

High intensity region segmentation in MR imaging of multiple sclerosis

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Abstract. Numerous pathologies are often manifest in Magnetic Resonance Imaging (MRI) as hyperintense or bright regions as compared to normal tissue. It is of particular interest to develop an algorithm to detect, identify and define those Regions of Interest (ROI) when analyzing MRI studies, particularly for lesions of Multiple Sclerosis (MS). The objective of this study is to analyze those parameters which optimize segmentation of the areas of interest. To establish which areas should be considered as hyperintense regions, we developed a database (DB), with studies of patients diagnosed with MS. This disease causes axonal demyelination and it is expressed as bright regions in PD, T2 and FLAIR MRI sequences. Thus, with more than 4300 hyperintense regions validated by an expert physician, an algorithm was developed to detect such spots, approximating the results the expert obtained. Alongside these hyperintense lesion regions, it also detected bone regions with high intensity levels, similar to the intensity of the lesions, but with other features that allow a good differentiation. The algorithm will then detect ROIs with similar intensity levels and performs classification through data mining techniques.

1. Introduction

Multiple Sclerosis is a disease of the central nervous system that affects more than 2.5 million people all over the world. There is no known cure for the disease so far; however, there are therapies that may slow its progression.

The neural regions where myelin is lost (plaques or lesions) appear as hyperintense regions in MRI studies, particularly on T2, PD and FLAIR sequences [1]. In MS, these lesions appear at different times and locations of the brain and spinal cord. Once identified, a growth in size or temporal spread of the lesions may occur. And so, it is very important to delimit all the lesions if it is meant to evaluate the development of the disease or the results of the treatment drugs [2].

However, the human ability to distinguish subtle variations in the images is quite limited. Another important fact is that delineating all lesions in a particular study is a tedious and time consuming task. This is where Digital Image Processing has a wide range of applications.

While MRI studies are widely used for the diagnosis of neurodegenerative diseases and monitoring their evolution, conventional methodology fails to detect the underlying disease process, and consequently, the correlation between the clinical findings and conventional MRI is very limited [3]. This discrepancy clinical/radiological is probably due to the difficulty of the analysis and detection of specific major pathologic patterns associated with each disease.



Physicians reporting studies must be trained based on certain conditions and perform a number of annual reports. Double reading of reports increases the sensitivity of lesion detection minimum 7% but at a high time cost [4].

From the observation of the evolution of hyperintense regions it can be analysed the development of the abnormalities caused by MS, which in turn serve to monitor the disease and assess the effectiveness of various drugs.

Therefore, the aim of this work was to develop an automatic algorithm based on statistical parameters that could delimit the regions acceptably, in comparison with a DB delimited by a specialist, after a validation process. This segmentation program might then be used with different artificial intelligence techniques in order to develop an automatic detector of MS lesions in MRI.

Tissue segmentation is one of the processing phases in medical imaging and defines different regions within images or volumes obtained from the different diagnostic techniques [5]. This process can be applied for the diagnosis or treatment of various diseases by detecting and tracking the injured areas.

Magnetic Resonance Imaging (MRI) is a method widely used in the analysis of neurological pathologies. To accomplish this, it is important to acquire different sequences that allow one to enhance particular characteristics of each tissue to detect pathologic regions. Among the sequences used, it can be mentioned: proton density, T1, T2, FLAIR, fMRI, Perfusion, Diffusion, DTI, etc. [6]. In the acquired images, the regions under evaluation are often presented as hyper or hypo-intense regions (see figure 1).

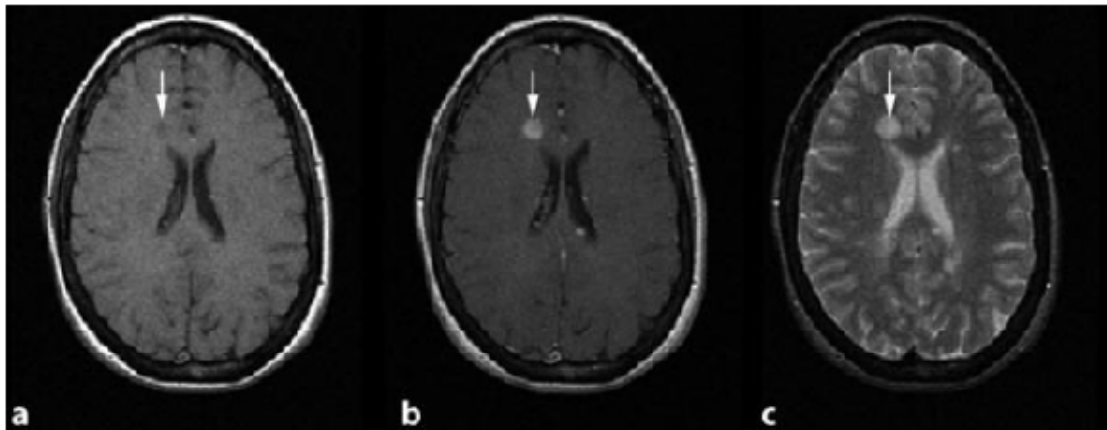


Figure 1. Axial images of sequences T1(a), T1 with contrast (b) and T2(c) of a patient with MS. In T1 sequences de lesion are defined as hypo-intense regions. While in T1 with Gd the lesions are shown as hyper-intense (courtesy of Sahraian M A and Radue E W 2008).

There are segmentation techniques based on the multi-sequence analyzing seeking the delimitation of just the MS lesions avoiding the reduction of false-positive [7], [8]. Other methods are based on fuzzy logic techniques intended to improve the detection of small lesions [9]. Akselrod-Ballin et al [5] propose a method of segmentation and classification using two data sets: PD-T1-T2 for 25 patients and FLAIR for 16 patients. Examples of MS lesions are shown in figure 2. Based on the proposed technique, they indicate that the sequence FLAIR has slight improvements in sensitivity and specificity. However, most of these studies use databases with a small number of studies, making it difficult to generalize these techniques.

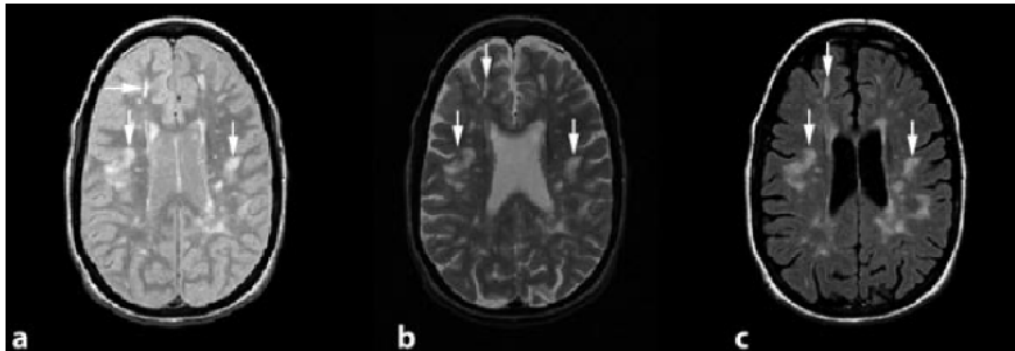


Figure 2. Axial images of sequences PD(a), T2(b) and FLAIR(c). It can be seen a better definition of the lesions in the last image (courtesy of Sahraian M A and Radue E W 2008).

For MS patients, FLAIR sequence shows the lesions as hyper-intense regions. In addition to these structures, there are other hyper-intense regions related with injuries of different etiology or bone structures. This paper aims to apply segmentation tools of hyper-intense regions. This algorithm is then used to classify them in lesions of MS or other structures, see figure 3.

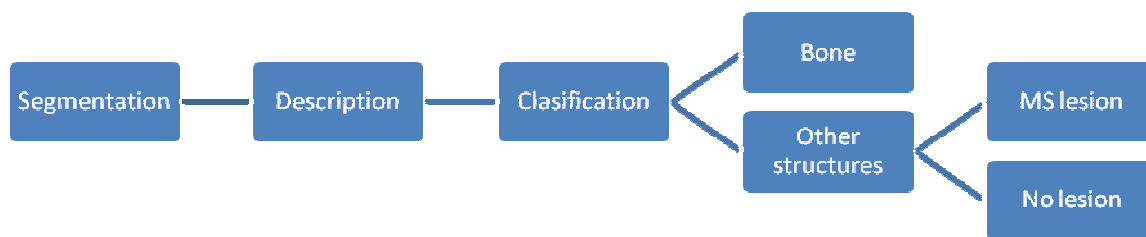


Figure 3. Steps of a usual Computer-Aided Diagnosis System.

This paper presents a segmentation technique based on adaptive thresholds and growth regions. Proposed techniques have highlighted a better sensitivity over the specificity, proposing for classification stages discrimination between segmented volumes corresponding to MS lesion or other structures.

2. Methods and Materials

2.1 Data Base

The database is composed of 100 studies of 68 patients with MS, acquired in a 0.5-T magnetic resonator develop by own project research [12]. These studies have multiple sequences, within which, in the Axial FLAIR series was conducted a process of delimiting regions of injury. This arduous process was carried out by a specialist in neuroimaging, which indicated 2 points for each lesion: the first inside the injury and the second in the periphery. This allowed subsequently delimit ROIs by growing seed point, to the gray level of the border point. The marks were recorded on an overlay under DICOM standards and all were validated by the same professional.

2.2 Automatic detection of hyperintense regions

Once defined the regions of injury, it was necessary to develop a system for automatic detection of regions with the same relative intensity of bright or gray level, which can be used, for example, in systems of Computer-Aided Diagnosis (CAD) for further classification process [10]. For this, it was used a Region Growing Technique.

It was necessary to solve two specific problems: the location of the seed points of growth and the amplitude of growth of these seeds.

Identifying regions of hyperintensity (seed points) was performed by dynamic threshold binarization according to the result of Equation 1, where P1 is a constant.

$$\text{Detection Threshold} = \frac{\text{Median}^2}{\text{Mean}} * P1 \quad (1)$$

The average value of the image is modified by the amount of extreme samples (hyperintensities), while the median value of the image has slight response to this variation. The greater amount of hyperintensities in the image, the greater the average and therefore the detection threshold will be reduced in order to detect every one of them. The result of this first binarization is a black and white image, where white regions correspond to the brighter pixels of the hyperintense areas in the original image. To perform the growth of the ROIs, using the centroid of these regions as seed points, a new gray level is determined by Equation 2, where P2 is a constant.

$$\text{Growing Threshold} = \frac{\text{Mean}^2}{\text{Median}} * P2 \quad (2)$$

This equation resembles to the idea that sometimes hyperintense regions do not present a strong contrast to neighbor regions that are also bright, so while brighter the image, the gray level thresholding should be increased to ensure well defined ROIs and avoid not desirable connection.

To set the value of the constants P1 and P2, which limit seed points and ranges of growth, it were analyzed all database studies. For this, it was used an exhaustive method by scanning a range in the P1-P2 space. This range was established based on a medium value of detection and growing of the lesions, after an iterative process. All this permitted to define superposition of regions automatically marked and labeled by the physician in order to detect errors.

The overlay, composed only by the automatic detected lesions, was analyzed by XOR (exclusive-or) resulting in 1 when the values of the both binaries images, automatic process and validated DB, were different. This means that XOR operation result is related with errors in segmentation. Therefore, lesion areas marked by the professional (I_{prof}) that overlap automatically marked regions (I_{autom}) are deleted, resulting in zero. Hence, the amount of white pixels is considered as a quality measure, the lower the best. The differences image is defined as show in Equation 3.

$$I_{diff} = XOR(I_{prof}, I_{autom}) \quad (3)$$

That is, the result is a "white value or 1" when automatically marked regions do not correspond to those marked in the database due to poor growth, to an excessive growth, or that are inconsistent with lesion marks (for example, bone).

This defines whether automatically labeled regions are smaller or larger than those of the database, and so, expect a minimum area resulting of XOR output when regions are as close as possible.

3. Results

The proposed method was used to perform scanning in the parameter space (P1, P2) to analyze the resulting area of the XOR output and obtained the result shown in figure 4. The scan was made on 100 studies with 18 images each, resulting in a total of 1800 images. It can be seen that the area increases as the parameter of growth increases because there are more variations with respect to the database. On the other hand, in the opposite direction, if the amount of seed points decreases, the number of ROIs detected will become smaller, so that the output area decreases, showing poor results.

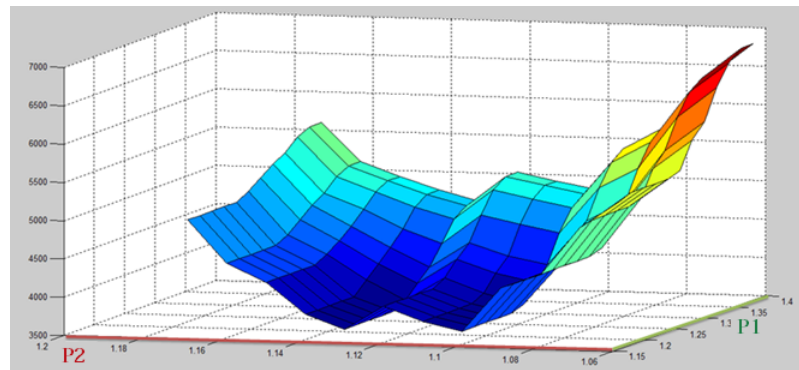


Figure 4.Resulting parameter space (P1, P2). The region with best results is shown in blue.

As can be seen, the image has an area of minimum values, which corresponds with the fewer error in the ROIs delimitation. As mentioned with regard to seed points, the best parameters values are those who result in a minimum value in the XOR-area surface. This is because all the lesion areas are indicated by a dot seed and the growth of these is consistent. On the other hand, if the “seed parameter” is set to low, there might be too many seed points, and the error would increase.

To evaluate better the response in this area and establish the best values for the parameters P1 and P2, a more extensive analysis was carried out in a minimum zone, using a smaller step to sweep both parameters. The final results are shown in the figure 5.

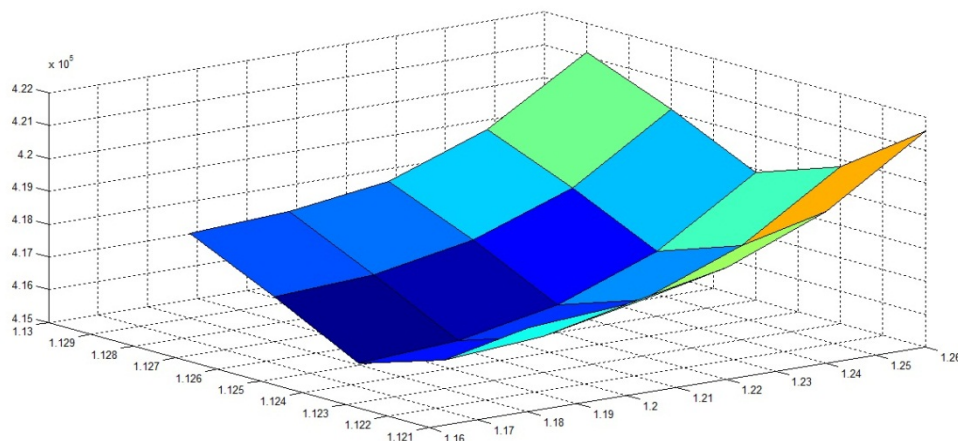


Figure 5.Resulting parameter space (P1, P2) with a more little step between parameters values.

With these values, the segmentation algorithm was tried out and validated against the data base in an automatic process based on verifying the pixels establish as ROI, using the optimum values of P1 and P2. This process gave the best result of a 91% of lesion segmentation, with an 8% of extra pixels and a 19% of fewer pixels, for the parameters P1=1.18 and P2=1.125. This means that all over the 100 studies the algorithm detects a 91% of the lesions but has the main problem in the growing parameter, which it seems to be too small, giving ROIs smaller than the ones of the data base. With the intention to improve this, a smaller value of the parameter was used but the results were worst, probably because an excessive delimitation. Nevertheless, a result of 91% is acceptable to start a real situation validation with the values found as optimal for P1 and P2 in equal acquisition conditions. This is, same equipment and image features.

These percentages correspond only to the lesions marked in the data base. The hyper-intensities due to bone and other structures are also delimited but were not took into account for the validation, because the mayor objective is to evaluate the lesions segmentation. As mentioned above, after the segmentation, a classification process should categorize all the structures detected.

The best values of P1 and P2 were then used in the detector with excellent delimitation results (see figure 6). The bone was eliminated of the segmentation process by using a classification stage not described in this work, based in features detection of bone regions and neural network classification [13].

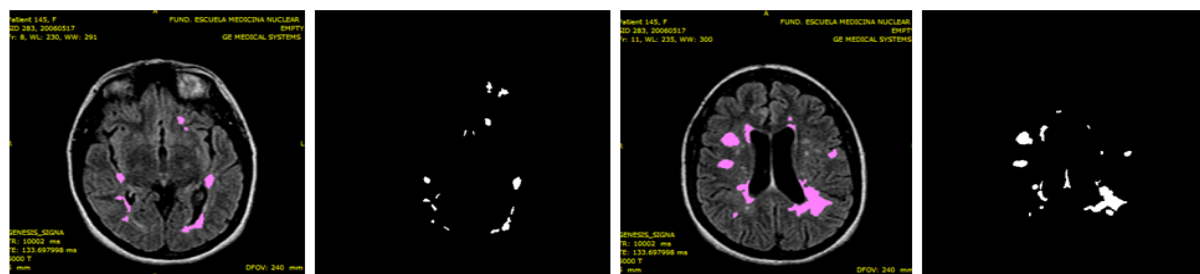


Figure 6. Specialist delimitations in pink next to automatic segmentation results on the right.

4. Conclusions

Detection of hyperintense regions in MRI studies is of great diagnostic value in clinical practice. Usually, this segmentation process is based on complex interpretation algorithms [11]. By systems that delimit these areas, similar to a medical specialist or maintaining similar parameters, it is possible to detect and classify hyperintense areas by specialized systems or obtain characteristics of these regions that might be used as clinical diagnostic support. For example, evaluate an increase in the size of lesions of a patient under a given treatment. The search of a better equation for the growing parameter is the main objective at the moment, basically trying to obtain bigger ROIs without detecting other adjacent structures.

Through this work we present an algorithm that detects hyperintense regions of MS, with a 91% validation but slightly more little lesions with respect to the data base, as a prelude to the classification of injury and other bright regions.

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