extended approach we have added a new constraint in order to avoid periventricular inflammatory regions, which usually appear as elongated regions. To this end, we have used the maximum probability tissue labels derived from the MICCAI 2012 Gran Challenge and Workshop on Multi-Atlas Labeling[4]. The data was labeled by Neuromorphometrics, Inc.[5] using MRI from the OASIS project[6]. This atlas belongs to the standard space used by SMP12 tissue segmentation; therefore, one can easily obtain the deformation fields to this space from any subject space. Since we already performed this process at the early steps, we are able to apply the inverse deformation fields with a nearest-neighbor interpolation to the labels belonging to the ventricles. This procedure allows to pullback any of the brain structures of this atlas (see Figure 1). Once the ventricles have been brought to the subject space, we obtain a smoothness region by applying morphological operations (dilation and erosion). All the lesions attached to this ventricle region and presenting elongated shapes are discarded. In Figure 1 there is an example of this scenario, where we show the ventricles and some elongated candidate regions that have been removed.

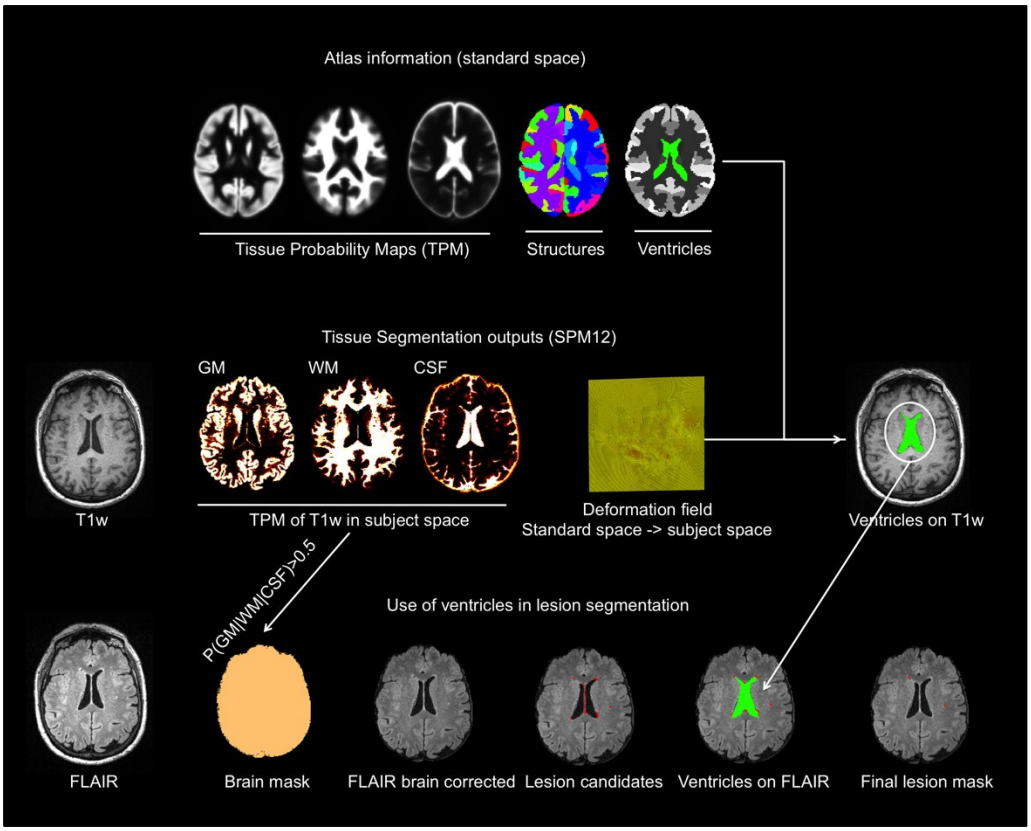

Figure 1: Scheme of the whole pipeline. The first line represents the atlas information used when segmenting the tissues and the ventricles of the T1w image in the second row. The bottom row shows all the steps over the FLAIR image when segmenting the white matter lesions.

[4] https://masi.vuse.vanderbilt.edu/workshop2012/index.php/Challenge_Details
[5] http://Neuromorphometrics.com/
[6] http://www.oasis-brains.org/

As described in Roura et al. [1], a simple iteration of the thresholding process changing the parameter α may avoid oversegmentation of lesions and ensure a more accurate application of the post-processing steps. We followed the same strategy in our experimental tests.

3. Experimental results

In our evaluation we have used the original FLAIR image space to perform the lesion segmentation, thus the parameter configuration differs slightly from the one presented in Roura et al. [1]. The 24 MS patients manually annotated in FLAIR images were used to test our approach, comparing the obtained results with those reported in Roura et al. [1] using the same patients.

For the first iteration we let the same α=3 reducing λ_{ts}=0.5 and λ_{nb}=0.5, detecting only large lesions. This allows to increase the λ_{ts} and λ_{nb} when detecting small lesions, therefore, for the second iteration we set the following parameters: α=1.75, λ_{ts}=0.9, λ_{nb}=0.9. The trade-off of this parameter setting has been done in a similar way than in Roura et al. [1]. The parameter α has been tested in both iterations from 1 to 3 each 0.1, while λ has been evaluated from 0 to 1 each 0.05.

Obtained results are shown in Figure 2, where the following segmentation and detection values were obtained. Average Dice Similarity Coefficient (DSC) = 0.35 ± 0.21, True Positive Rate (TPR) = 0.40 ± 0.19 and Positive Predictive Value (PPV) = 0.58 ± 0.30. A slightly performance increase with respect to the work of Roura et al. [1] was observed with a DSC Δ0.05, TPR Δ0.04 and PPV Δ0.05.

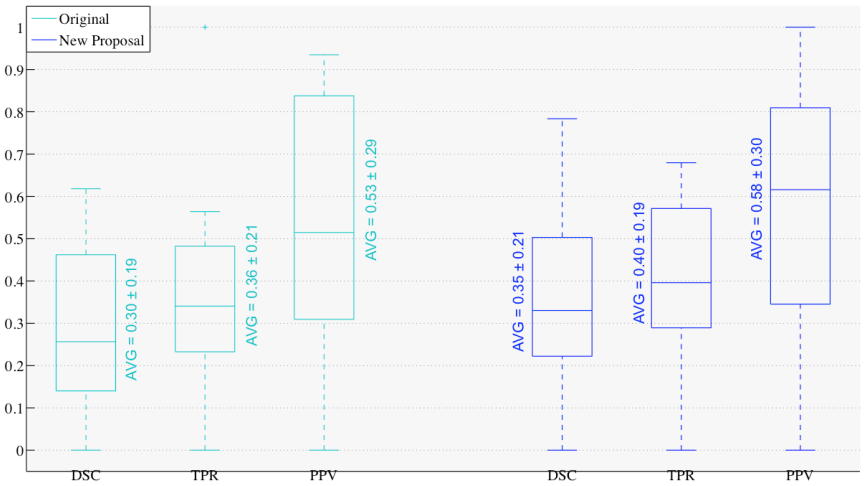

Figure 2. Boxplots representing DSC, TPR, and PPV measures obtained with the Roura et al. [1] and the new proposal.

An improvement of the new proposal can be seen in Figure 3, where the FP detections close to the ventricles have been removed. Looking at the 3D representation, one can see how the TP is fairly similar while FN and FP are reduced in the new approach. The computation time required by each patient is less than 5 minutes. However, nearly 4 of these minutes are required by the SPM tissue segmentation step.

Besides, the original approach [1] was tested also with different private datasets at different magnetic field strength (3T and 1.5T) in order to prove its robustness. The tool was also compared to the state-of-the-art works evaluating the well-known MICCAI MS Challenge 2008, for both training and testing dataset (total score = 82.344). We observed better

results then those of the state-of-the-art when evaluating the training dataset for the two hospitals (UNC: DSC=30%, TPR=68%, PPV=38%; CHB: DSC=38%, TPR=46%, PPV=69%).

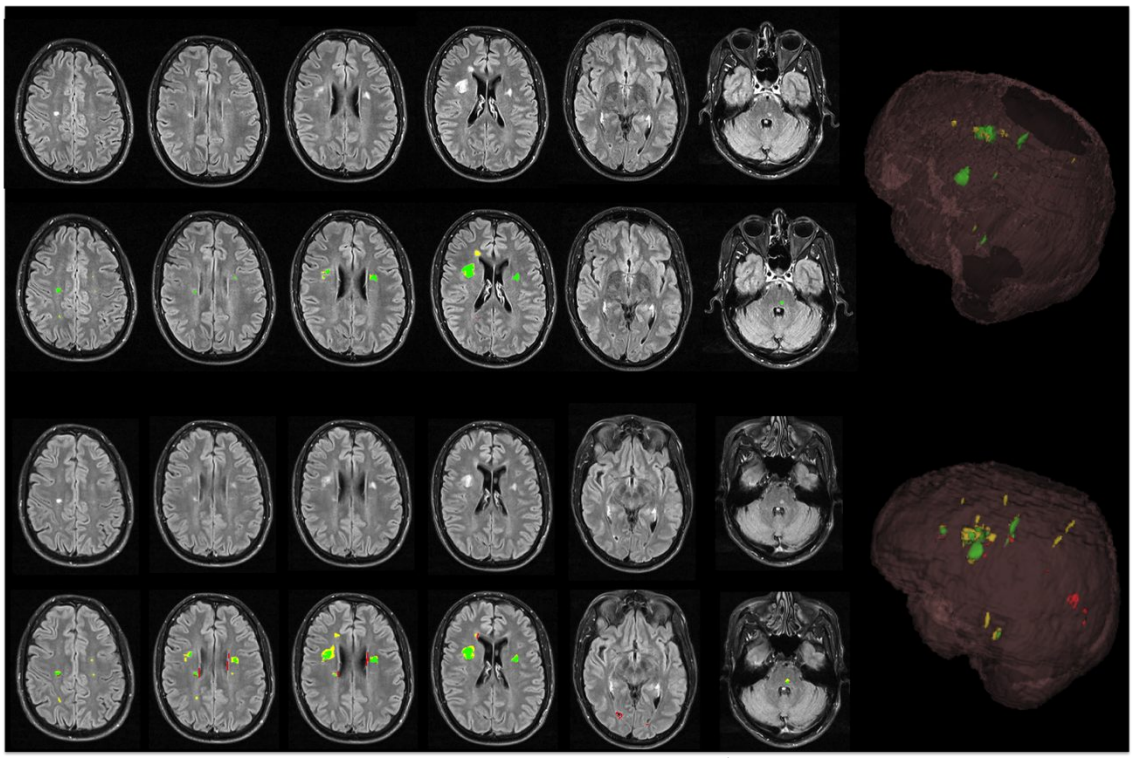

Figure 3. Qualitative example of the results of the new proposal (1st and 2nd rows) and the Roura et al. [1] approach (3rd and 4th rows). Notice that 1st and 2nd row have lower resolution in z-index, which means that the slices may differ (TP=green, FP=red, FN=yellow).

Novelty of the proposed method

Given that inflammatory periventricular regions can present elongated hyperintensities in FLAIR images, they can be misclassified as MS WML. This issue has been solved as a new post-processing rule to reduce FP. Furthermore, we have integrated all the pre-processing steps into the same SPM framework (SPM12 compatible).

4. Conclusions and future work

We have introduced an update of the automatic MS lesion segmentation approach presented in Roura et al. [1]. The performance has been slightly improved by adding a new restriction, which allows reducing FP detections while maintaining TPR. On the other hand, as stated in Roura et al. [1], the use of external pre-processing libraries, sometimes not easy to install and configure, was advised for an optimal performance of the approach. In this work, we have also improved this issue implementing new pre-processing steps which have been integrated into the own SPM framework, being therefore a multiplatform MS segmentation tool more straightforward to use. In order to optimize our code, we would like to explore the possibility of using a GPU based implementation to achieve the necessary parallelization and hardware acceleration.

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