Characterizing Scars in the Cerebral Cortex by Analyzing Intensities in T2/MRI Sequences

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Abstract. The detection of scars in the cerebral cortex usually involves a manual process performed by radiologists, who have to face multiple troubles. For example, the bad calibration of the equipment used to get images of the cerebral cortex can cause spacial and geometrical distortions in the MRI (Magnetic Resonance Imaging) sequences. Owing to the advances in algorithms capable of analyzing MRI sequences, it is possible to automatically detect scars in the cerebral cortex in a successful way. In addition, an automatic process for finding scars can decrease the subjectivity of human interpretations and serve as a tool to support diagnoses of diseases. In this paper, we propose a new methodology to detect scars in the cerebral cortex by means of the analysis of intensities in T2/MRI sequences. In particular, we implement three main algorithms: the region growing, thresholds, and artificial neural networks.

Keywords: Detection of scars, cerebral cortex, intensity, Magnetic Resonance Imaging.

1 Introduction

Nowadays, some manual processes performed by humans, such as the analysis of medical images, have been automated in order to accomplish different objectives. Several researchers have been focused on the development of projects that employing computing algorithms allow humans to get a fast and less subjective response regarding diagnoses of diseases. The kind of systems created to automate the manual processes that experts in the medical field perform is known as Computer Aided-Diagnosis (CAD) [18, 30].

There exist different kinds of medical images, e.g., Ultrasound, Computed Tomography (CT), and X rays, which are processed by CAD tools. In particular, MRI sequences are built considering the intensities of human body tissues, which

are captured by the receiving antennas of a MRI machine. Later, these intensities are transformed into images, which are analyzed by radiologists and neurologists, to find anomalies in tissue structures, malfunctions, diseases, etc. Specifically talking about the brain, the analysis of intensities in MRI sequences facilitates the detection of multiple sclerosis, Alzheimer, tumors, etc.

There are different types of MRI sequences, being T1 and T2 the main ones. Each one of them has a different range of intensities, which represents a difficulty when analyzing imaging sequences through algorithms. In particular, the MRI segmentation task becomes more complex, because it is not possible to establish ranges in which organs can be located, as in the case of CT. If there were ranges of intensities established, such as the Hounsfield values in CT [28], it would be simpler to classify tissues when performing automatic imaging analysis, since their intensities are located in those ranges. Another problem is that those intensities change each time images of an organism are taken, because the MRI machine works with hydrogen spin atoms present in the patient's body at the moment the images are taken. Thus, even when the captured images correspond to the same person, their intensity values will not remain constant.

Digital analysis of medical images is an important topic of Artificial Intelligence, since a computer should have a knowledge degree in order to make decisions. That knowledge is derived from a learning phase, in which it is necessary to process labeled data. In this paper, we propose a new methodology to automate the detection of scars in the cerebral cortex. Our methodology focuses on the analysis of intensities in MRI sequences of the cerebral cortex, in particular, in T2 sequences. This analysis is made by using segmentation and pattern recognition algorithms, such as growing regions [26] and thresholding [27]. To make the final decision about the nature of a detected object, the use of artificial neural networks [13] is proposed.

This paper is organized as follows. In section 2, related work regarding the detection of cerebral injuries is presented in order to expose their strong and weak points. In section 3, the proposed methodology to automatically detect scars in the cerebral cortex is explained in detail. Following, section 4 describes the established parameters of the experimentation phase and analyzes the obtained results. Finally, in section 5, the conclusions and future work are presented.

2 Related Work

Thanks to Computer Science, the analysis of data has been automated by means of algorithms. One of the most common approaches is the statistical one. Under it, several research works have been made, such as Khayati et al.'s [15], whose objective is to find multiple sclerosis injuries in the cerebral cortex by using FLAIR sequences, specially on axial cuts. To find these injuries, they propose a Bayesian approach, which employs Markov random fields [11, 24] and adaptive mixtures [4] to compute *a priori* probabilities stored in a feature vector that is used to classify the types of analyzed tissues. Radiologists and neurologists have manually performed the selection of images in which injuries are present. They

have analyzed spatial characteristics and regions of the brain to extract it from images. The feature vector is built from the intensities of FLAIR sequences. The advantage of using Markov random fields and adaptive mixtures is that it is not necessary to perform a training phase, in order to make the system learn and make decisions, since *a priori* information is already known.

Kobashi et al. [16] propose the SoS system, which consists in analyzing different types of medical images. Among them, MRI sequences are processed to get relevant information about neonates, e.g., the brain volume, the brain deformity index, the *sulcal* deformation index, the *gyral* area, and the brain representation. From these measures, the SoS model provides data that can be analyzed lately by radiologists and neurologists. The SoS model gives useful information and provides a degree of certainty, even if it relies on fuzzy methods [14].

Nakamura et al. [22] focus on measuring the brain volume when it presents multiple sclerosis injuries. Since these are known as black holes, neurologists consider that the brain loses volume when presenting such holes. To extract the brain from images, an anisotropic mask filter [3, 6] is used. This mask filter attenuates the background of images to improve the contrast of the noise or irrelevant information. Like Kobashi et al., Nakamura et al. classify different tissues (e.g., white matter, gray matter, and cerebrospinal fluid) by processing some probabilities, which are obtained from the intensities, anatomy, and morphology of the brain tissues and are used to create masks for each class.

Klöppel et al. [25] make a comparison of different methods to detect injuries in white matter, analyzing MRI sequences. They employ algorithms from the statistical approach e.g., the k-nearest neighbor algorithm [7] and support vector machines [21]. Multiple thresholds are also established based on the intensity of MRI images. On their research, Klöppel et al. combine T1 and FLAIR sequences from demented patients. It is important to notice that Klöppel et al. normalize their images, i.e., they do not work with pure intensities of tissues.

Arimura et al.'s project [2] has been in development for several years; that is why it includes the automated detection of various diseases. To start, during data processing, they use normalization and smoothing filters [8]. Depending on the injury and the extracted features, different methods are used. In case of aneurisms, Arimura et al. use a 3D Gaussian filter [29] considering the shape of injuries. Some other segmentation techniques have been employed, such as the growing regions [26], snake [9], watermarks [1], and level set [23] algorithms. For multiple sclerosis, the shape of injuries is also taken into account to establish candidates. Afterwards, the distance is measured between the places where injuries are located and the lateral ventricles, because Arimura et al. claim that sclerosis is located at a certain distance from the center of the brain. For detecting Alzheimer, support vector machines are used to measure some characteristics, such as the volume of the cerebrospinal fluid.

To detect tumors, Arimura et al. propose a neural network with the following architecture: fifteen neurons on the input layer in which each neuron corresponds to a characteristic, e.g., location of a tumor, whether it involves an edema or not, heterogeneity, etc. In the hidden layer, there are six neurons and, in the

output layer, there are four neurons for: high-grade glioma, low-grade glioma, metastasis, and malignant lymphomas, respectively.

Arimura et al.'s work is extensive and really complete. They have used different algorithms, which give a wide outlook of which techniques should be used to obtain better results, when detecting a specific injury. In this case, the detected problems have involved the brain, but in a similar way, these algorithms could work with any part, type of tissues or organs of the human body.

Fu et al. [10] propose the use of artificial neural networks [13], Expectation-Maximization [5], and the C-means algorithm [20] to classify the brain tissues into white matter, gray matter, and cerebrospinal fluid.

Finally, Yamamoto et al. [30] use a false-positive reduction scheme [19], a rule-based algorithm, and support vector machines to detect multiple sclerosis. In this work, T1, T2 and FLAIR MRI sequences are analyzed.

All these research works deal with a specific illness. In this paper, we propose a new approach, which objective is to detect scars in the cerebral cortex, no matter the illness, by analyzing intensities in MRI sequences. This new approach aims at providing radiologists and neurologists with a second opinion.

3 Methodology for the Automatic Detection of Scars in the Cerebral Cortex

The following section describes the methodology proposed in this paper to automate the detection of scars in the cerebral cortex by analyzing MRI sequences. The images of these sequences have a size of 256x256 pixels in grayscale and can be represented as T1 with contrast and simple, T2 with contrast and simple, FLAIR, among others. In practice, radiologists use T2 sequences to identify scars in the cerebral cortex, since the human eye can identify lesions in the brain easily, owing to perceptible changes in the intensity of pixels. In the case of T1 sequences, intensities and shapes change with respect to T2 sequences for both the human eye and the computer. Consequently, the identification of scars in T1 sequences is not as straightforward as in T2 sequences.

3.1 Cerebral Tissue Extraction Through the Region Growing Algorithm

In all imaging sequences, tissues of all kinds can be observed, e.g., skull, ocular, fat, nerve, etc., and must be removed in order to extract the tissue of interest. This step can be accomplished through the region growing algorithm [26] with variable seed to only extract the brain tissue area, which is the target tissue of the proposed methodology. It is also possible to carry out a histogram analysis [12] because of the difference in the imaging intensities.

The main objective of the region growing algorithm is to group pixels, according to the similarity degree among the intensity values of neighboring pixels. There are two types of algorithms, semi-automatic and automatic. The former type involves an operator, while the latter only requires an operator to verify

the result. Sant'anna et al. [26] propose two main tasks for the region growing algorithm: 1) to divide images into a number of homogeneous regions, where each region is labeled only once, and 2) to separate homogeneous regions from the rest with different properties. The steps of the region growing algorithm are:

1. **Selection of the seed.** In a manual way, a physician or a radiologist selects a starting point in an image that serves as seed, which will provide the coordinates of the initial pixel depending on the tissue to be extracted.
2. **Determination of the t threshold.** Necessary conditions for the algorithm to classify pixels into regions and the t threshold are determined.
3. **Establishment of the neighborhood.** Pixels are selected in order to be included in the neighborhood of the seed (see lines 7-14 from Algorithm 1).
4. **Iteration and recursion.** The neighborhood is defined for each visited pixel, so a path is determined in order to visit pixels not visited yet (see lines 1-18 from Algorithm 1).

Algorithm 1 Region growing segmentation

Require: An image, (x, y) coordinates of the seed, intensity, t threshold
Ensure: Brain tissue region extraction

```
 1: while (stack r ≠ empty) do
 2:     if (neighVisited(x, y) = 0) then
 3:         region ← image(x, y)
 4:         if (region<= (seed+ t)) & (region>= (seed-t)) then
 5:             neighVisited(x, y) ← 1
 6:             segmentedImage(x, y) ← image(x, y)
 7:             pendingNeigh.push(x-1, y-1)
 8:             pendingNeigh.push(x-1, y)
 9:             pendingNeigh.push(x-1, y+1)
10:             pendingNeigh.push(x, y+1)
11:             pendingNeigh.push(x+1, y+1)
12:             pendingNeigh.push(x+1, y)
13:             pendingNeigh.push(x+1, y-1)
14:             pendingNeigh.push(x, y-1)
15:         end if
16:         seed ← region
17:     end if
18: end while
```

Within these steps, it is important to take into account three criteria. The first one corresponds to the way the seed is determined. Let us recall that the region growing algorithm can be automatic or semiautomatic. In the automatic algorithm, no intervention is required from a user to determine the coordinates of the seed. The algorithm becomes semi-automatic when the user indicates such coordinates as done in this work. This algorithm has been used because it is necessary to select a seed that corresponds to a pixel, which value is within

the intensity range of the brain tissue, preventing the algorithm from selecting another tissue, such as eyes or skull. Since the segmentation process described in this paper is bi-dimensional, the seed has to be selected on each image.

The second criterion is the measure of homogeneity to determine whether a pixel belongs or not to a region of interest. At this point the t threshold is determined. We have obtained an approximate value of the brain tissue by means of the DICOM viewer called Osirix [17], a special tool for visualizing medical images. In this way, we have calculated and proposed the t threshold used for the experiments detailed in section 4.

The t threshold corresponds to the range established according to the intensity values of the region that requires segmentation. The similarity of pixels with respect to the seed is indicated by the absolute difference between the intensity of each pixel and the one of the seed. The t threshold is used to establish the following condition: if the absolute difference is less than t, then that pixel is added to the region of interest. If a large value of t is considered, there may be areas far apart, so the degree of homogeneity is lower. More, by setting a small value of t, the segmented region is more homogeneous and the data loss is less.

Finally, the third criterion refers to the conditions the algorithm must follow to stop, i.e., how and when. We have used a stack, in order to establish a path that allows the algorithm to return and to verify whether there is a neighbor that has not been visited. In this way, this stack allows the algorithm to go over the whole image looking for pixels that correspond to the brain tissue.

3.2 Detection of Suspicious Regions Using Thresholding

Thresholding is one of the simplest techniques for separating or labeling pixels in an image [27]. This technique determines a value, called threshold, that decides the class (i.e., a region) a pixel belongs to according to its intensity value. The definition of the t threshold can be expressed as follows [31]:

Let p be the analyzed pixel of an image, which has to be assigned to either a class P_0 or P_1 according to the conditions $I(p) < t$ or $I(p) > t$.

The intensity is an imaging characteristic, so the t threshold measures this property, in order to separate an object from the image background. The t threshold can be fixed or variable, i.e., its value changes according to the segmentation needs. If the intensity of the pixel being analyzed exceeds the t threshold, that pixel belongs to the class of the object of interest. On the contrary, if the intensity of that pixel is less than t, it is considered as a part of the background.

3.3 Determination of Scars Using Artificial Neural Networks

All the regions obtained during the detection phase of suspicious spots are processed, in order to be placed into two classes: scar or non-scar. An artificial neural network is used in the classification process, which input neurons correspond to the location (x, y) and the intensity of the pixels belonging to such regions.

To display the results, it is necessary to implement a scientific visualization technique, such as 3D reconstruction, and to use colors that allow radiologists to

distinguish suspicious tissue regions, i.e., the system suggests a tissue susceptible to be a scar. The development of this tool is out of the scope of this paper.

4 Experiments and Results

In this section, we describe two tests of the proposed methodology when applying it on the MRI sequences provided by the Mexican Neurology and Neurosurgery National Institute. On these MRI sequences, scars were previously detected through the traditional method used by experts in the medical area, i.e., observation. In particular, we describe the characteristics of T2 sequences, the parameters used in the experimental stage and the results obtained when processing medical images using the proposed methodology.

4.1 The Former Sequence

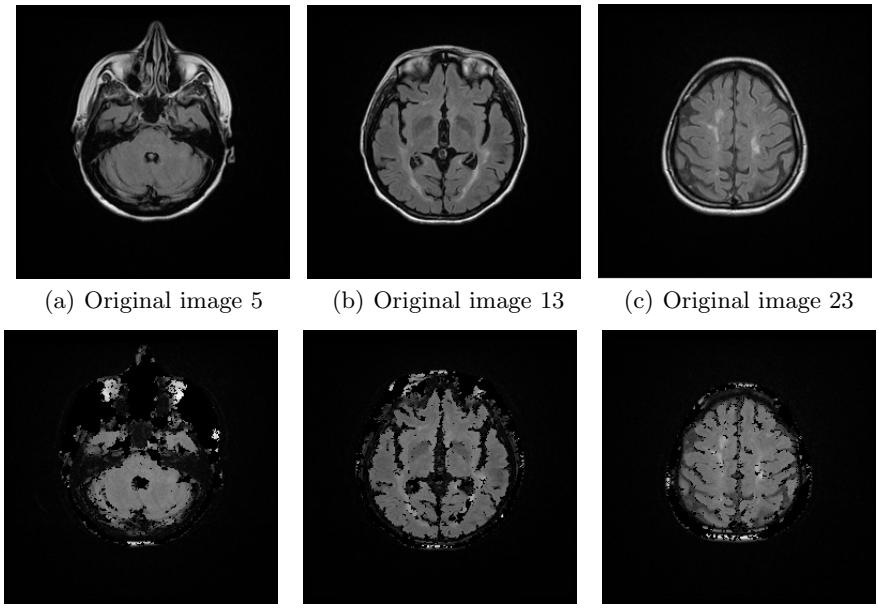
In this section, we present the results obtained from processing the former MRI sequence, which consists of 24 images of axial cuts from the T2 type. The patient is a 42 years-old female, whose disease is multiple sclerosis. Sequence values are in a range of intensities from 0 to 4052.

1) Extraction of the brain tissue region. Extracting the soft tissue is part of the preparation process of the images that are analyzed in the detection phase of scars. The main task of this first phase is the extraction of brain tissue, while avoiding losing information, e.g., removing the skull and other tissues irrelevant to this study. The parameters needed to carry out the former segmentation of images by means of the region growing algorithm are: 1) the coordinates of the seed, which are (100, 125) pixels, 2) the intensity value, corresponding to the average of the region of interest in Osirix, which according to the coordinates of the seed is 1089, and 3) the t threshold, which is 72.

Figure 1 shows some segmented images from the former sequence. Let us notice that some traces of skull and other tissues, such as eyes, are still present in the segmented images. The existence of these residues is due to the fact that the intensity values of the brain are taken as a basis to define the t threshold, so it is possible for this intensity value to be present in some other tissues, which is considered when running the region growing algorithm.

2) Detection of suspicious regions. As mentioned in Section III.B once the cerebral and skull regions have been separated, the next step is to identify, within the brain tissue, regions that can be labeled as scars (suspicious spots). It is necessary to carry out another segmentation process, in order to extract information about each one of the regions that will be considered as suspicious scars.

The viewer Osirix allows us to obtain the corresponding intensity values of each tissue. This viewer has a tool that gives the average value of the selected region. In this way, we have obtained the approximate value of a scar and established the threshold values. The proposed thresholds for extracting the brain tissue and detecting scars in T2 sequences are ± 72 and ± 385, respectively. These parameters are useful for testing both the former and latter sequences.



(a) Original image 5 (b) Original image 13 (c) Original image 23

(d) Brain extraction in image 5 (e) Brain extraction in image 13 (f) Segmented image 23

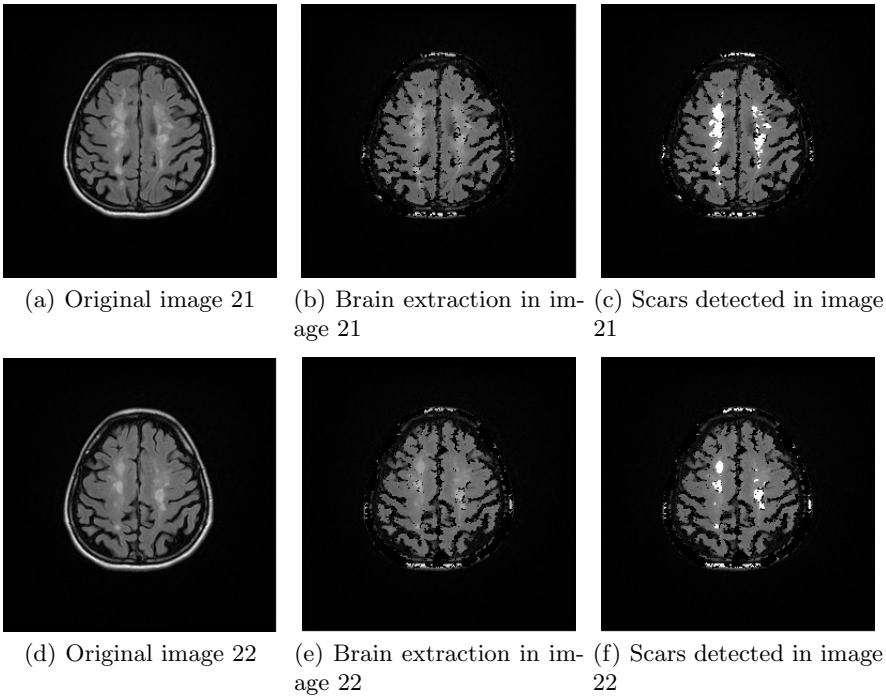
Fig. 1. Segmentation of the former sequence. We can see at the top, three images from the original sequence and, at the bottom, the corresponding segmented images, in which the brain tissue has been isolated. These two sets of images allow us to make a comparison between the original sequence and another where the skull and other tissues have been removed from each image. In figures (a), (b) and (c) there are some tissues that are not part of the brain, e.g., eyes. Once the segmentation process has been done, there are still tissues that do not correspond with the brain tissue, as shown in figures (d), (e) and (f)

Figure 2 shows the results regarding the images 21 (c) and 22 (d). The suspicious spots can be seen in (e) and (f). Once detected by the histogram analysis algorithm, the scars are highlighted by means of an intense white color, in order to be clearly identifiable. The value for the region of interest, i.e., the areas corresponding to the scars, is 1950 and the t threshold is 390.

4.2 The Latter Sequence

The latter sequence consists of 24 images of axial cuts from the T2 type that correspond to a 43 years-old female patient with multiple sclerosis. The intensity levels are approximately between 0 and 3384.

Figure 3 shows the results of the segmentation performed. In particular, figures (a), (b), and (c) correspond respectively to the 18, 19 and 20 images of the original sequence. In these images, there are visually distinctive scars. Using the region growing algorithm, the cerebral tissue was obtained as observed in figures



(a) Original image 21 (b) Brain extraction in image 21 (c) Scars detected in image 21

(d) Original image 22 (e) Brain extraction in image 22 (f) Scars detected in image 22

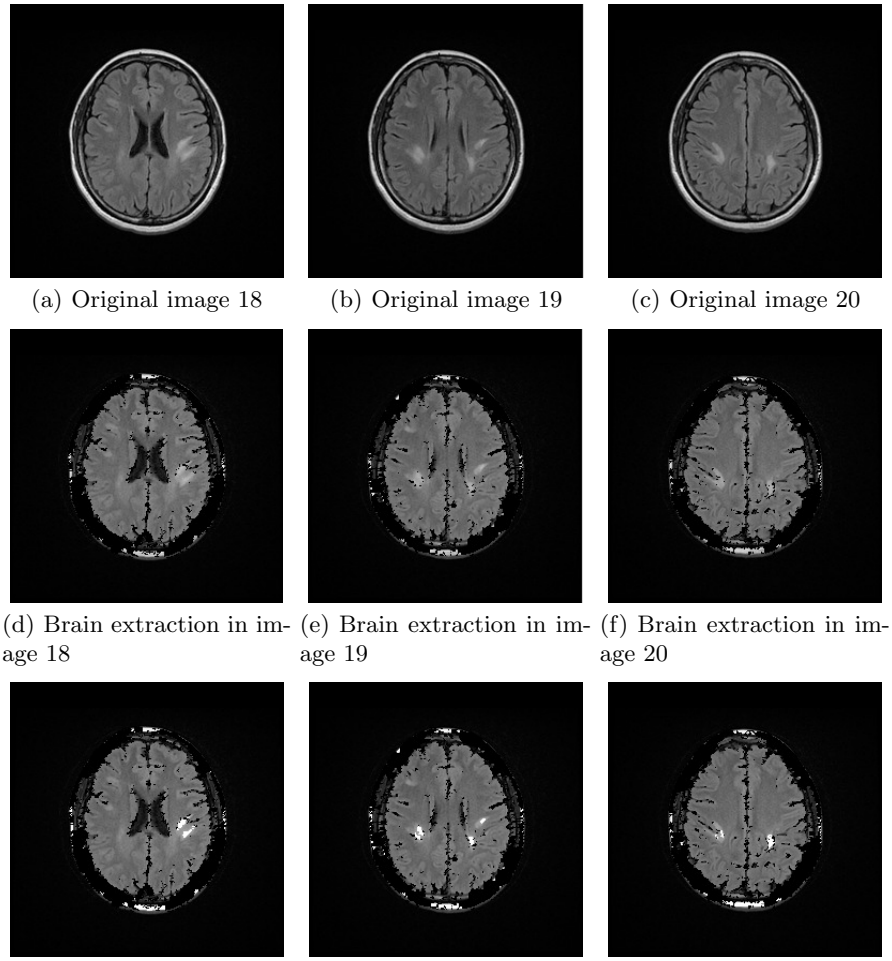
Fig. 2. Figures (a) and (b) show respectively the images 21 and 22 before being processed. Figures (c) and (d) correspond to the results of the former segmentation phase: the brain extraction. Finally, in figures (e) and (f) scars have been highlighted with a more intense color. In this case, there are other pixels that, according to the intensity values, have answered to the threshold as if they were scars, e.g., the skull tissue. This is the reason that indicates that another process has to be done: the use of artificial neural networks, so a decision of whether a tissue is or not a scar can be made.

(d), (e) and (f). Finally, in figures (g), (h) and (i), there can be distinguished some scars from the remaining tissue. In order to standardize results, the values of the parameters used to test this latter sequence were the same as those used in the former sequence.

It is important to notice that the values of parameters were tested in both sequences and that, despite the intensity variations between these sequences, it is possible to remove soft tissue and identify regions considered as scars. We have decided to analyze T2 sequences, because neurologists rely on this type of sequences when it is necessary to identify scars through manual processes.

4.3 Discussion

According to the performed tests and obtained results at applying our methodology, some observations are made.



(a) Original image 18 (b) Original image 19 (c) Original image 20

(d) Brain extraction in image 18 (e) Brain extraction in image 19 (f) Brain extraction in image 20

(g) Scars detected in image 18 (h) Scars detected in image 19 (i) Scars detected in image 20

Fig. 3. Segmentation of the latter sequence. Figures (a), (b) and (c) correspond to images 18, 19 and 20, respectively from the original sequence. Figures (d), (e) and (f) show the results obtained from the brain extraction phase done by the region growing algorithm. Figures (g), (h) and (i) show scars detected by the t threshold

MRI sequences present different ranges of intensities due to: 1) the type of sequence (e.g., T1 or T2) and their respective variants (e.g., T1 with and without contrast) and 2) the conditions of the patient's organism, which generate changes in intensities when taking images. Despite this fact, variations are not so important, i.e., a T1 sequence can be well differentiated from a T2 sequence, because the intensity values belong to an average range more or less established in both types of sequences. Nevertheless, these intensity variations make the

work performed by the computer difficult, specially during the extraction of the cerebral tissue and the detection of scars.

However, most of the cerebral tissue region is segmented, it is necessary to establish the way the t threshold should be computed, in order to be highly accurate and flexible to changes in the ranges of intensities for each sequence. To identify suspicious regions, it is necessary to establish a robust t threshold, as in the case of the former segmentation, due to intensity variations.

For the methodology proposed in this paper, we have considered variations in the range of intensities for each sequence. Thus, we have established a t threshold that allows the region growing algorithm to be flexible enough to segment the greater part of the brain tissue. During the latter phase of this methodology, using another t threshold, it is possible to extract suspicious regions once the brain has been segmented.

5 Conclusions and Future Work

Through the development of this research work, a new methodology to automatically detect scars in the cerebral cortex is proposed. The work done by other researchers has been focused on creating Computer Aided-Diagnosis tools specialized in the study of diseases causing brain scars, e.g., epilepsy, multiple sclerosis, etc. Instead, the proposed methodology relies on pattern recognition algorithms to find scars in the cerebral cortex, regardless the type of disease provoking these scars. These algorithms act as a basis to create a tool that decreases the subjectivity of diagnosis and that makes the research tasks that neurologists perform at hospitals easier. Another contribution of the proposed methodology consists in making Computer Sciences stronger and wider, owing to the interdisciplinary nature of this project, which brings together different fields of study, such as neurology, physics, and bioinformatics.

Some important extensions of this work are now stated. First, we aim at reinforcing the computing of thresholds, since they must present a flexible behavior, i.e., they should adapt themselves to different intensities for the same type of sequences, T1 or T2, and to the difference existing in the range of each sequence, e.g., intensities for T2 are between 0 and 3900 in average.

As we want to extract the cerebral tissue region in three dimensions, it is necessary to adjust the region growing algorithm so that, according to the seed, this algorithm would work not only into the current image, but also into the previous and following images.

To make a final decision regarding the identified object, currently, a neural network is in development. It would decide whether such an object is a scar or not. We also aim at building a three dimensional representation of the brain to show the location of the scars in a graphical way. Finally, a multispectral analysis would be made, in order to find scars in T1 sequences.

It is important to emphasize that Computer Aided-Diagnosis tools are not accurate. Instead, they provide a closer look of what is happening inside a human organism, in order to help radiologists and physicians in the diagnosis of diseases.

The response of these tools is a second opinion, which should be verified by an expert of the medical field.

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