A Multi-Level Thresholding Method based on Histogram Derivatives for Accurate Brain MRI Segmentation
Un método de umbralización multinivel basado en derivadas del histograma para la segmentación precisa de imágenes cerebrales de RM

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Resumen: Este trabajo describe la implementación y evaluación cuantitativa de un método automático para la segmentación precisa de imágenes cerebrales de resonancia magnética (RM). El método se basa en la umbralización adaptativa multinivel del histograma de la imagen con el fin de clasificarla en un número variable de clases de tejidos cerebrales. Inicialmente, se realiza una etapa de preproceso para eliminación de ruido y realzado de la imagen. Después, se calcula el histograma de la imagen que es suavizado usando un filtro piramidal. La derivada de dicho histograma se usa para determinar una lista de picos y valles en la correspondiente función. El número de clases de tejidos cerebrales a segmentar se corresponde al número de umbrales buscados en el histograma más uno, y dichos umbrales se determinan usando los valores los valles de la función derivada que minimizan los errores en la clasificación de los píxeles de la imagen. El método propuesto se usó para segmentar cuatro clases de tejidos en las imágenes cerebrales (materia blanca, materia gris, líquido cefalorraquídeo y fondo, respectivamente) correspondientes a un conjunto de imágenes sintéticas de resonancia magnética cerebral obtenidas usando la base de datos BrainWeb. El método propuesto se comparó con otros dos métodos de segmentación implementados: el primero basado en modelos de mezcla de gaussianas y el segundo basado en el algoritmo de las k medias. Nuestra propuesta produjo resultados de clasificación correcta por encima del 95%, que son equivalentes a los de los algoritmos comparados.

Palabras clave: Análisis de imágenes médicas; imágenes cerebrales de resonancia magnética; segmentación automática; umbralización multinivel; derivada de histograma;BrainWeb.

Abstract: This work describes the implementation and quantitative evaluation of an automatic and accurate brain magnetic resonance image segmentation method. This is based on adaptive multi-level thresholding to classify the images into variable number brain tissue classes of interest. The method includes a denoising and enhancement image preprocessing stage. After that, the image histogram is computed and smoothed using a pyramid filter. Then, this histogram is differenced to determine a list of peaks and valleys (i.e. local minima) on it. As the number of considered tissue classes to segment is the number of searched histogram thresholds plus one, the histogram thresholds were chosen using the values of valleys that minimize the classification errors. The proposed method was used to segment four tissue classes (i.e. white matter, gray matter, cerebrospinal fluid and background, respectively) in a collection of synthetic brain MR slice from BrainWeb database. The method was compared to other two implemented segmentation approaches: one based on Gaussian mixture models and other one based on k-means clustering. Our multi-level thresholding segmentation algorithm produced equivalent correct classification results (above 95%) than the other two compared methods of the literature.

Keywords: Medical image analysis; magnetic resonance (MR) brain images; automatic segmentation; multi-level thresholding; histogram derivative;BrainWeb.

1. INTRODUCTION

Current neuroimaging techniques allow researchers and doctors to detect the activity and/or possible complications within the human brain without needing invasive neurosurgery [1]. There exists a number of safe imaging techniques accepted nowadays in hospitals throughout the world. Methods for creating structural and functional human brain images include among other ones: Electro-Encephalography (EEG), Magneto-Encephalography (MEG), Positron Emission Tomography (PET), Single-photon

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emission computed tomography (SPECT), Transcranial Magnetic Stimulation (TMS), Structural Magnetic Resonance Imaging (MRI) and Functional Magnetic Resonance Imaging (fMRI) [1][2].

Structural magnetic resonance imaging (MRI) [3][4] is a radiology technique that uses magnetic fields, radio waves and computers to produce 2D or 3D high-quality images of certain body structures. A MRI scan has the advantage of avoiding the X-ray radiation exposure and with not known side effects. Moreover, MRI presents a precise accuracy in detecting structural abnormalities in the body internal organ being explored [2]. MR brain image segmentation into several tissue classes has significant interest to visualize and quantify individual anatomical structures. This segmentation task was first performed manually by the radiologist in a clinical environment and it could be difficult to reproduce. Currently, many different algorithms have been presented in the literature for the computerized segmentation of brain MR images (see for example [5], [6], [7] and [8]). However, the brain medical image segmentation is an open question [4], considering the variety of individual pathologies and the related clinical requirements for accuracy. The automatic brain segmentation methods (or the semi-automatic ones with minimal interaction for human operators) are still current topics of research for the cases of large number of tissue classes [9] or for some specific applications [10].

Image segmentation [11][12] is an essential process in most subsequent tasks of image analysis. The goal of image segmentation is to cluster its pixels into salient image regions that correspond as closely as possible with the objects in the scene. The segmentation result could be used for object recognition. In particular, many of the existing techniques for image description and recognition depend highly on the segmentation results.

Thresholding [11][12] is perhaps the simplest approach used for image segmentation. It allows separating the objects from the background in an image by using a threshold value to transform one gray-level image into a binary one. According to Sezgin and Sankur [13], these thresholding methods can be classified into six main categories: *histogram-based* where the peaks and valleys of the smoothed histogram are analyzed, *clustering-based* where the gray-level values are clustered in two groups (i.e. background and objects) or modeled as a mixture of two Gaussians, *entropy-based* that compute the entropy of the objects and background to separate both regions, *object attribute-based* that search a similarity measure between the gray-levels and the binarized images, *spatial methods* which use higher-order probability distribution of the pixels, and *local methods* which adapt the threshold value on each pixel to the local image characteristics.

The simpler thresholding methods only use one threshold value to extract the objects of interest, which in many situations, doesn't result to be a good segmentation of the image. Multi-level thresholding is an extension of this segmentation method category which uses several thresholds

and enables the partitioning of an image into multiple classes [14][12]. Several multi-level thresholding methods have been proposed in the literature. Tsai [15] suggests a method based on the conservation of moments of the histogram. Bolon et al. [16] present a thresholding method, based on distribution histograms of gray levels, which applies the minimization of the sum of inertia criterion to determine the thresholds between the different classes. Ritter and Wilson [17] describe an approach for multilevel segmentation that extends the bimodal approach proposed by Otsu [12]. Cheriet et al. [18] suggest a general recursive solution that is also an extension of Otsu's method. Three other thresholding approaches were proposed by Yan [19]: Yan-Otsu, Yan-Kittler and Yan-Huang methods, respectively, referred as a whole as the unified thresholding method by Yan. AboudNeta et al. [20] present a method, based on the division of the histogram into sub-regions, where a threshold is determined for each of these sub-regions. In general, many of these thresholding methods produced good segmentation results. However, some of the approaches demand a high processing time, which making these methods impractical when the number of thresholds used exceeds three for multi-class segmentation [21]. Other approaches are not fully automatic, requiring a prior knowledge of the classes in the histogram. Finally, other methods are sensitive to the uniformity of the histogram, which is a factor extremely important for the success in the segmentation. As the MRI images contain non-uniformities that introduce a substantial variability in the intensities of pixels from the same tissue class [22], these last methods are not applicable in many situations.

This paper presents an automatic and accurate multi-level thresholding method for brain MR image segmentation, which can handle successfully the abovementioned difficulties from other approaches. The proposed method is a substantial extension of a preliminary work [23] by the same authors. The rest of the paper is organized as follows. In Section II, the theoretical basis of the proposed multi-level thresholding method is briefly described. Moreover, this section sketches the two used segmentation algorithms for comparison purposes and it enumerates the performance metrics applied in the evaluation. In Section III, we describe the experimental framework for the qualitative and the quantitative validation of our method, and also compare it to other two implemented brain MRI segmentation methods. Finally, the conclusions of this study are drawn in Section IV.

2. MATERIALS AND METHODOS

In this section, we first review histogram-based multi-level thresholding types and proposals. Next, the proposed multi-level thresholding method is explained. As this segmentation method is compared to two implemented segmentation approaches, these algorithms are summarized. Finally, we outline the quantitative evaluation metrics used to compare the presented brain MRI segmentation method with the other considered segmentation approaches.

2.1 Histogram-Based Multi-Level Thresholding

Segmentation by histogram thresholding is based in grouping image pixels into regions with different gray level ranges when choosing one or more thresholds to find the best separation among these regions. Thresholding is a simple but often effective image segmentation technique when the different image elements (i.e. objects and background) have contrasting intensities. In consequence, the image histogram can be partitioned into a number of peaks (where each one could correspond to an image region) and there exist some local minima or valleys between pairs of adjacent peaks where the histogram thresholds are located.

When selecting one single histogram threshold, the image objects are separated from the background. More formally, thresholding converts an input gray level image input image *f(x,y)* into an output binary image defined as follows:

$$g(x,y) = \begin{cases} 1, & if f(x,y) \geq T \\ 0, & if f(x,y) < T \end{cases} \quad (1)$$

where pixels labeled as 1 in *g(x,y)* can correspond to the objects (or to background), whereas pixels labeled as 0 correspond to the background (or to objects).

Several methods have been proposed to find the histogram peaks and then to select the threshold value as the minimal point between them, in order to obtain a better separation among regions. The main difficulty in automatic thresholding is to select an appropriate *T* value that produces the best segmentation result. However, due to the possibility of finding many possible local minimum values in the image histogram, the determination of relevant peaks and valleys can be a difficult problem.

When just one threshold is used to segment the image, the process is called global thresholding. However, in most cases the histograms of real images present more than two distinct peaks. The non-uniform image lighting conditions or the presence of noise, for example, can produce changes on the gray levels of the objects and on the background making the use of a single threshold inappropriate for the segmentation. In this case, better results can be obtained by analyzing the intensities of the pixels in an image region to determine several local thresholds. Global thresholding can be generalized to consider an arbitrary number of threshold values. In multi-level thresholding, the purpose is to determine several T_i values (where *i* > 1) that effectively extract the different regions of interest (i.e. the objects) in the image, as illustrated in Figure 1.

Using multi-level thresholding using *i*=3 threshold values, the image *g (x, y)* can be segmented as follows.

$$g(x,y) = \begin{cases} L_1, & if\ f(x,y) \leq T_1 \\ L_2, & if\ T_1 < f(x,y) \leq T_2 \\ L_3, & if\ T_2 < f(x,y) \leq T_3 \\ L_4, & if\ f(x,y) > T_3 \end{cases} \quad (2)$$

where: Li+1 are the four regions of pixels (i.e. the classes) obtained after the application of the three T_i thresholds. This is illustrated by the histogram example shown in Fig. 1.
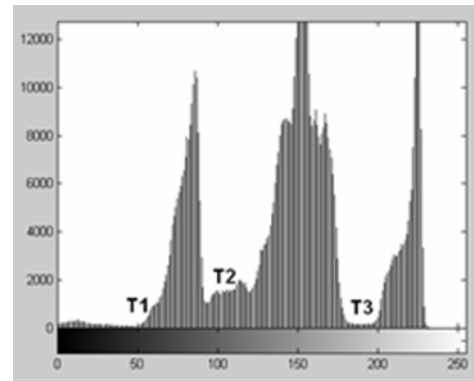

Figure 1. Multi-level thresholding example for i=3

2.2 Proposed Segmentation Method

The proposed automatic and adaptive method for multi-level thresholding of a brain MR histogram image consists of two main stages: pre-processing and histogram thresholding, respectively.

In the *pre-processing stage*, the initial brain MR image is filtered with a Gaussian filter (with σ=0.5 and kernel size of 3×3) to reduce the impulsive noise. After that, a decorrelation stretch stage is applied on the result (using the decorrstretch function of MATLAB) as a way to enhance the image contrast. Next, the image histogram *h* is calculated and then smoothed using a pyramid filter *p* of size 1×*N*, where *N* is defined by the user. The pyramid-type filter has the edges increased symmetrically in one unit until the central pixel, which has the largest value. For example, if *N*=5 then the filter is defined as *p* = [1, 2, 3, 4, 5, 4, 3, 2, 1]. This filter is applied (i.e. convolved) to the image histogram in order to minimize the presence of shallow valleys and short peaks that could cause an excessive detection of histogram thresholds.

In the *histogram thresholding stage*, a one-dimensional array *z* is created by the derivative of the histogram *h* as follows:

$$z(i) = \begin{cases} 1, if h(i+1) - h(i) < 0 \\ 0, if h(i+1) - h(i) \geq 0 \end{cases} \quad (3)$$

where: *h(i)* and *h(i+1)* correspond to consecutive histograms bins.

After that, the derivative of z is computed as:

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$$z'(i) = z(i) - z(i+1) \qquad (4)$$

Two lists of the intensities in the histogram corresponding to the peaks *PL* (Eq. 5) and to the thresholds *TL* (Eq. 6) are determined next:

$$PL = \{i \mid (z'(i) = -1) \cap (0 \leq i \leq 255)\} \qquad (5)$$

$$TL = \{i \mid (z'(i) = 1) \cap (0 \leq i \leq 255)\} \qquad (6)$$

The number of possible classes in the segmented image is equal to the number of histogram thresholds increased by one. As the number of classes to be found in the brain MR image segmentation and also the minimal percentage of image pixel belonging to each class are known in advance, then a test isperformed on each histogram class. The goal is to determine if each class contains this corresponding minimum percentage of pixels in relation with the image size. The threshold whose class fulfills this parameter for the class is accepted; otherwise, this threshold is rejected and the class is grouped to the next one in the histogram, so that all segmented classes finally contain the minimum percentage of pixels required.

Optionally, in a *post-processingstage*, it is possible to assign different colors to the pixel classes according to the list of thresholds produced. This way, as a final result, a color image representing the segmentation result can be returned. Fig. 2 summarizes the proposed multi-level thresholding algorithm for segmenting the brain MR images.

Inputs: I = Brain MR image
   N = Size of pyramid-type filter mask
   k = number of classes to segment the brain image I
p_k = minimum percentage of pixels in each segmented class k

Output: I' = Image with pixels labeled to one of classes

Algorithm:

I_1 = RGB_Gray (I); //Convert image I into a gray level one
I_2 = GaussianFilter (I_1,G_σ); // Convolve I_1 with a Gaussian filter G_σ to reduce noise
I_3 = ContrastEnhancement (I_2); // Increase contrast of I_2 by decorrelation stretch
h = ImageHistogram (I_3); // Compute image histogram of I_3
p_N = PyramidFilter (N); // Create a pyramid-based filter of size 1xN
h' = FilterHistogram (h, p_N); // Smooth image histogram h with a filter pyramid p_N
z = DifferenceHistogram (h'); // Construct array z of the histogram derivative
z' = SecondDifferenceHistogram (z); // Second derivative of the histogram
PL = PeaksList (z'); // Compute list of peaks of the smoothed histogram z'
TL = PeaksList (z'); // Compute list of thresholds of the smoothed histogram z'
TL' = CheckHistogramClasses (z', k, p_k, PL, TL); // Check histogram classes to see if they have
 // the minimum percentage (%) of pixels and
// to set the final list of thresholds TL'
I' = LabelClasses (I, TL') // Label pixel classes in final image I' using final list of thresholds TL'

Figure 2.Pseudo-code of proposed histogram-based multi-level thresholding algorithm.

2.3Other segmentation approaches considered

In this Subsection, we summarize the two other implemented brain MR image segmentation algorithms that will be compared to our proposed multi-level thresholding method on the same test images.

The first algorithm is an adaptation of the hybrid Bayesian segmentation and classification

approaches proposed by Mignotte et al [24]. This algorithm produced good results when segmenting brain SPECT images into three tissue classes: white matter, grey matter and cerebrospinal fluid, respectively. Both the segmentation and classification methods apply a Bayesian estimation stage to determine, from the training images, the parameters of a Gaussian Mixture Model (GMM) using the iterative Expectation-Maximization (EM) algorithm. The parameter estimation step, used in the segmentation, considers the diversity in the distribution mixture of the SPECT images. Next, a set of features extracted both from edge segmentation and from Gaussian mixture distribution are combined into a feature vector describing each image database. Mignotte et al. applied *k*-means clustering to classify these feature vectors into two brain classes: "healthy" and "diseased" ones. We adapted this approach for segmenting our brain MR images into four classes (i.e. by adding the background region to the three previous classes). Before estimating the parameters of the GMM for the brain segmentation, a pre-processing for the enhancement and denoising of the MR images was performed as follows. First, the image was multiplied by an appropriate scalar value to correct non-uniform illumination. Next, the difference between the application of the top-hat and bottom-hat morphological filters (a disk-shaped structuring element of size 5 was used for both filters) on the previous MR image was computed to increase the contrast. Finally, a decorrelation stretch stage was applied on the resulting image as a way to enhance the color differences in it.

The second brain MR image segmentation algorithm to be compared with our method uses the same pre-processing for the enhancement of MR images in the previous algorithm. After that, the *k*-means clustering procedure (with *k* = 4) was applied separately to segment each color channel of the brain image. Finally, the three segmented channel are combined to produce the segmentation result.

2.4 Statistical Validation Metrics used for Evaluation

The classification errors of each segmentation method is determined by comparing the results produced by the manual segmentation created by the radiologist (and considered as ground truth) and by the automatic segmentation produced by each of the three implemented algorithms. The following quantitative measures were used to evaluate the quality of the tested brain MR segmentation methods: *Jaccard similarity coefficient* (*JC*) [25], *Positive Predictive Value* (*PPV*) or *Precision,* and *Accuracy* (*AC*), respectively. Next, we summarize each of the considered evaluation metrics.

- Jaccard *similarity coefficient* (*JC*):

In general, this coefficient determines the similarity between two sets, and it is defined as the size of the intersection divided by the size of the union of these sets. This measure can be adapted to compare two digital images *RI* and *SI*, with spatial resolution *M*×*N*, as follows:

$$JC(RI, SI) = \frac{\sum_{i=1}^{M} \sum_{j=1}^{N} \begin{cases} = 1, \text{if } RI(i, j) = SI(i, j) \\ = 0, \text{if } RI(i, j) \neq SI(i, j) \end{cases}}{M \times N} \qquad (7)$$

The coefficient varies between zero when the compared images do not have any similarity and one when both images are identical.

- *Positive Predictive Value* (*PPV*) or *Precision*:

Let *TP* and *TN* be the respective number of correctly classified pixels as positive and as negative ones after the segmentation task in the final image *SI*, and *FP* and *FN* the respective numbers of false positive and false negative pixels in this same image. ThePositive Predictive Value (PPV) or Precision is defined as follows:

$$PPV(SI) = \frac{TP_{SI}}{TP_{SI} + FP_{SI}} \qquad (8)$$

- *Accuracy* (*AC*):

In a similar form, the accuracy measure describes the ratio of positive cases (i.e. pixels) which were classified correctly.

$$AC(SI) = \frac{TP_{SI} + TN_{SI}}{TP_{SI} + TN_{SI} + FP_{SI} + FN_{SI}} \qquad (9)$$

3. RESULTS AND DISCUSSION

First, a short description of the brain images used in the experiments is presented. Next, we continue with the quantitative results achieved. These results are compared to other segmentation approaches using the same validation metrics. Finally, a short discussion on the results is given.

3.1 Brain MRI Datasets.

The effectiveness of the proposed segmentation method was tested on the *Simulated Brain Database* (*BrainWeb*) [26][27] which is a database of realistically simulated MRI data volumes. This method was also compared to other two segmentation approaches implemented in this work (referred as *GMM method* and *k-means method*, respectively, in the experiments).

The MRI data volumes of the *BrainWeb* Database are produced by a MRI simulator developed in the McConnell Brain Imaging Centre of the Montreal Neurological Institute, at McGill University (Canada). Simulated brain MRI data can be based on two anatomical models: "normal" and "multiple sclerosis" ones. In our experiments, most of the images were created using the following MRI acquisition parameters: T1-w (weighting) mode, 1 mm thickness slices and resolution of 181×217×181 voxels (i.e. 181×217 slice size), noise levels of 0% and 3%, and non-uniform intensity levels of 20%, repetition time (RT) equal to 18 ms and echo time (ET) equal to 10ms in an angle of 30 degrees at MINC stored in the 16 bit little endian format for integers.

3.2 Experimental Results.

We present both qualitative (i.e. visual) and quantitative results for the *BrainWeb* images used, where the ground truth segmentation is known. The corresponding results on the same MR slices are compared for all the segmentation algorithms being tested.

Next, the qualitative results achieved with several slices (of the same MR volume) for the three segmentation method are shown. Four tissue classes are considered in the segmentation: white matter (WM), gray matter (GM), cerebrospinal fluid (CFS) and background (BG), respectively.

The results are also compared to the segmentation produced for each slice using the SPM8 tool [28]. SPM is a software analysis tool (suite of MATLAB) available for the interpretation of neuroimaging data. The SPM8 version was released in 2009 and it includes a segmentation algorithm (i.e. the *unified segmentation algorithm*) adapted from [29].

Figure 3 shows the 4-class segmentation results of different brain MR slices of the same volume acquired using *BrainWeb* database (for the T1-w MRI modality). Each column corresponds to one brain slice and, for each of them, the following images are visualized: original slice, corresponding ground truth image, segmentation produced by the SPM8 software (for 4 classes), and respective automatic segmentation produced by the GMM method, the *k*-means method and the proposed multi-level thresholding method.

In Figure 4 we visualize the segmentation results achieved with our proposed method for the same brain slice acquired using the respective weighted MRI modalities T1-w (i.e. longitudinal relaxation time) and T2-w (i.e. transverse relaxation time). The result produced by the pre-processing (i.e. denoising and contrast enhancement) stage of the multi-level thresholding method is shown in the third column in this figure. It can be noticed that the proposed algorithm achieved accurate segmentation results for both modalities.

Quantitative results corresponding to the statistical validation metrics described in the previous section are presented next.

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These results, shown by Table 1, correspond to the three segmentation methods experimented.

It can be noticed that the proposed multi-level thresholding algorithm produces very similar results to the other two compared ones (GMM and k-means, respectively) with respect to three considered metrics. Moreover, our method outperforms in average the SPM8 segmentation for these metrics as follows: 1.88% using Jaccard coefficient, 5.35% in precision and 3.5% in accuracy, respectively.
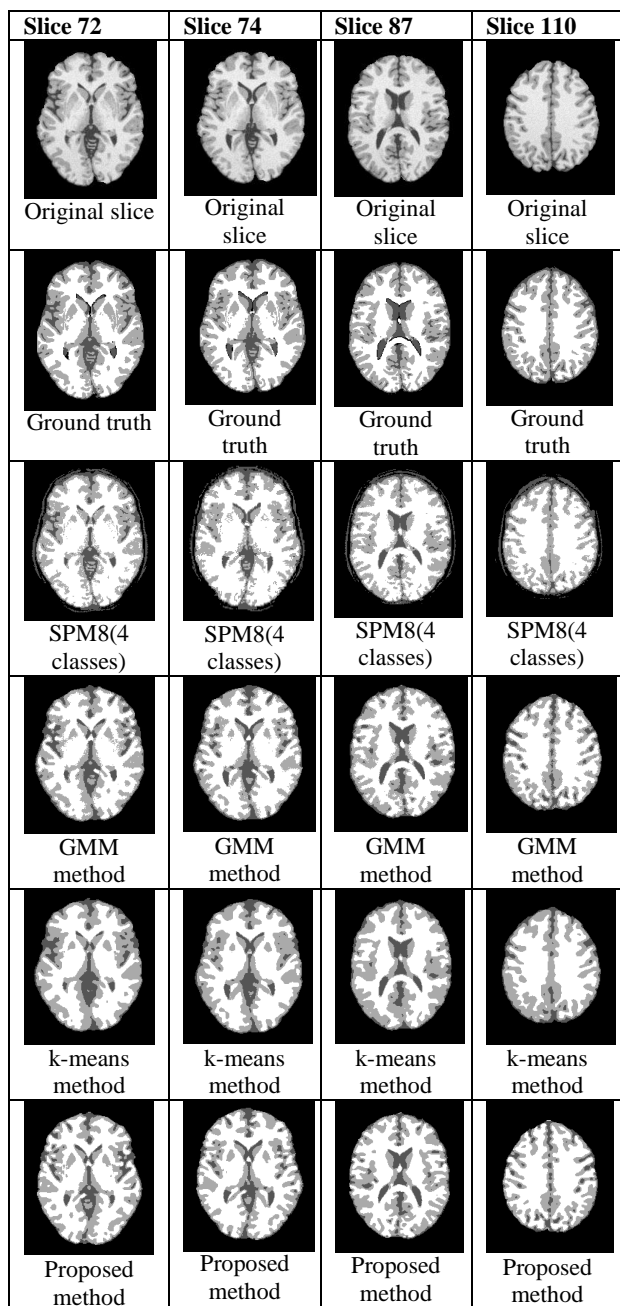

Figure 3. Visual comparison of the different implemented segmentation methods (where each column corresponds to a brain slice): original slice, ground truth, SPM8 segmentation, and respective GMM, *k*-means and proposed multi-level thresholding automatic segmentation results
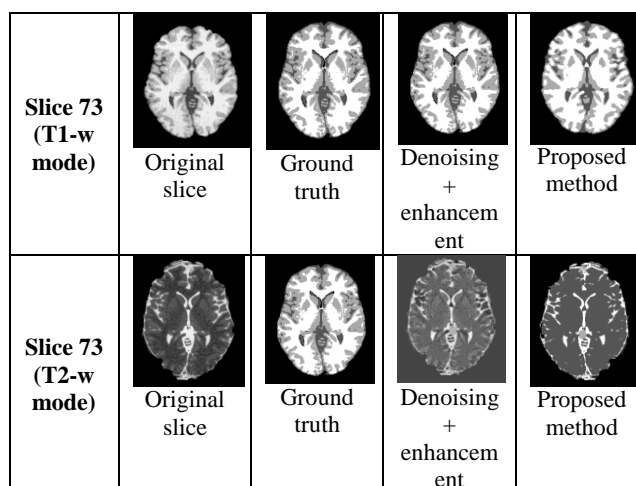

Figure 4. Segmentation results produced by our multi-level thresholding algorithm for the same brain slice acquired under the weighted MRI T1-w and T2-w modalities.

Table 1. Quantitative results produced by the compared segmentation methods.

Slice	Metric	SPM8	GMM method	*k*-means method	Proposed method
72	Jaccard	0.9561	0.9801	0.9831	0.9760
	Precision	0.9221	0.9727	0.9786	0.9699
	Accuracy	0.9220	0.9626	0.9682	0.9551
74	Jaccard	0.9574	0.9817	0.9848	0.9767
	Precision	0.9246	0.9750	0.9810	0.9713
	Accuracy	0.9245	0.9657	0.9714	0.9566
87	Jaccard	0.9625	0.9838	0.9862	0.9763
	Precision	0.9303	0.9765	0.9818	0.9707
	Accuracy	0.9303	0.9683	0.9728	0.9540
110	Jaccard	0.9681	0.9878	0.9886	0.9873
	Precision	0.9296	0.9930	0.9958	0.9932
	Accuracy	0.9296	0.9712	0.9732	0.9702

3.3 Discussion.

Several authors consider that segmentation methods based on Gaussian Mixture Models (GMM) produce good results in the automatic segmentation of brain MR images [30][31][32].

In particular, those models which are based on finite mixtures. With the addition of the preprocessing stage, the proposed automatic segmentation algorithm is works well on difficult images that originally present a low contrast (i.e. the quantitative segmentation metrics on the test MR slices produce similar results than those achieved by the GMM method).

Moreover, the denoising and contrast enhancement pre-processing stages included by our method clearly improve the original image quality and make the histogram analysis task much more manageable.

Additional favorable comparisons with the unified segmentation algorithm (implemented in SPM) also give value to the algorithm proposed in this work. For the three

analyzed metrics, correct classification results above 90% were achieved for all the images tested with our method. In this sense, the results on the precision and the accuracy metrics above 60% on smaller brain structures and above 80% on large structures make our algorithm applicable on real clinical brain MR images.

4. CONCLUSIONS

This paper presented a multi-level thresholding segmentation method applied to brain MR images. The method includes a denoising and enhancement pre-processing stage to improve quality of the original images. After that, the image histogram is computed, and detection of peaks and valleys through the derivative of the smoothed histogram was fast and flexible making it possible the effective location of the multiple thresholds in an unsupervised form.

Our method produced accurate segmentation results (i.e. above 95% of precision and accuracy on the tested brain slices) which are equivalent to the other two compared algorithms, and better than those produced by the SPM software on the same test images. The method was also successfully experimented using brain slices acquired under the two weighted MRI T1-w and T2-w modalities.

These achieved results make the proposed segmentation method applicable on real clinical images as a future work. Moreover, as the presented method remains sufficiently general, as another future work we aim to apply it to other types of images (i.e. SPECT) or to other medical data classification problems (i.e. for breast tissues).

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