

Detection of Hyperintense Regions on MR Brain Images using a Mamdani Type Fuzzy Rule-Based System

Application to the Detection of Small Multiple Sclerosis Lesions

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Abstract—In this paper we present an algorithm for detecting hyperintense regions in brain images acquired by Magnetic Resonance Imaging. The work is part of a more general research oriented to the design of support tools that assist the healthcare experts in their research activities on brain diseases. The algorithm has been focused on the detection of small multiple sclerosis lesions in PD- and T2-weighted images. In the design of the algorithm we have considered a fuzzy approach to deal with the uncertainty and vagueness characteristic of these lesions in magnetic resonance images. The core of the work is the introduction of a Mamdani type Fuzzy Rule-Based System to optimize the detection taking into account the necessary trade-off between true and false positives in this kind of problems. Results show a very good sensitivity of the algorithm in the detection of hyperintense regions associated with small multiple sclerosis lesions, and a low false positive rate with regard the number of pixels analyzed.

Keywords—component; fuzzy rule-based systems; fuzzy reasoning; magnetic resonance imaging; multiple sclerosis

I. INTRODUCTION

Multiple Sclerosis (MS) is a disease of the central nervous system characterized by multifocal inflammation and destruction of the myelin that encases the axons. This demyelinating process results in an inhibition of neural transmission and causes the appearance of several clinical symptoms, such as motor and sensory disturbances, paralysis or visual alterations ([1], [2], [3]). These areas of demyelination, or lesions, can be observed by magnetic resonance imaging (MRI).

Magnetic resonance imaging (MRI) is the modality of choice for clinical evaluation of MS because it provides an

objective and direct assessment of the evolving pathology in multiple sclerosis [4], and it has also been recognized as a diagnostic criterion of this disease [5]. Moreover, quantitative analysis of MR images to measure and monitor lesion load and tissue volumes has become invaluable for patient follow-up and evaluation of therapies [6].

In a MRI examination, MS lesions can be visualized using different sequences. Dual acquisition of proton density (PD-) and T2-weighted images is one of the most common sequences used to evaluate MS lesion volume ([4], [6]). In these weighted images pixels belonging to MS lesions show hyperintensity, a lighter gray level in relation to its surroundings. So, the detection of MS lesions in these weighted images is based on the location of the hyperintense regions.

However, segmentation of MS lesions in PD- and T2-weighted images is a challenging task which stems from several reasons. Among them it is worth to highlight the following: MS lesions are not the only regions presenting hyperintensity within the images; detection of MS lesions in MRI involves the analysis of several images with different anatomical features, and presents a high dependence of contrast-to-noise ratio in the images; the presence of noise, partial-volume effects and motion can have significant consequences on the performance of segmentation algorithms [7].

One of the main challenges in developing an automated MS segmentation algorithm within MRI images is the minimization of false-positive. Beside aforementioned drawbacks, the presence of small MS lesions is one of the main problems to avoid false detections. The size of small lesions gives a greater weight to the boundary pixels and, consequently, the detection

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of small MS lesions without false detections is difficult due to the presence of factors such as noise or non-homogeneities of magnetic resonance images. Therefore, the greater the sensitivity for detecting small lesions, the greater the chance of false positives.

Moreover, MS lesions are inherently fuzzy with an uncertainty component mainly in the definition of their boundaries [4]. This consideration made that some authors ([8], [9]) introduced fuzzy techniques in the design of their MS detection and segmentation algorithms.

Although some authors, [10], [11], [12], [13], have developed crisp and fuzzy algorithms for detecting MS lesions, within them false detections must be manually removed or require that the detection excludes regions below a minimum size. Then, the design of an automatic algorithm for this purpose has the risk of removing small lesions.

Thus, in order that an automatic MS lesions detection algorithm can ensure high sensitivity in the detection of hyperintense pixels, while avoiding a large number of false positives, it seems necessary to introduce a trade-off between the number of true and false positives. This trade-off may also help in the selection of optimal parameters to combine the multiple features involved in an algorithm.

Taking into account previous considerations, our research is oriented to the development of automatic algorithms for detecting small MS lesions. A successful detection of these lesions would be useful to avoid manual removing of false positives using an existing MS lesion segmentation algorithm, or to be used as an starting point in the design of a new automatic MS lesion segmentation algorithm.

In this paper, we present an approach based on a *Mamdani* type *Fuzzy Rule-Based System (MFRBS)* [14] to design the detection step of this kind of algorithms. In our approach, we start from an algorithm developed in previous works ([15], [16]), and we introduce this fuzzy scheme to improve the design of the previous detection step using also an MRI sequence more sensitive to the presence of small lesions.

The rest of the paper is organized as follows. Section II described the system proposed in [15] for detecting multiple sclerosis small lesions. The section III outlines the proposed algorithm. The results are presented in section IV, and the last section is devoted to presenting the conclusions and future research works.

II. AN APPROACH TO MS SMALL LESIONS DETECTION

Present paper, as some previous works of the authors, is part of a more general research activity oriented to a general methodology for the development of automatic algorithms oriented to offer support tools that can assist to radiologists and other healthcare professionals in the diagnosis and research activity on neurological diseases that require medical imaging.

With this aim in [15] authors developed a fuzzy-based algorithm for detecting small MS lesions in whose design it was implemented the protocol followed by the experts for detecting MS lesions. With this in mind, lesions detection was based on the location of pixels showing hyperintense behavior

regarding its local neighbouring pixels. However, since the hyperintensity may also appear in regions that do not correspond to lesions, fuzzy rules were introduced allowing differentiating lesions from other hyperintense regions.

The proposed algorithm consisted of four main stages: *Preprocessing, Fuzzy characterization and evaluation of hyperintensity characteristics, Defuzzification, and Filtering of false detections*. The image database considered for the development of the system was acquired with a Spin Echo sequence (TR / TE / matrix / FOV: 2200ms / 12-80ms / 192x256 / 250mm) that provided 5mm thick slices separated 1mm.

1) *Fuzzy characterization and evaluation of hyperintensity characteristics*: On the images obtained from the preprocessing step, the extraction of hyperintensity due to the presence of MS small lesions was based on next definitions:

Definition 2.1

A pixel, p_{ij} , presents hyperintensity if its gray level, $g(p_{ij})$ in PD- and T2-weighted images is high enough in relation to its near surrounding.

Definition 2.2

A region, R_k , is a small MS lesion if:

- i.- R_k is located within the encephalic parenchyma,
- ii.- $\forall p_{ij} \in R_k$, p_{ij} presents hyperintensity, and
- iii.- R_k is contained within a 5x5 raster window with a minimum size of 3 pixels.

Then, the *hyperintensity characterization and evaluation* was carried out considering a 9x9 raster window centered on the pixels of the MS small lesions marked by the neuroradiologists, and applying next rules:

Rule 2.1

The higher the gray level of pixels in a region, the greater its hyperintense behavior.

Rule 2.2

A pixel has hyperintense behavior if its gray level is sufficiently distinguishable from the gray levels of two adjacent pixels for a sufficiently large number of radiuses within a 9x9 window centered at that pixel.

Rule 2.3

A region can be associated with MS lesion if its pixels present hyperintense behavior in both PD- and T2-weighted images.

The implementation of these rules provided the values $\mu_D^r(p_{ij})$ and $\mu_{T2}^r(p_{ij})$, or degrees with which the pixel p_{ij} is sufficiently differentiable at each radius r_k ($1 \leq k \leq 8$) of the 9x9 window in PD and T2-weighted images, respectively.

Figure 1 shows the 9x9 window, $W(p_{ij})$, used by the algorithm to study the local hyperintensity behaviour of the pixel p_{ij} (black square in the image). The black lines correspond to the eight considered radiuses, and the gray squares under them the pixels considered.

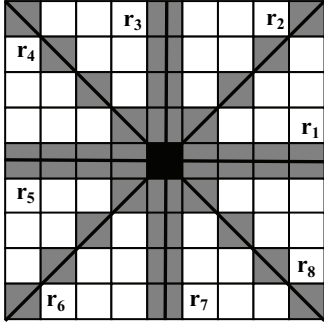


Figure 1. Example of 9x9 window considered for evaluating the hyperintensity. Gray-levels of the pixels under the eight radius (black lines), together with the gray-level of central pixel (black lines), are used for evaluating the hyperintensity of the last one.

Finally these degrees were aggregated for obtaining the membership degree of each pixel to the hyperintensity fuzzy set, $\mu_H(p_{ij})$.

2) *Defuzzification and Filtering of false detections*: To obtain the agrupations associated with small MS lesions we applied a defuzzification process to the membership functions previously obtained. Then, with the aim of eliminating false detections, due to hyperintense pixels do not associated with MS small lesions, a filtering process was carried out in which size, location and regional restrictions were applied.

III. PROPOSED ALGORITHM DESCRIPTION

The aim of the algorithm here presented is to increase lesion detection ratio obtained by our previous system, but maintaining both its general structure and the trade-off between true and false detections.

With this in mind, our approach takes into account the greater sensitivity to show small MS lesions of MRI sequences used at present in MS examinations. This greater sensitivity is mainly due to the acquisition of images with contiguous 3 mm thick sections. As Molyneux et al. showed [17], the reduction of the section thickness from 5 mm to 3 mm increases the MR-visible lesion volume by about 9%.

Next section presents the images considered in this paper. The differences introduced by the MRI acquisition parameters with regard to the previous works ([15], [16]) were taken into account in the design of the algorithm here proposed.

A. Images

The images were acquired in a Magnetom Vision 1.5T (Siemens, Erlangen, Germany) equipment using a Turbo Spin Echo (TSE) sequence that enables dual acquisition of PD and T2 weighted images with the same sequence. The acquisition was performed with interleaved contiguous 3mm-thick axial sections (TR / TE / matrix / FOV: 3000ms / 14-80ms / 256x256 / 250mm). Two blocks of 23 interleaved slices were required to cover the whole brain.

The data set considered for our study consisted of 8 T2-, PD-weighted couples of slices selected from the images

obtained from two clinically definite MS patients. The selected images corresponded to axial slices associated with representative brain locations.

For having into account the aforementioned sources of problems, the half of the images showed low lesion volume and the other half high lesion load. For designing the algorithm we considered two out of the eight slices, one of a patient with reduced lesion volume, Im_R , and the other of a patient having high lesion load, Im_H .

The images obtained by the TSE sequence showed some differences at contrast level regarding the images considered at previous approach. These differences were more noticeable at the PD weighted images, where the differentiation between the gray levels of parenchyma and fluid regions was lower than the appreciated at the images acquired with the SE sequence. Moreover, with the new acquisition in the case of T2-weighted images the differentiation between lesions and fluid regions is more complex in some locations due to the similarity of their gray levels.

B. Study Design

With the aim of facing up to the differentiating factors introduced by the new acquisition method, the algorithm was overhauled looking for the steps that should be modified. After the analysis carried out it was showed that, though the methodology applied for local assessment of hyperintensity should be preserved, was necessary to perform some modifications within the "Fuzzy characterization and evaluation of hyperintensity" stage developed at previous algorithm.

Specifically, the changes came about in the way the hyperintensity fuzzy set was obtaining throughout the radial analysis. Thus, following previous algorithm, after applying the rules 2.1 and 2.2, the degrees with which a pixel p_{ij} is sufficiently differentiable at each radius r_k ($1 \leq k \leq 8$) of the window $W(p_{ij})$ were obtained for PD- ($\mu_D^{r_k}(p_{ij})$) and T2- ($\mu_{T2}^{r_k}(p_{ij})$) weighted images.

Then, as shown in the gray shaded region of Figure 1, the new proposal for obtaining the hyperintensity fuzzy set was carried out by means of a Mamdani type Fuzzy Rule-Based System (MFRBS) which took into account previous membership functions, rules 2.1 and 2.2 and the knowledge of experts.

1) *Obtaining the PD and T2 Hyperintensity Membership Functions $\mu_{H,D}$ and $\mu_{H,T2}$* : According to rule 2.2, for determining the degree with which a pixel is hyperintense at both weighted images must be imposed that *for a high enough number of radii the pixel is sufficiently differentiable*. Our proposal for implementing this restriction consisted on aggregating the differentiability degrees of the pixel at each radius ($\mu_P^{r_k}(p_{ij})$ ($P=PD, T2$)) using an OWA operator [18], i.e.

$$\mu_{H,P}(p_{ij}) = f_{WP}(\mu_P^1(p_{ij}), \dots, \mu_P^8(p_{ij})) \quad (1)$$

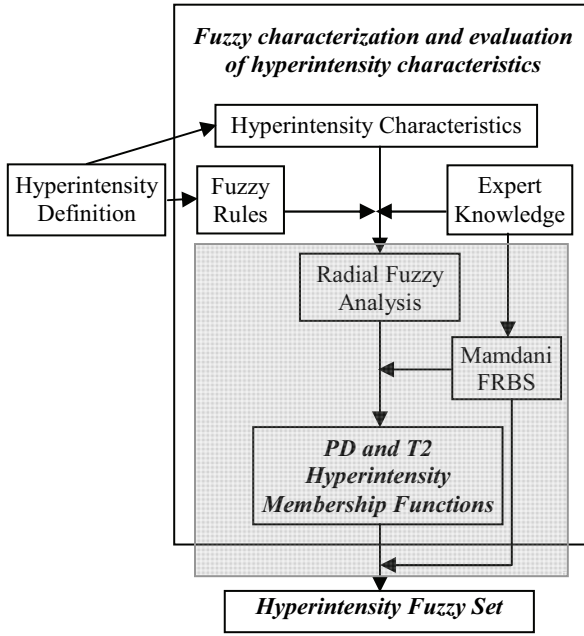


Figure 2. Gray-shaded region shows the step of the proposed algorithm that has been modified regarding the previous proposal.

To get the vectors w_P to be considered in the definition of $\mu_{H,PD}$ and $\mu_{H,T2}$ we followed the next two steps: a) *Sensitivity analysis* of $\mu_{H,PD}$ and $\mu_{H,T2}$ to the consideration of the vectors $w_P^1 = (1,0,\dots,0)$, $w_P^2 = (0,1,0,\dots,0)$, ..., and $w_P^8 = (0,\dots,0,1)$, which correspond to consider 1, 2, ... and 8 radii respectively; b) Implementation of a *MFRBS* to the results of the *sensitivity analysis* to determine w_{PD} and w_{T2} .

a) *Sensitivity analysis*: To perform this analysis we considered the following quality indexes: Correction Factor associated with the detection level of small lesions, *CF*; Sensitivity to the Detection of pixels of small lesions, *SD*; and Efficiency for Avoiding False Positives; *EAFP*.

Since the minimum size for a region to be considered small lesion is of three pixels, if the number of pixels of a region R_k detected by the algorithm is greater or equal to 3 the region can be associated with lesion, otherwise, although it can not be considered as lesion, may be recovered as such at subsequent steps. However, a lesion would not be recovered if the algorithm did not detect any pixel of this lesion.

Taking into account previous considerations the first quality index was introduced as follows:

Definition 2.3

Let L be the set of lesions, l_i , marked by the experts at a given image I , $Alg(L)$ the set of lesions detected by the algorithm, and $N=\#(L)$. Then the *Correction factor associated with the detection level of small lesions* at I is given by

$$FC = \frac{1}{1 + \sum_{i=1}^N \max(\chi_{Alg(L)}(l_i), DP_{Alg(L)}(l_i))}. \quad (1)$$

where $\bar{\chi}_{Alg(L)}(l_i)$ is the complementary of the characteristic function of $Alg(L)$, and $DP_{Alg(L)}(l_i)$ is equal to 0.5 if the algorithm detects less than 3 pixels of lesion l_i and equal to 0 in other case.

This factor was considered as a weighting factor of the true positives fraction for defining the *Sensitivity to the Detection of pixels of small lesions*, as follows:

Definition 2.4

Let TP be the number of voxels in the image I detected as of lesion by experts and by our algorithm, and FN the number of image voxels detected as of lesion by experts but not by our algorithm. Then, the *Sensitivity to the Detection of pixels of small lesions* in I is given by:

$$SD = FC \frac{TP}{TP + FN}. \quad (3)$$

This Sensitivity index provides information regarding the possibility for detecting lesion pixels of an image and penalizes the cases of missed lesions, although some pixels of those lesions have been detected by the algorithm.

Whereas previous indexes are related to sensitivity and ability of the algorithm for correctly detecting lesion pixels, the third index focuses on its accuracy for avoiding false detections.

Definition 2.5

Given an image I , let $card(ICR)$ be the number of pixels within the Intracranial Region (*ICR*) of I , or number of image pixels analyzed by the algorithm. Then, the *Efficiency for Avoiding False Positives* in I is given by:

$$EAFP = 1 - \frac{FP}{card(ICR)} = 1 - \frac{FP}{TP + FN + TN + FP}. \quad (4)$$

where TN (true negatives) is the number of *ICR* image pixels neither marked by experts nor detected by the algorithm, and FP (false positives), is the number of *ICR* image pixels detected by the algorithm but unmarked by experts.

These quality indexes were evaluated on the PD- and T2-weighted images of the design database. To do it, for each pixel p_{ij} situated at position (i, j) on Im_R and Im_H , its hyperintensity values $\mu_{H,D}^k(p_{ij}) = f_{w_D^k}(\mu_D^1(p_{ij}), \mu_D^2(p_{ij}), \dots, \mu_D^8(p_{ij}))$ and $\mu_{H,T2}^k(p_{ij}) = f_{w_{T2}^k}(\mu_{T2}^1(p_{ij}), \mu_{T2}^2(p_{ij}), \dots, \mu_{T2}^8(p_{ij}))$ were obtained for the PD- and T2- weighted images, and the 8 weighting vectors, $1 \leq k \leq 8$. Then these values were defuzzified applying an α -cut with $\alpha = 0.5$, since for this value there is a balance between being and not be hyperintense.

The quality values obtained after the defuzzification process for the PD- and T2-weighted images are shown in tables I and II. Rows two to nine of these tables display the mean results obtained for the 8 weighting vectors for images Im_R (columns 2, 4 and 6) and Im_H (columns 3, 5 and 7).

TABLE I. VALUES OF QUALITY INDEXES FOR PD-WEIGHTED IMAGES

Vector Weights	FC		SD		EAFP	
	Im_R	Im_H	Im_R	Im_H	Im_R	Im_H
w_{PD}^1	1.0	1.0	1.0	1.0	0.579	0.596
w_{PD}^2	1.0	1.0	1.0	0.980	0.718	0.732
w_{PD}^3	1.0	1.0	1.0	0.961	0.809	0.819
w_{PD}^4	1.0	1.0	0.850	0.922	0.894	0.89
w_{PD}^5	0.667	1.0	0.433	0.843	0.946	0.933
w_{PD}^6	0.667	0.667	0.4	0.471	0.977	0.963
w_{PD}^7	0.4	0.333	0.16	0.137	0.993	0.985
w_{PD}^8	0.333	0.2	0.1	0.047	0.999	0.997

TABLE II. VALUES OF QUALITY INDEXES FOR T2-WEIGHTED IMAGES

Vector Weights	FC		SD		EAFP	
	Im_R	Im_H	Im_R	Im_H	Im_R	Im_H
w_{T2}^1	1.0	1.0	1.0	1.0	0.539	0.589
w_{T2}^2	1.0	1.0	1.0	0.980	0.674	0.720
w_{T2}^3	1.0	1.0	0.95	0.961	0.775	0.815
w_{T2}^4	1.0	1.0	0.850	0.824	0.875	0.892
w_{T2}^5	0.667	0.667	0.433	0.458	0.938	0.943
w_{T2}^6	0.5	0.4	0.275	0.235	0.974	0.973
w_{T2}^7	0.4	0.25	0.18	0.108	0.993	0.992
w_{T2}^8	0.286	0.154	0.071	0.024	0.999	0.999

In the analysis of these values was borne in mind that the best weighting vector for each weighted image ought: 1) allow detecting a minimum of 3 pixels in all (or the maximum of) lesions, and 2) furnish high detection level of lesion pixels but maintaining the number of false positives as small as possible.

From definitions 2.3, 2.4 and 2.5 it follows that the higher the value of FC the closer we will be to meet first condition, and the higher the values of SD and $EAFP$ the more will be fulfilled condition 2). Moreover, the larger number of considered radii the more the restriction of lesion size will be satisfied, and the lower the possibility that correct and false detections show connectivity. As can be observed looking at tables I and II, these characteristics have significantly influence in the values of SD and $EAFP$, making that as the number of radii increases the first increases and the second decreases.

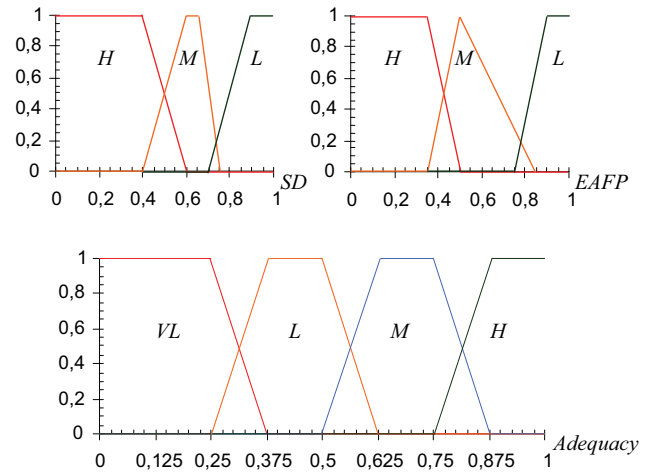
Given the above, the obtaining of the weighting vectors considered for defining $\mu_{H,PD}$ and $\mu_{H,T2}$ was performed using a *Mamdani type Fuzzy Rule system* because besides its high level of description, this type of system provides a natural framework for including expert knowledge in the form of linguistic rules, and possesses a high degree of freedom for selecting the most suitable fuzzification, defuzzification and inference components.

b) *Application of the MFRBS for determining w_{PD} and w_{T2}* : The *Knowledge Base (KB)* of the proposed system was obtained from experience and knowledge of experts. So, taking into account experts experience and the relationship between FC and SD , the *Data Base (DB)* was constituted by SD and $EAFP$, as input variables, and the *Adequacy* of the weighting vector as output variable. Moreover the linguistic terms, or labels, related to input and output variables were: $L_{SD} = \{High, Medium, Low\}$, $L_{EAFP} = \{High, Medium, Low\}$ and $L_{Adequacy} = \{High, Medium, Low, Very Low\}$.

For defining the membership functions associated with the linguistic labels considered for SD we studied the behavior of FC in cases where for some lesion the algorithm detected less than 3 pixels. From this study it appeared that there was a reverse proportionality factor between the increasing of lesions for which less than 3 pixels were detected by the algorithm and the value of FC . Furthermore, given the relationship between FC and SD , this factor made diminishing the SD value in the same proportion than FC if there are not false negatives, and at a higher rate in case of false negative detections.

In addition to previous considerations it was considered that the value of $EAFP$ decreases as FP increases and, the greater the number of false positives the easier these pixels can present connectivity with the false positives, making that small lesions appear larger than their actual size. With the aim of avoiding this situation, we should be very restrictive in defining the membership functions associated with the variable $EAFP$.

Given the above considerations, as well as the knowledge of the experts, the semantics of the linguistic variables were defined by the membership functions shown in the graphs of figure 3.

Figure 3. Membership functions of the labels associated with the input (SD and $EAFP$) and output (*Adequacy*) variables.

The *Rule Base (RB)* considered in the *KB* was constituted by the nine linguistic rules represented by the *decision table* shown in table III.

TABLE III. DECISION TABLE OF THE KB CONSIDERED FOR DEFINING $\mu_{H,D}$ AND $\mu_{H,T2}$

Decision Table		SD		
		High	Medium	Low
EAFP	High	R_1 : High (H)	R_4 : Medium (M)	R_7 : Low (L)
	Medium	R_2 : Medium (M)	R_5 : Low (L)	R_8 : Very Low (VL)
	Low	R_3 : Low (L)	R_6 : Very Low (VL)	R_9 : Very Low (VL)

Once the *KB* of the considered *MFRBS* was identified, we went on to define the *Inference Engine (IE)* which, by means of previous rules, put into effect the inference process on the system inputs.

The *IE* here considered was the classic of Mamdani, i. e. the t-norm minimum was used as conjunction and implication operators, and the mode A-FATI (first aggregate, then infer) as defuzzification interface. Finally in the *Defuzzification interface* the aggregation operator was modeled by the t-conorm maximum, while the defuzzification was carried out by the *Gravity Center* method, i.e. we considered the usually called *max-min-CG* inference engine

Tables IV and V show the results obtained by applying the proposed *MFRS* to the PD- and T2-weighted images, respectively. Having a look at these results it can be observed that for both weighted images the best performance is given for the weighting vectors that consider 4 radii (values highlighted in bold at both tables). This fact is better appreciated at figure 4 wherein blue triangles, red ellipses, green squares, black crosses, and brown triangles have been used for representing the *GCs* obtained for the weighting vectors w_P^1 , w_P^2 , w_P^3 , w_P^4 and w_P^5 , while the *GCs* obtained for the weighting vectors w_P^6 , w_P^7 and w_P^8 , are represented by purple ellipses. Therefore, the membership degrees of a pixel p_{ij} to the *PD* and *T2* hyperintense fuzzy sets are given by:

$$\mu_{H,P}(p_{ij}) = (0,0,0,1,0,0,0,0) \bullet (\mu_P^{r\sigma(1)}(p_{ij}), \dots, \mu_P^{r\sigma(8)}(p_{ij}))^T. \quad (5)$$

TABLE IV. RESULTS OBTAINED APPLYING THE PROPOSED MFRBS TO THE PD-WEIGHTED IMAGES OF THE DESIGN DATABASE

	w_{PD}^k	SD	EAFP	Rules	GC
Im_R	$k=1$	1	0.579	R_2	(0.687, 0.342)
	$k=2$	1	0.718	R_2	(0.687, 0.179)
	$k=3$	1	0.809	R_1, R_2	(0.741, 0.055)
	$k=4$	0.85	0.894	R_1	(0.897, 0.346)
	$k=5$	0.433	0.946	R_4, R_7	(0.484, 0.32)
	$k=6$	0.4	0.977	R_7	(0.437, 0.417)
	$k=7$	0.16	0.993	R_7	(0.437, 0.417)
	$k=8$	0.1	0.999	R_7	(0.437, 0.417)
Im_E	$k=1$	1	0.596	R_2	(0.687, 0.324)
	$k=2$	0.98	0.732	R_2	(0.687, 0.161)
	$k=3$	0.961	0.819	R_1, R_2	(0.83, 0.068)
	$k=4$	0.922	0.89	R_1	(0.90, 0.406)
	$k=5$	0.843	0.933	R_1	(0.895, 0.331)
	$k=6$	0.471	0.963	R_4, R_7	(0.530, 0.256)
	$k=7$	0.137	0.985	R_7	(0.437, 0.417)
	$k=8$	0.047	0.997	R_7	(0.437, 0.417)

TABLE V. RESULTS OBTAINED APPLYING THE PROPOSED MFRBS TO THE T2-WEIGHTED IMAGES OF THE DESIGN DATABASE

	w_{T2}^k	SD	EAFP	Rules	GC
Im_R	$k=1$	1	0.539	R_2	(0.687, 0.382)
	$k=2$	1	0.674	R_2	(0.687, 0.235)
	$k=3$	0.95	0.775	R_1, R_2	(0.744, 0.1)
	$k=4$	0.85	0.875	R_1	(0.897, 0.346)
	$k=5$	0.433	0.938	R_4, R_7	(0.484, 0.320)
	$k=6$	0.275	0.974	R_7	(0.437, 0.417)
	$k=7$	0.18	0.993	R_7	(0.437, 0.417)
	$k=8$	0.071	0.999	R_7	(0.437, 0.417)
Im_E	$k=1$	1	0.589	R_2	(0.687, 0.332)
	$k=2$	0.98	0.72	R_2	(0.687, 0.177)
	$k=3$	0.961	0.815	R_1, R_2	(0.83, 0.165)
	$k=4$	0.824	0.892	R_1	(0.894, 0.291)
	$k=5$	0.458	0.943	R_4, R_7	(0.515, 0.272)
	$k=6$	0.235	0.973	R_7	(0.437, 0.417)
	$k=7$	0.108	0.992	R_7	(0.437, 0.417)
	$k=8$	0.024	0.999	R_7	(0.437, 0.417)

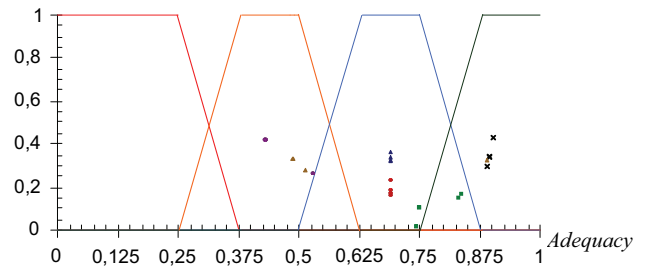


Figure 4. Gravity centers obtained applying the proposed MFRBS. Black crosses, and brown triangles represent the *GCs* obtained for the weighting vectors w_P^4 and w_P^5 , respectively.

2) *Obtaining the Hyperintensity Membership Function μ_H* : According to rule 2.3, a pixel is hyperintense if it presents hyperintense behavior at both PD- and T2-weighted images. So, for obtaining the membership degree of a pixel to the hyperintense fuzzy set, its membership degrees to the *PD* and *T2* hyperintense fuzzy sets had to be aggregated.

Given the characteristics of $\mu_{H,PD}$ and $\mu_{H,T2}$ it was considered that the aggregation operator used for defining μ_H should be a not too restrictive "logical and" (to provide similar importance to both membership functions), and ought take into account the process followed for obtaining the functions to be aggregated.

Bearing in mind the above restrictions as well as the characteristics of the lesions within the images, we studied the operators that could better adapt to them. After this study it was decided that the best operators were: the T-norms Minimum (Min) and Product (Prod), and Averaging Operator Geometric Mean (GM).

For determining which of these operators was better suited to our model we applied a *MFRBS* similar to the considered at previous step. The differences regarding previous system were at the *KB*. So, at the *DB* the linguistic variables and the membership functions associated to the output variable were modified. This change involved the modification of the *RB*.

The set of linguistic terms associated to the output variable was $L'_{Adequacy} = \{\text{High, Medium, Low}\}$. The semantics associated with this variable, as well as the Rule Base, which were determined from the information provided by the experts, are shown at figure 5 and table VI, respectively.

The results obtained after applying the proposed MFRBS are shown at table VII. Moreover, for a better understanding of these results, the GCs obtained from the defuzzification step for the minimum, product, and geometric mean have been depicted as blue, red, and black points at figure 5.

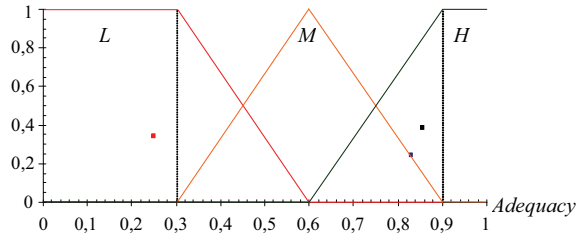


Figure 5. Membership functions of the output variable considered in the DB of the MFRBS designed for determining the aggregation operation used in the definition of the hyperintensity membership function. Blue, red and black points are the GCs obtained for the operators *Min*, *Prod* and *GM*, respectively.

TABLE VI. DECISION TABLE OF THE KB CONSIDERED FOR DEFINING μ_H

Decision Table		SD		
		High	Medium	Low
EAFP	High	R_1 : High (H)	R_4 : Medium (M)	R_7 : Low (L)
	Medium	R_2 : Medium (M)	R_5 : Medium (M)	R_8 : Low (L)
	Low	R_3 : Low (L)	R_6 : Low (L)	R_9 : Low (L)

TABLE VII. RESULTS OBTAINED APPLYING THE PROPOSED MFRBS TO THE DESIGN DATABASE FOR OBTAINING μ_H

Operator	FC	FSD	EAFP	Rules	GC
Min	1	0.8	0.948	R_1	(0.835, 0.23)
Prod	0.667	0.433	0.964	R_4, R_7	(0.246, 0.345)
GM	1	0.88	0.924	R_1	(0.856, 0.376)

In analyzing the results it is appreciated that the product T-norm has clearly the worst fitting to the data, since its *Adequacy* is Low. As for the T-norm minimum, though its *Adequacy* is High, the CG obtained after the defuzzification is very close to *Adequacy* Medium. Therefore, since for the Geometric Mean aggregation Operator the Adequacy obtained was clearly High, the hyperintensity membership function (μ_H) was defined as:

$$\mu_H(p_{ij}) = \sqrt{\mu_{H,D}(p_{ij})\mu_{H,T2}(p_{ij})} \quad (6)$$

IV. RESULTS

The proposed algorithm was evaluated on the 8 PD- and T2-weighted images of the data set. To do it, once the hyperintensity degrees of all the pixels were obtained using (6), we applied a 0.5-cut in order to maintain the balance between being and not be hyperintense. Then we evaluated the quality indexes *FC*, *SD*, and *EAFP*, obtaining the results shown at table VIII.

It must be emphasized that the algorithm showed a high sensitivity detecting hiperintensity regions associated with MS lesions, as can be inferred from the mean value of *SD* that appears at table VIII. In the evaluation of this value must be taken into consideration the hard penalization introduced by the *correction factor FC*. However this index showed also a high mean value (close to 1), and a minimum value of 0.5, what points out that the vast majority of pixels belonging to MS lesions were detected throughout the detection of hiperintensity within these images. Moreover, although we had a small number of false negatives, and the size of MS lesions can be very small, we checked out that all small lesions previously marked up by the experts were detected after applying the proposed algorithm.

On the other hand, the values obtained for *EAFP* indicate a low presence of false detections (*FP*) with regards to the number of pixels within the intracranial region (*card(ICR)*). The small difference between minimum and maximum values for this index, depicted at last column in fourth and fifth rows of table VIII, also allow us to infer that the detection of false positives showed no dependence of the different anatomical features that appear on different slides.

TABLE VIII. RESULTS OBTAINED TROUGH THE LOCAL ANALYSIS OF THE IMAGES DATABASE

	FC	SD	EAFP
Mean	0.94	0.85	0.93
σ	0.177	0.195	0.008
Minimum	0.5	0.43	0.92
Maximum	1.0	1.0	0.94

However, it must be taken into consideration that though a mean value obtained for this index is very high, this not implies necessarily that the number of FP were extremely low because *card(ICR)* is much greater than the possible number of *FP*. In this regard, should be noted that, although it would be desirable, in our implementation of the proposed trade-off it was not imposed that the results provided by the algorithm were free of false detections, instead it was decided to prioritize correct detections, as can be inferred from the definition of the semantic of the output linguistic variable shown in figure 3.

V. CONCLUSIONS AND FUTURE WORK

In conclusion, we have presented an algorithm to detect small hyperintense regions in PD- and T2-weighted MR images of the brain, and we have applied it to the detection of small multiple sclerosis lesions. The algorithm is designed based on a trade-off between true and false positive detections

that has been assessed by the introduction of quality indexes defined for this purpose. Then, a Mamdani type *FRBS* designed considering knowledge and experience of experts, and whose *KB* has fed on the results of the quality indexes obtained for the design images, has provided the aggregation operators defining the hyperintensity fuzzy set. Results have shown that the algorithm is very efficient detecting hyperintense regions associated with small MS lesions.

Future work will involve the introduction of new strategies for reducing false detections without removing true detections. Also the algorithm will be applied to a greater data set to achieve a better validation.

REFERENCES

- [1] A. Compston and A. Coles, "Multiple sclerosis," *The Lancet*, vol. 359, no. 9313, pp. 1221–1231, 2002.
- [2] J. R. Mitchell, S. J. Karlik, D. H. Lee, and A. Fenster, "Computer-assisted identification and quantification of multiple sclerosis lesions in mr imaging volumes in the brain," *J Magn Reson Imaging*, vol. 4, no. 2, pp. 197–208, Mar–April 1994.
- [3] M. K. Edwards and J. M. Bonnin, "White matter diseases in magnetic resonance imaging of the brain and spine," in *Magn Reson. Imaging of the Brain and Spine*, ed., Atlas. S. W, Raven Press, 1991, pp. 467–477.
- [4] D. H. Miller, R. I. Grossman, S. C. Reingold, and H. F. McFarland, "The role of magnetic resonance techniques in understanding and managing multiple sclerosis," *Brain*, vol. 121, no. 1, pp. 3–24, Jan. 1998.
- [5] W. I. McDonald, A. Compston, G. Edan, et al., "Recommended Diagnostic Criteria for Multiple Sclerosis: Guidelines from the International Panel on the Diagnosis of Multiple Sclerosis," *Annals of Neurology*, vol. 50, no. 1, pp. 121–127, 2001.
- [6] D. H. Miller, M. Filippi, F. Fazekas, et al., "Role of magnetic resonance imaging within diagnostic criteria for multiple sclerosis," *Annals of Neurology*, vol. 56, pp. 273–278, 2004.
- [7] D. L. Pham, C. Xu, and J. L. Prince, "A survey of current methods in medical image segmentation," *Annual Review of Biomedical Engineering*, vol. 2, pp. 315–337, 2000.
- [8] M. Hasanzadeh and S. Kasaei, "Multispectral brain MRI segmentation using genetic fuzzy systems," 9th Int. symposium on signal processing and its applications, pp. 1–4, Feb. 2007.
- [9] P. Wang and H. Lei Wang, "A modified FCM algorithm for brain image segmentation," *Int. seminar on Biom. Informat. Eng.* pp. 26–29, 2008.
- [10] K. Van Leemput, F. Maes, D. Vandermeulen, A. Colchester, and P. Suetens, "Automated segmentation of multiple sclerosis lesions by model outlier detection," *IEEE Trans Med Imaging*, vol. 20, no. 8, pp. 677–688, Aug. 2001.
- [11] F. Admiraal-Behloul, D. M. J. van den Heuvel, H. Olofsen, M. J. P. van Osch, J. van der Grond et al., "Fully automatic segmentation of white matter hyperintensities in MR images of the elderly," *Neuroimage*, vol. 28, no. 3, pp. 607–617, Nov. 2005.
- [12] B. R. Sajja, S. Datta, R. He, M. Mehta, R.K. Gupta et al., "Unified Approach for multiple sclerosis lesions segmentation on brain MRI", *Ann. Biomed. Eng.*, vol.34, no. 1, pp. 142–151, Jan. 2006.
- [13] A. Askelrod-Ballin, M. Galun, J.M. Gomori, M. Filippi, P. Valsasina, et al., "Automatic segmentation and classification of multiple sclerosis in multichannel MRI", *IEEE Trans. On Biomedical Engineering*, vol. 56, no. 10, pp. 2461–2469, Oct. 2009.
- [14] E. H. Mamdani, "Application of fuzzy algorithms for control of a simple dynamic plant," *Proc. Inst. Electr. Eng.*, no. 121, pp. 1585–1588, 1974.
- [15] F. X. Aymerich, P. Sobrevilla, J. Capellades, E. Grivé, J. Gili et al., "Fuzzy detection of multiple sclerosis small lesions", in *Proceedings of the fifth conference of the European Society for Engineering and Medicine (ESEM)*, pp. 197–198, 1999.
- [16] F. X. Aymerich, P. Sobrevilla, E. Montseny, and J. Gili J, "Detección mediante técnicas difusas de lesiones de esclerosis múltiple en imágenes de resonancia magnética," XVIII Congreso Anual Sociedad Española de Ing. Biomédica (CASEIB), pp. 269–273, 2000 (not available in english)
- [17] Molyneux P.D., Tubridy N., Parker G.J., et al., "The effect of section thickness on MR lesion detection and quantification in multiple sclerosis," *AJNR Am J Neuroradiol.*, vol. 19, pp. 1715–1720, 1998.
- [18] R. R. Yager, "Families of OWA Operators," *Fuzzy Sets and Systems*, vol. 59, pp. 125–148, 1993.