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Multiple Sclerosis lesion segmentation using an automated multimodal Graph Cut

Jeremy BEAUMONT Olivier COMMOWICK Christian BARILLOT

VisAGeS U746 INSERM / INRIA, IRISA UMR CNRS 6074, Rennes, France

Abstract. In this paper, we present an algorithm for Multiple Sclerosis (MS) lesion segmentation. Our method is fully automated and includes three main steps: 1. the computation of a rough total lesion load in order to optimize the parameter set of the following step; 2. the detection of lesions by graph cut initialized with a robust Expectation-Maximization (EM) algorithm; 3. the application of rules to remove false positives and to adjust the contour of the detected lesions. Our algorithm will be tested on the FLI 2016 MSSEG challenge data.

Keywords: Graph Cut, Expectation-Maximization, Multiple sclerosis, Tissue classification

1 Introduction

Multiple Sclerosis (MS) is a chronic demyelinating disease that affects the central nervous system. Brain lesions detection plays an important role in Multiple Sclerosis (MS) studies, as it is used to evaluate patient disease and its future evolution. Currently, lesions are detected by manual or semi-automatic segmentation methods, which are very time consuming and which show a high inter and intra-raters variability [8]. This issue can be solved with fully automated MS lesion segmentation methods. Here, we present one, based on the combination of graph cut and robust EM tissues segmentation using multiple sequences of Magnetic Resonance Imaging (MRI). Our process is applied to the FLI 2016 MSSEG challenge data.

2 Challenge data and evaluation criteria

2.1 Data and pre-processing

15 MS patients data sets are available to allow challengers to optimize their segmentation algorithms. These data sets contain pre-processed and unprocessed data, available for challengers who would rather do their own pre-processing on the data, the ground truth and the seven manual segmentations used to compute it.

The challenge data sets include T1-w, T1-w Gadolinium, T2-w, PD and FLAIR sequences. It will not be described further in this paper, more details

can be found on the challenge website¹. The pre-processed data are denoised with the NL-means algorithm [5], rigidly registered [3] towards the FLAIR images, brain extracted using the volBrain platform [10] and bias corrected using the N4 algorithm [11]. As data are brain extracted, brain masks are provided in the pre-processed data sets. We decided to use the pre-processed data. Therefore, the method we described below will focus only on the MS lesions segmentation itself.

2.2 Evaluation criteria for the MS-SEG challenge

The qualitative evaluation of the proposed segmentation algorithm is made through two categories of evaluation metrics: lesion detection (are the lesions well detected independently of the contour quality?) and segmentation precision (are the lesion contours close to those of the ground truth?). For the MS-SEG challenge, the different segmentation workflow results will be compared to a ground truth for each MS patient using several evaluation metrics and will be ranked using two of them²:

F1 score: A metric used to assess the capacity of an algorithm to detect lesions. The F1 score is a combination of the lesion sensitivity (SensL), i.e. the proportion of detected lesions in the ground truth, and the lesion positive predictive value (PPVL), i.e. the proportion of true positive lesions inside the result of segmentation algorithms.

Dice score: A well known overlap metric used to assess the capacity of an algorithm to be accurate in lesion delineation.

The ground truth is computed with the Logarithmic Opinion Pool Based STAPLE (LOP STAPLE) method [1], using seven independent manual segmentations for each patient.

3 MS lesions segmentation workflow

3.1 Lesions detection using graph cut

The segmentation algorithm relies on a graph cut approach previously presented in [6] and [2]. 3 MR sequences and the brain mask are required for this algorithm. We choose to use T1-w, T2-w and FLAIR sequences. We do not use PD as it generally shows less MS lesion contrast than T2-w and FLAIR.

Graph cut principle: MS patient images are used to generate a graph which will be exploited to segment in an optimal way MS lesions from both contour and regional information. This graph is initialized in a manner that each of its

¹ <https://portal.fli-iam.irisa.fr/msseg-challenge/data>

² More details are provided on the challenge website: <https://portal.fli-iam.irisa.fr/msseg-challenge/evaluation>

nodes corresponds to a voxel and is connected to two other nodes representing the object class for MS lesions and the background class for normal appearing brain tissues (NABT). These two nodes are respectively called terminal source and sink. The image nodes are connected with their spatial neighbors by n-links, whose values are computed using a spectral gradient [6] and depend on the similarity of the two considered voxels. The t-links connect nodes in the image to their corresponding terminal source and sink nodes and represent how voxels fit into given models of the object and background. The simplest way to estimate object and background models is to use seeds chosen by a user. However, user interactions are prohibited if we want to develop an automated algorithm. This is why we compute the seeds in images with a 3-class multivariate Gaussian Mixture Model (GMM), where each class is equivalent to a brain tissue: White Matter (WM), Grey Matter (GM) and Cerebrospinal Fluid (CSF). MS lesions are considered as the outliers of this model.

Seeds computation: To be robust to outliers, the 3-class multivariate GMM is estimated using an Expectation Maximisation (EM) algorithm [7] which optimizes a trimmed likelihood. This EM algorithm has a parameter, h , representing the portion of voxels that are removed from the estimation. Its value needs to be adjusted to reject MS lesions as well as other outliers like veins or skull stripping errors from the estimation of the NABT model.

The obtained parameters of the GMM are used to compute a Mahalanobis distance [4] between each voxel of the images and each class of the NABT model. From this distance, a p-value, used to represent the probability not to fit into each of the 3 classes, can be computed. For each voxel i , we keep the lowest p-value among the three classes, denoted p_i . Sinks should have a high value when their corresponding voxels are close to the NABT model. The sinks t-links weights W_{bi} are then computed as:

$$W_{bi} = 1 - p_i \quad (1)$$

All voxels that do not fit in the NABT model have a high p-value, therefore, we wish to differentiate MS lesions from other outliers (vessels, skull stripping errors . . .) using a priori knowledge about lesion intensities. MS lesions are usually hyperintense compared to WM in T2-w and FLAIR images. A fuzzy logic approach has been chosen to model this expert's knowledge. Instead of defining a binary threshold for hyper intensity, a fuzzy weight, computed for each sequence from the two parameters *slope beginning* S_b and *slope end* S_e , is characterized (see [6] for more details). The final sources weights W_{oi} are computed by taking the minimum value between the p-value and the fuzzy weights W_{T2} and W_{flair} :

$$W_{oi} = \min(p_i, W_{T2}, W_{flair}) \quad (2)$$

Parameters definition: The presented algorithm works with three parameters: h , S_b and S_e . In order to obtain the best segmentation results, we optimize

these parameters with the provided training data set. We note that the parameter h depends on the proportion of outliers in an image, and as such is directly linked with the Total Lesion Load (TLL) of MS patients. Therefore, the algorithm parameters have to be adapted to the MS patient TLL, which has to be estimated before performing the segmentation. We define two parameter sets: one for mild lesion load ($TLL < 25 \text{ cm}^3$), and the other one for severe lesion load ($TLL \geq 25 \text{ cm}^3$). These sets are presented in Table 1. A rough TLL estimation is automatically computed with the following steps:

1. Non-linear registration of an atlas on the T1-w image. This atlas contains CSF, GM and WM probability maps plus a brain mask without the cerebellum and the brainstem.
2. Masking the T2-w and FLAIR images to keep only the WM in the two hemispheres (the amount of lesions is usually lower in the cerebellum and the brainstem and can be removed of the rough TLL estimation), using the atlas WM probability map and brain mask without the cerebellum and the brainstem.
3. Segmentation of the T2-w and FLAIR masked images with the K-means algorithm [9]. T2-w and FLAIR images are segmented respectively in 4 and 3 classes. This segmentation is performed to extract MS lesions, regrouped in one class in each image, from WM.
4. Intersection of the T2-w and FLAIR MS lesions classes.
5. Computation of the volume from the resulting image, which corresponds to an approximation of the TLL.

	h	S_b	S_e
Mild Lesion Load	0.1	2.0	4.0
Severe Lesion Load	0.4	3.0	4.0

Table 1: Values of our segmentation algorithm parameters, optimized on the training data.

3.2 Post-processing

After the detection of candidate lesions, some false positives still remain. To remove these artifacts, we add a post-process, made of the following steps:

1. lesions which have a size lower than 3 mm^3 are removed
2. lesions touching the brain mask border are removed, as they are probably false positives due to vessels or skull stripping errors
3. lesions not sufficiently located in WM are removed, as MS lesions are typically located there

4. lesions which do not touch a mask computed from MS patient T2-w and FLAIR sequences are removed. Lesions are considered as hyper intense in these two modalities, so it is possible to build a mask of “probable lesions”, i.e. regions where lesions may appear and out of which no lesion may be seen. This mask is built by automatically thresholding the T2-w and FLAIR images and intersecting those masks. Our segmentation method generates several false positives in the brainstem, therefore, the mask used in this post-processing step also excludes this region.
5. lesions delineations are improved using the mask of “probable lesions” computed in the previous step

4 Results

4.1 Sample results

Table 2 presents an evaluation of the whole segmentation algorithm with a post-processing step on the training data. An example of segmentation result is shown in Figure 1.

	Dice scores	SensL	PPVL	F1 scores
Mild Lesion Load	0.4703	0.4124	0.5698	0.4441
Severe Lesion Load	0.7219	0.2775	0.4605	0.3061
Mean	0.5709	0.3584	0.5260	0.3889

Table 2: Evaluation of our segmentation algorithm on the training data

4.2 Implementation and Computation Times

The algorithm benefits of a multi-threaded implementation, based on ITK and available in open-source software Anima³. The total computation time to process each segmentation of the data set on a computer with an Intel(R) Xeon(R) CPU E5-2660 v3 @ 2.60GHz (8 cores) is approximately 10 minutes.

5 Conclusion

A fully automated MS lesion segmentation method using a graph cut initialized with a robust EM algorithm was presented. The results of the segmentation depend on the algorithm input parameters, which are directly linked with the MS patient TLL. The TLL is difficult to estimate and an error could result in a bad choice of these parameters, which may influence the segmentation workflow leading to worse results. Consequently, the automation of the presented method

³ <https://github.com/Inria-Visages/Anima-Public>

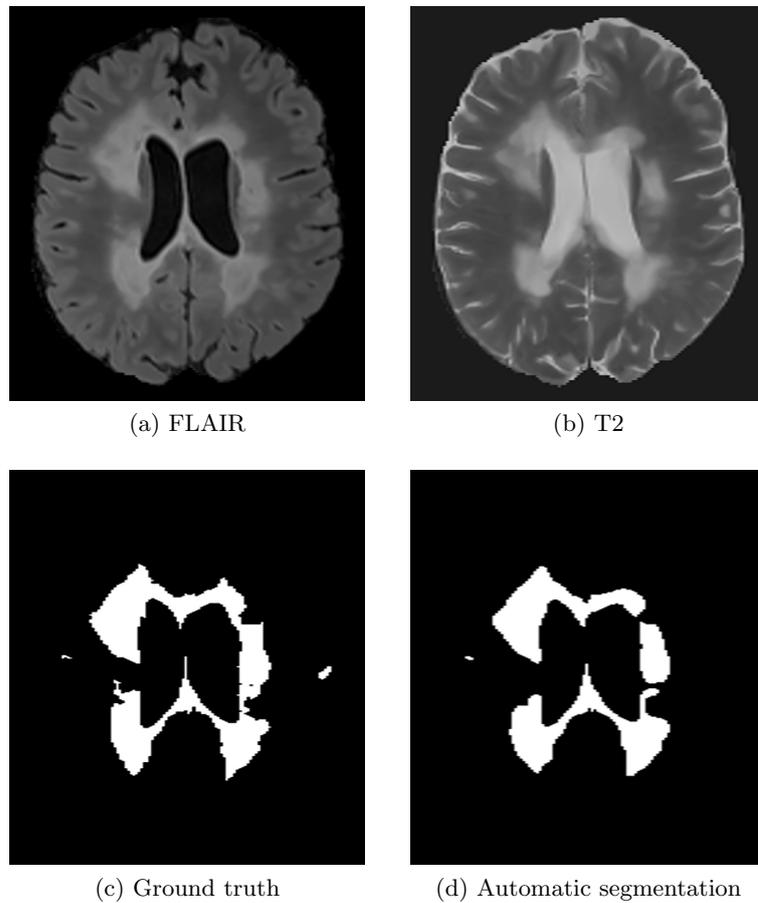


Fig. 1: Automatic segmentation of the data set 01016SACH

is a complicated task where the initialization of the parameters is very important to reach satisfactory results. These results are improved with a post-processing step in order to reduce the number of false positives to be as close as possible to the ground truth.

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