An automatic method for Multiple Sclerosis Lesion Detection in Fluid Attenuated Inversion Recovery Magnetic Resonance Images

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ABSTRACT
This paper proposes a method for automatic detection of Multiple Sclerosis lesion in Fluid Attenuated Inverse Recovery (FLAIR) Magnetic Resonance Images (MRI). The majority of proposed automatic methods require the acquisition of T1-weighted images, in addition to the FLAIR images, which are commonly acquired within a clinical setting. The T1 images are used to identify the main brain structures (white matter, gray matter and cerebrospinal fluid). The approach described in this paper intends to replace the T1 images by probabilistic atlases used for the same purpose. The analyzed results of this method show a significant high rate of lesion detection.

CCS Concepts
• Computing methodologies ➞ Image processing; • Applied Computing → Imaging;

Keywords
MRI, White Matter Hyperintensities; Multiple Sclerosis; Lesion Locating; FLAIR

1. INTRODUCTION
Multiple sclerosis (MS) is an autoimmune inflammatory disease that affects the central nervous system (CNS). According to S. Warren[1], MS is the most common primary neurological disorder that occurs on young adults and is characterized by an immune attack on the myelin sheath. This attack results in White Matter Lesions (WML), well observable as hyperintense (bright) regions in T2-weighted or FLAIR images.

These characteristics made the usage of Magnetic Resonance Images (MRI) the most common method for manual diagnosis. Due to the fact that FLAIR images tend to eliminate the cerebrospinal fluid (CSF) signal (which also appears hyperintense in T2-weighted images), this modality is used more often on automatic segmentation methods ([2][3][4]).

Despite being the standard in the clinical practice, the manual diagnosis is very time-consuming and sometimes unaffordable to run in large-scale. Besides that, different professional diagnostics can lead to different results or even the same professional can end up with two different diagnostics for the same patient in distinct moments.

Thus, the development of automatic methods proves to be necessary for reducing the variability derived from human interactions, and allowing an efficient locating of MS Lesions in a large amount of MRIs[5]. In the main MS automatic segmentation/quantification methods[6], it is noticeable the need for acquiring MRI images in at least two modalities: a FLAIR or a T2 image, where WML areas present a higher intensity, and T1 MRI images that present a better contrast between the brain tissues, thus allowing the segmentation of the brain tissues(Figure 1).

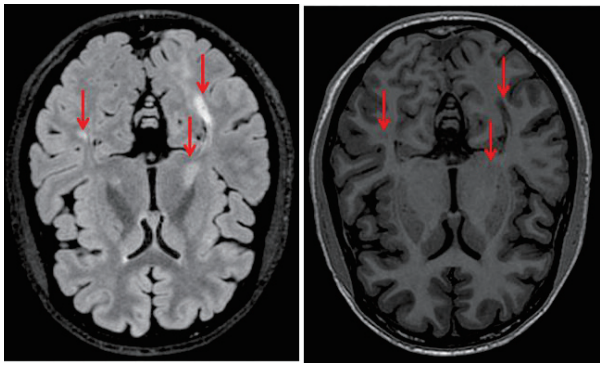

Figure 1 – Difference between FLAIR (top) and T1 Images (bottom). Arrows indicate some WM lesion areas.

This procedure is observed in automatic segmentation methods like the used as a golden standard (Lesion segmentation toolbox – LST)[2] for validating our proposed method. However, adding an extra modality to the pipeline incurs in a more time-

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consuming and costly process[3] and makes impossible to reproduce the method in pre-existing exams, unless the T1-weighted images are available. That said, the creation of an automatic locating method for WML that uses only FLAIR images is proposed.

This paper presents, in the next section, a description of the MRIs and the atlas used on this method. The following section presents the proposed automatic MS lesion locating method. Then, the results obtained with the method implementation on a set of images deriving from a MS study are presented. Finally, the conclusions that arose from analyzing this method implementation and the obtained results are presented, as well as the future work perspectives.

2. MATERIALS

For this paper, images from 10 patients were used for the application of this method, provided from a MS research project. Our institutions ethics committee approved this project and written consent was obtained from all subjects for the use of these images. The MRIs were acquired in a 3 Tesla GE HDxT scanner using an 8 channel cranial coil. The FLAIR images were acquired with a spin echo sequence with TR=8000ms, TE=102ms, flip angle=90, isotropic voxels of 1mm^3, with a 256x256 matrix and 180 slices. T1 volumetric images were acquired in a sequence with TR=34ms, TE=4ms, flip angle=20, and with the same dimensions as the FLAIR images.

In order to replace the usage of T1-weighted images from the automatic lesion-detecting pipeline, the usage of a probabilistic atlas containing brain structures is proposed. The probabilistic atlas used in this paper is the GG-366[7], developed by the Glahn Group (GG), from the Institute of Living of the Hartford Hospital in Connecticut, USA. The atlas is composed by a set of images with the brain atlas in FLAIR and T1-weighted and probability atlas for WM, GM and CSF. The FLAIR weighted brain atlas (Figure 2a) and the white matter probabilistic atlas (Figure 2b) were used from this set of images.

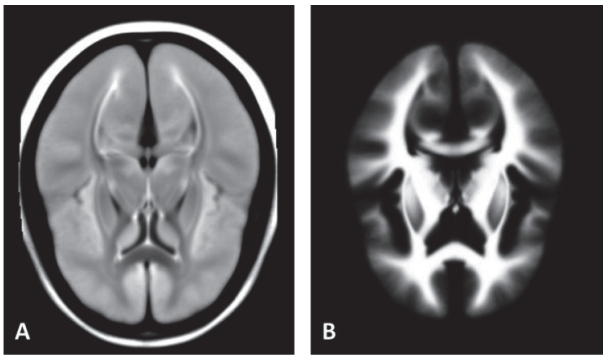

Figure 2 – Slice of the GG's FLAIR (A) and WM probabilistic (B) atlases.

3. PROPOSED METHOD

This paper aims at implementing a MS lesion locating method that requires only one MRI modality (FLAIR), combined with the usage of a registered probabilistic atlas to identify the brain tissues. The proposed execution pipeline consists in: registering the probabilistic atlas image to patient's FLAIR image; segmenting the WM in the FLAIR image using the registered WM of the probabilistic atlas as a prior; and identifying the WML by selecting the hyperintensies in the resulting WM segmentation[8].

The proposed method, illustrated in Figure 3 starts by registering the patient's FLAIR image with the GG-366 template, thus guaranteeing that the voxels in both sequences are spatially correspondent in the brain space. In this step, the brain atlas and the WM probability atlas are registered into the patient's brain space. This transformation is made through the usage of the linear registration routines from the AFNI[9] software and the Brain Extraction Tool, available in the FSL library [10].

The next step consists in the binarization of the WM probability map, in order to select all the voxels with at least 50% probability of being white matter, which is represented by a value of or greater than 0.5 in the voxel. In this process, as described in Equation 1, each voxel (v_i) of the probabilistic atlas image is checked. If its value is equal or greater than 0.5, the voxel is labeled 1; if not, it is labeled 0.

$$v_i = \begin{cases} 0 \; if \; v_i \leq 0.5 \\ 1 \; if \; v_i > 0.5 \end{cases} \quad \textbf{(1)}$$

Following that, all the voxels in the FLAIR image with no correspondence to the mask generated in the previous step are removed, leaving only the voxels that are classified as WM, according to the probability atlas.

After determining the WM region in the patient exam, a binarization is applied through a threshold (t), in order to identify hyperintensity regions presented in this tissue, which, in consequence, shows WML regions. The threshold value was determined by 2 standard deviations (d) above the mean of intensities (m) on the slice (ignoring background voxels), using an idea similar to the presented by Wu et al. [4](Equation 2). All regions with intensity greater than (t) were defined as MS lesion area. A thresholded image is shown in Figure 4.

$$t = m + 2d \quad \textbf{(2)}$$

The remaining voxels were three-dimensionally grouped in clusters. It was considered a 3x3x3 voxel neighborhood to determine if two voxels were adjacent and, thus, part of the same cluster. A 3d Flood Fill method was used to run through the clusters. This voxels grouping process was done in both, method and LST results, in order to generate one list of clusters for each method. These lists will be compared during the validation process, as described in next section.

Due to its inexpressive size, all clusters with less than 40 voxels (approximately 10mm³) were removed from the method's cluster list. This removal is made based on the definition that a WML must be larger than 3mm in cross section, comprising 27mm³[11].

4. RESULTS VALIDATION

In order to evaluate the accuracy of the results obtained with the proposed method, the obtained results were compared to the Lesion Segmentation Tool (LST) [2] results. LST is considered, nowadays, one of the state of the art methods, when it comes to automatic MS lesion segmentation and quantification.

From a qualitative point of view, as can be observed in Figure 5, the results obtained with the application of a threshold in the WM regions are close to those obtained with the LST.

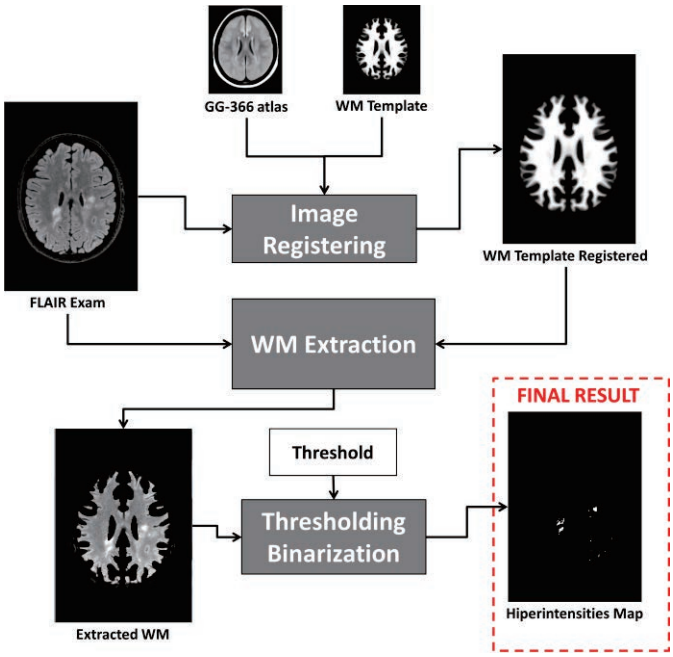

Figure 3 – Slice of the GG's FLAIR (A) and WM probabilistic (B) atlases.

In these images, areas where both the proposed method and the LST found lesion voxels (true positives) are marked in green. Yellow areas are clusters where the method indicated lesion occurrences, but the LST does not confirm its existence (false positives). Finally, the false negative clusters are showed in red.

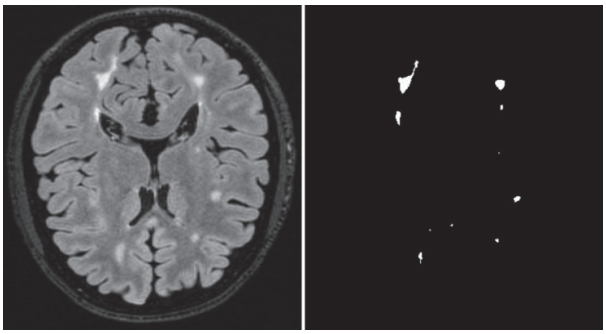

Figure 4 – FLAIR image (left) and hyperintensities map (right) after threshold binarization.

It is important to notice that the usage of LST was only possible because the available set of images contained T1-weighted images.

To evaluate the results, clusters from the method's list and clusters from the LST's list were compared and those clusters that overlapped were annotated. The acquired results demonstrate that most of the lesions indicated by the method are correspondent to some part of the lesion indicated by the state of the art method. Despite the method not quantifying the whole volume of the lesions, the identification of the areas where those lesions occur allows a quick location of the regions where WML exists, which is an important tool for MS diagnosis.

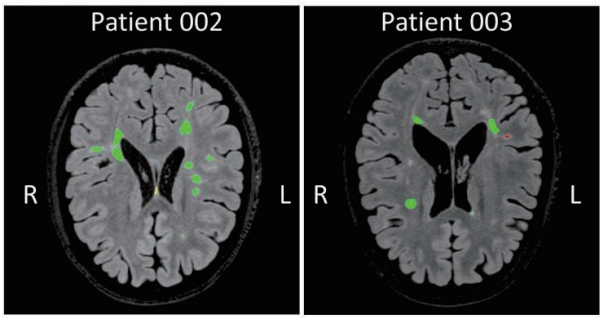

Figure 5 - Visual comparison of results obtained with the LST and with the proposed method usage, overlapping the FLAIR images

It is observable, when overlaying the WM mask to the FLAIR exams, that the result from the WM Atlas binarization does not cover all the tissue that it represents. This happens due to the fact that the GG-366 atlas is created based on an average of FLAIR images. The result of this average is an image blurred and with little detail of the brain structures (as can be noticed in Figure 2a).

From a quantitative point of view, the following statistical measures proposed on systematic reviews[5][6] were used as metrics: Dice similarity coefficient (DSC), sensitivity (Sen), overlap fraction (OF) and extra fraction (EF). The results are presented in Table 1 along with the False Positives (FP), False Negatives (FN) and True Positives (TP) cluster count and the number of clusters found with the LST.

In order to calculate the values of this evaluating metrics, the hyperintense clusters found with the method and its location in relation to LST clusters were taken into account.

Based on the acquired results, we observed a significantly high accuracy rate for the majority of the cases. The observed False Negative rate was 11% (average). The graphic in the Figure 6 shows the results of the method application compared to the LST. It can be observed that results from the method are similar to the state of the art results.

5. CONCLUSIONS AND NEXT STEPS

By eliminating the need for acquiring another MRI modality (T1 weighted), the application scope of automatic WM lesion detection methods is expanded, allowing its usage in both new and old exams, which makes it easier to follow up the progression of the disease on patients.

For future developments, the possibility of a region growth algorithm implementation is studied. Thus, the neighborhood of hyperintense voxels will be evaluated, in order to enhance lesion clusters, making this method completely automatic for segmentation and volumetric calculus of MS as it is for detection.

Even facing the restrictions observed in the results from the application of this method, it can be noticed that only using the thresholding method presented results significantly close to the state of the art. The main impediment for an accurate locating of the MS lesions was the lack of precision in the white matter mask, which did not comprise the tissues that it represents in its totality.

For this method, the linear registration was chosen since it is the same registration method that is used at the state of the art [2].Due to its unsatisfactory results on identifying WM areas, the implementation of non-linear registering methods is studied for future work, as an attempt to make the white matter probabilistic atlas registration more accurate.

Table 1- Comparative analysis between quantitative evaluation metrics data from the analyzed patient's MRIs.

Patient	Clusters				DSC	Sen.	OF	EF
	FP	FN	TP	LST				
002	9	6	34	40	0,819	0,85	0,85	0,225
003	14	4	46	50	0,836	0,92	0,92	0,28
004	40	4	34	38	0,607	0,894	0,894	1,052
006	107	3	20	23	0,266	0,869	0,869	4,652
007	152	2	11	13	0,125	0,846	0,846	11,692
101	43	0	6	6	0,218	1	1	7,166
102	20	4	24	28	0,666	0,857	0,857	0,714
103	41	4	23	27	0,505	0,851	0,851	1,518
105	53	3	16	19	0,363	0,842	0,842	2,789
106	42	2	40	42	0,645	0,952	0,952	1
Mean	**52,1**	**3,2**	**25,4**	**28,6**	**0,505**	**0,8881**	**0,8881**	**3,1088**

FP: False Positives; FN: False Negatives; TP: True Positives; LST: number of clusters found with the LST; DSC: Dice similarity coefficient; Sen: sensitivity; OF: overlap fraction; EF: extra fraction;

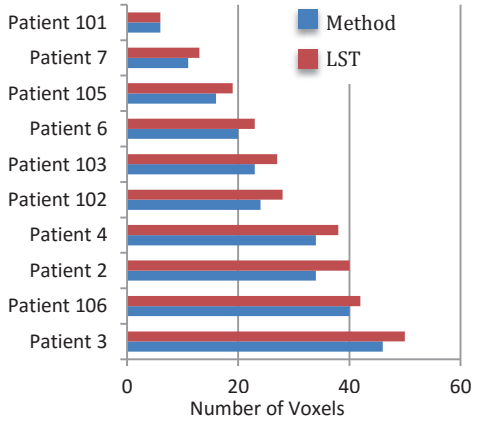

Figure 6 – Comparison between proposed method and LST results.

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7. COMPETING INTERESTS

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