WML Detection of Brain Images Using Fuzzy and Possibilistic Approach in Feature Space

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Abstract: - White matter lesions are small areas of dead cells found in parts of the brain that act as connectors are detected using magnetic resonance imaging (MRI) which has increasingly been an active and challenging research area in computational neuroscience. This paper presents new image segmentation models for automated detection of white matter changes of the brain in an elderly population. The main focus is on unsupervised clustering algorithms. Clustering is a method for dividing scattered groups of data into several groups. It is commonly viewed as an instance of unsupervised learning. In machine learning, unsupervised learning refers to the problem of trying to find hidden structures in unlabeled data. Unsupervised clustering models, Fuzzy *c*-means clustering, Geostatistical Fuzzy *c*-means clustering and Geostatistical Possibilistic clustering algorithms partition the dataset into clusters according to some defined distance measure. The Region of Interest (ROI) is then extracted on the membership map. Much more accurate results are obtained by GFCM, which better localized the large regions of WMLs when compared to FCM.

Key-Words: - Fuzzy clustering, geostatistics, image segmentation, magnetic resonance imaging, possibilistic clustering, white matter changes

1 Introduction

1.1 Background

Medical Imaging is the technique and process used to create images of the human body for clinical or medical science which is often perceived to designate the set of techniques that produce images of the internal aspect of the body. This means that cause is inferred from effect. White matter changes (lesions) are often seen in elderly people. White matter lesions coincidentally also appear as patches of white, or a very light grey, on MRI. Accurate quantification of white matter changes may contribute to determining if it is possible to affect the evolution of white matter changes with Evaluation of WMLs in MRI is conventionally performed using skill and knowledge of experts [2]. This manual assessment on WML results in different ratings [1],[3], which make it non reproducible and difficult for a general agreement. Cluster analysis or clustering is the task of assigning a set of objects into groups (called clusters) so that the objects in the same cluster are more similar (in some sense or another) to each other than to those in other clusters. The proposed system applies

clustering models like Fuzzy-set and Geostatistic frameworks with application to unsupervised detection of white matter changes of the brain in elderly people. The proposed segmentation models are derived by extending the objective functions of FCM and Possibilistic clustering with a Geostatistical (spatial) model.

1.2 Medical Image Segmentation

Segmentation techniques developed for medical images are non-universal, and image modality and application specific. Compared to other segmentation approaches, clustering techniques can be made adaptive and are relatively simple to implement with acceptable accuracy. Segmentation by clustering does not require a training set. Therefore it is not as limited to image modality and application as some other segmentation approaches such as the active shape model. K-means, and fuzzy C-means are some of the most well-known and often used clustering techniques. However, both are initialization dependent. In practical application, interaction is desirable during human not clustering segmentation process. Image and categorization is a means for high-level description of image content. The goal is to find a mapping of the archive images into classes (clusters) such that the set of classes provide essentially the same information about the image archive as the entire image-set collection. The generated classes provide a concise summarization and visualization of the image content that can be used for different tasks related to image database management. Image clustering enables the implementation of efficient retrieval algorithms and the creation of a userfriendly interface to the database. A common approach to image clustering involves addressing the following issues:

1.Image features – how to represent the image.

2. Organization of feature data – how to organize the data.

3. Classifier – how to classify an image to a certain cluster.

1.3 White Matter Lesions

The white matter, also known as substantia alba, is a neuron that is made up of extending, myelinated nerve fibers, or axons. It composes the structures at the center of the brain. like the thalamus and the hypothalamus. It is found between the brainstem and the cerebellum. It is the white matter that allows communication to and from grey matter areas, and between grey matter and the other parts of the body [3]. There are three different kinds of tracts within the white matter: 1. Projection tracts, which send action potentials from the cortex to other brain regions, out of the brain to muscles, or into the brain from sense receptors. 2. Commissural tracts, which carry information between the left and right hemispheres of the brain over bridges known as commissures. These tracts allow the two hemispheres of the brain to communicate with one another.3.Association tracts. which carrv information between lobes within the same hemisphere. Long association fibers connect different lobes of a hemisphere with one another and short association fibers connect different gyri within a single lobe [5]. The brain's white matter transmits signals between areas of the brain that process information, known as grey matter. When white matter dies, vital communication between two collaborating areas of grey matter slows and can even stop. White matter lesions coincidentally appear as patches of white, or a very light grey, on Since MS lesions present MRI. different characteristics from lesions in elderly individuals, the existing methods are not directly applicable because of the decreased contrast between white matter and grey matter in elderly [6]. Conditions caused by white matter lesions are generally incurable. The main form of treatment is to combat symptoms and slow the condition's progress using prescription medications. White matter is actually affected by a number of different diseases and conditions. such as multiple sclerosis and Alzheimer's disease. Virtually all categories of pathology may cause white matter abnormalities. White matter hyperintensities are more common and extensive in patients with cardiovascular risk factors and symptomatic cerebrovascular disease. White hyperintensities can be measured matter quantitatively and non-invasively on large population samples and have been proposed as an intermediate marker, which could be used for the identification of new risk factors and potentially as a surrogate end point in clinical trials. White matter abnormalities may be seen in congenital. inflammatory, neoplastic, posttraumatic, metabolic, toxic, vascular, degenerative and demyelinating diseases. The primary white matter disorders are classically divided into two groups: dysmyelinating disorders (usually metabolic), in which normal myelin fails to form, and the demyelinating diseases, in which normal myelin has formed and is later destroyed by a myelinoclastic process. The imaging appearance of white matter disease caused by all disease categories is often nonspecific. Developing white matter lesions is a normal part of the aging process. The lesions are very common in the elderly and are present in older people even if they have no health problems. Controlling blood pressure is an important way to help stop white matter problems from getting worse. In addition, many patients receive migraine treatment since these treatments open the blood vessels to further reduce blood pressure.

1.4 Multiple Sclerosis Lesions

In multiple sclerosis, lesions, also known as plaques, are patches of inflammation (An inflammation is a manifestation of the immune system's response to an invading organisms or substances. These may be viruses, bacteria, fungi, allergens, or, in the case of autoimmune diseases, the body's own tissue. A typical example of inflammation that most people are familiar with is the painful red swelling associated with acne.) in the central nervous system (CNS) in which the nerve cells (neurons) have been stripped of their myelin, an insulating fatty protein. Lesions tend to be randomly distributed in the CNS white matter. The neurons of the white matter are responsible for sending communication signals both within the CNS and between the CNS and the rest of the body. Demyelinated neurons do not function efficiently and it is these lesions that give rise to the symptoms of multiple sclerosis (Fig. 1). As the disease progresses, the neurons themselves can become damaged. Modern technologies such as MRI scans and to a lesser extend CT scans can produce images of the brain and spinal cord showing the distribution of the lesions.



Fig.1 Nerve axon with myelin sheath.

In relapsing-remitting MS, there is significant recovery as the inflammation dies down. Special maintenance cells called glial cells are responsible for the repair of the damaged nerves. One type of glial cell, called an oligodendrocyte, lays down new myelin and another type, called an astrocyte lays down scar tissue. In progressive forms of MS, recovery is less significant. Examination of MRI scans show that the vast majority of lesions do not produce clinical symptoms. These are known as silent lesions. Why this is, is not well understood although it is thought that other parts of the central nervous system take over the function that was done by the damaged neurons. Recent research indicates that there may be at least four different types of lesion indicating four different forms of multiple sclerosis or even that MS is in fact four different diseases. At the cellular level, what happens at the site of a lesion is very complex and varied. Immune system component cells (leukocytes) especially

Helper T-cells, Macrophages and possibly mast cells appear to be involved. A complex mix of cellar signalling molecules called cytokines and chemokines mediates the destruction. As well as damaging the myelin, oligodendrocytes are often killed which at the very least delays remyelination.

1.5 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of the brain is a safe and painless test that uses a magnetic field and radio waves to produce detailed images of the brain and the brain stem. An MRI doesn't use radiation, which is one way it differs from a CAT scan (also called a CT scan or a computed axial tomography scan). MRI can detect a variety of conditions of the brain such as cysts, tumors, bleeding, swelling, developmental structural and abnormalities, infections, inflammatory conditions, or problems with the blood vessels. It can determine if a shunt is working and detect damage to the brain caused by an injury or a stroke.



Fig.2 CT Scan Vs MRI Scan.

With the aid of Magnetic Resonance Imaging (MRI), neuroscientists can see inside the brain to discover any problem areas, such as bleeding after a stroke. MRI is a precise and accurate method of diagnosis. Unlike some other imaging techniques, MRI can provide images in multiple planes; a feature that makes the technique even more versatile as shown in Fig.2.

As magnetic resonance imaging has become widely available and brain magnetic resonance imaging is increasingly being carried out in various clinical settings, clinicians often have to deal with the incidental discovery of white matter lesions, appearing as hyperintensities on T2 weighted images. In the general population the prevalence of white matter hyperintensities ranges from 11-21% in adults aged around 64 to 94% at age 82. Pathological findings in regions of white matter hyperintensity include myelin pallor, tissue rarefaction associated with loss of myelin and axons, and mild gliosis. These lesions are located in the deep white matter, typically sparing sub cortical U-fibres. The affected vessels are presumed to induce the lesions in deep white matter through chronic hypo perfusion of the white matter and disruption of the blood-brain barrier, leading to chronic leakage of plasma into the white matter.

2 Related Works

Anbeek et al. [7] proposed k-nearest neighbors algorithm (k-NN) for automatic segmentation of WMLs. This is a supervised learning method and used the information from T1-weighted, inversion recovery (IR), proton density-weighted (PD), T2weighted, and fluid attenuation IR (FLAIR) scans in order to estimate the probability of voxels. A voxel (volumetric pixel or, more correctly, Volumetric *Picture Element*) is a volume element, representing a value on a regular grid in three dimensional space. This is analogous to a pixel, which represents 2D image data in a bitmap (which is sometimes referred to as a pixmap). As with pixels in a bitmap, voxels themselves do not typically have their position (their coordinates) explicitly encoded along with their values. Instead, the position of a voxel is inferred based upon its position relative to other voxels (i.e., its position in the data structure that makes up a single volumetric image). In contrast to pixels and voxels, points and polygons are often explicitly represented by the coordinates of their vertices. A direct consequence of this difference is that polygons are able to efficiently represent simple 3D structures with lots of empty or homogeneouslyfilled space, while voxels are good at representing regularly-sampled that are nonspaces homogeneously filled.



Fig.3 Comparison of T1W, T2W and FLAIR

T1-weighted scans are a standard basic scan, in particular differentiating fat from water - with water darker and fat brighter. This is one of the basic types of MR contrast and is a commonly run clinical scan. T2 - weighted scans are another basic type. Like the T1-weighted scan, fat is differentiated from water - but in this case fat shows darker, and water lighte as shown in Fig. 3. For example, in the case of cerebral and spinal study, the CSF (cerebrospinal fluid) will be lighter in T2-weighted images. By combining the results of these techniques binary segmentation results are obtained from the selected threshold values, and therefore the relation between an optimal threshold and lesion volume was separately chosen for each patient.

A probability mixture model and the Bayesian classifier was used by Khayati et al. [8] in order to extract normal tissue, abnormal tissue and cerebrospinal fluid (CSF) which serves primary purpose like buoyancy, protection and chemical stability. Normal tissue refers to white matter and grey matter of brain whereas abnormal tissue refers to lesions of brain in FLAIR-MR images. This method does not focus on the lesions of small size or irregular shape.

Beare et al. [9] applied a morphological watershed model and statistical classifiers for segmenting age-related cerebral white matter hyper intensities (WMH) on MRI scans. This approach can enhance the segmentation of small and peripheral lesions, but different white matter mask generations, which may yield different results.

Lao et al. [10] proposed an approach for segmenting WML in which support-vector machine (SVM) classifier was used in order to classify new scans, and post processing analysis was carried out to eliminate false positives. The strength of SVMbased classifiers is the ability to separate overlapping features, but selecting effective features for classifying a particular difficult problem is one of the key issues in pattern classification that should be first identified, where the results are based on only expert-defined information. This method is less accurate. Therefore WML image intensities cannot be visually distinguished.

Lesions are irregular voxels that do not belong to GM, WM and CSF and can be classified as outliers in grey and white matter regions. This method was proposed by Seghier et al. [11]. After combining the segmentation and normalization of images, fuzzy clustering was applied to identify outlier voxels as lesions in normalized grey and white matter segments. Spatial smoothing was done using Gaussian kernel, which affect the sensitivity and specificity of the method.

Hernandez et al. [12] presented a multispectral MRI approach for segmenting normal and abnormal brain tissue. The procedure was carried out by combining pairs of different MRI sequences and modulated them in the red-green color space to enhance the tissue discrimination. Fully automated method for CSF, GM and WM segmentation based on multimodal MRI data is optimized and extended with WML segmentation was proposed by R. de Boer, H. A. Vrooman and F. van der Lijn [13].

M. L. Seghier, A. Ramlackhansingh presented a new procedure to identify any type of brain damage given a single anatomical image. This procedure is based on the assumption that the lesion comprises atypical voxels that disclose themselves as outliers in grey and white matter segments. Atypical voxels are those that do not correspond to the expected tissue types; i.e., are neither Grey Matter (GM), White Matter (WM) nor Cerebrospinal Fluid (CSF). To avoid misclassification, they proposed a modified version of the unified segmentation scheme to segment healthy and damaged brain tissue.

3 Proposed Scheme



Fig.4 Overall process of the system.

The proposed system applies clustering models like Fuzzy-set, Possibilistic approach and Geostatistic frameworks with application to unsupervised detection of white matter changes [1] of the brain in elderly people as in shown Fig.4. The first step of automated quantification of WML involves Image Segmentation. The goal of segmentation is to simplify and/or change the representation of an image into something that is more meaningful and easier to analyze. Image segmentation is typically used to locate objects and boundaries (lines, curves, etc.) in images. In multiple sclerosis, lesions, also known as plaques, are patches of inflammation of the central nervous system (CNS).

Since MS lesions present different characteristics from lesions in elderly individuals, those methods are not directly applicable because of the decreased contrast between white matter and grey matter in MRI [4]-[6] in elderly. The proposed segmentation models are derived by extending the objective functions of FCM with a Geostatistical (spatial) model and PSO method was used to optimize the membership functions of the fuzzy model, where the results show that the optimized MFs provided better performance.

3.1 Fuzzy C-Means Clustering

Fuzzy c-means has been a very important tool for image processing in clustering objects in an image. Fuzzy c-means (FCM) clustering is an unsupervised method derived from fuzzy logic that is suitable for solving multiclass and ambiguous clustering problems. The FCM clustering algorithm is used to calculate the minimization of the fuzzy objective function [11]. It works by assigning membership to each data point corresponding to each cluster center on the basis of distance between the cluster center and the data point. More the data is near to the cluster center more is its membership towards the particular cluster center. Clearly, summation of membership of each data point should be equal to one. Its advantages include a straightforward implementation. fairly robust behaviour. applicability to multichannel data. Fuzzy c-means (FCM) clustering is an unsupervised technique that has been successfully applied to feature analysis, clustering, and classifier designs in fields such as astronomy, geology, medical imaging, target recognition, and image segmentation. An image can be represented in various feature spaces, and the FCM algorithm classifies the image by grouping similar data points in the feature space into clusters. This clustering is achieved by iteratively minimizing a cost function that is dependent on the distance of the pixels to the cluster centers in the feature domain. A major disadvantage of its use in imaging applications, however, is that FCM does not incorporate information about spatial context, causing it to be sensitive to noise and other imaging artifacts.

There are many acceleration techniques for FCM; there are very large data versions of FCM that utilize both progressive sampling and distributed clustering; there are many techniques that use FCM clustering to build fuzzy rule bases for fuzzy systems design; and there are numerous applications of FCM in virtually every major application area of clustering. Main objective of fuzzy c-means algorithm is to minimize the objective function.

$$J(U, V) = \sum_{i=1}^{n} \sum_{j=1}^{c} (\mu_{ij})^{m} ||x_{i} - v_{j}||^{2}$$
(1)

3.1.1 FCM Algorithm

S1 Randomly select 'c' cluster centers.

S2 Calculate the fuzzy membership.

S3 Calculate the fuzzy centre.

S4 Repeat steps 2) and 3) until the minimum 'J' value is incorporated as in equation (1).

J (U, V) =
$$\sum_{i=1}^{n} \sum_{j=1}^{c} (\mu_{ij})^{m} ||x_i - v_j||^2$$

where $'/|x_i - v_j|/'$ is the Euclidean distance between i^{th} data and j^{th} cluster center.

3.2 Geostatistical Fuzzy Clustering

The fuzzy C-means objective function is generalized to include a spatial penalty on the membership functions. The fuzzy C-means algorithm (FCM) has been utilized in a wide variety of image processing applications such as medical imaging and remote sensing. Its advantages include a straightforward implementation, fairly robust behavior, applicability to multichannel data, and the ability to model uncertainty within the data. A major disadvantage of its use in imaging applications, however, is that FCM does not incorporate information about spatial context, causing it to be sensitive to noise and other imaging artifacts. Therefore geostatistical fuzzy clustering is proposed. The advantages of the new method are the following: (1) it yields regions more homogeneous than those of other methods, (2) it removes noisy spots, and (3) it is less sensitive to noise than other techniques (4) it removes noisy spots, and (5) it is less by extending the into the FCM objective function.. It is derived by extending the into the FCM objective function. The clustering is a two-pass process at each iteration. The first pass is the same as that in standard FCM to calculate the membership function in the spectral domain. In the second pass, the membership information of each

pixel is mapped to the spatial domain, and the spatial function is computed from that. The FCM iteration proceeds with the new membership that is incorporated with the spatial function. The iteration is stopped when the maximum difference between two cluster centers at two successive iterations is less than a threshold A distinctive observation of the incorporation of the geostatistical modeling into the fuzzy clustering is that it is able to accurately detect the WMLs as the regions of interest of an elderly population and provides the bidirectional association between depression and vascular disease. The main aim of is to minimize the objective function, where kriging variance is incorporated It is a derived function.

$$J_{GP}(U, v) = \sum_{i=1}^{N} \sum_{j=1}^{c} (u_{ij})^{m} [d(x_{i}, v_{j})]^{2} + \sum_{j=1}^{c} (e_{j})^{2} \sum_{i=1}^{c} (u_{ij}-1)^{m}$$
(2)

where $(e_j)^2$ is the kriging (geostatistical) variance of estimating v_i using x_i, x=1,2...N-1.

3.2.1 GFC Algorithm

S1 Randomly select 'c' cluster centers.

S2 Calculate the fuzzy membership.

S3 Calculate the spatial variability.

S4 Incorporate spatial variability into objective function as in equation (2).

S5 Minimise the objective functions by setting a Lagrangian function.

3.3 Geostatistical Possibilistic Clustering

Although FCM is a very useful clustering method, its memberships do not always correspond well to the degree of belonging of the data, and may be inaccurate in a noisy environment. To improve this weakness of FCM and to produce memberships that have a good explanation for the degree of belonging for the data, Possibilistic approach was proposed. It is a variation over fuzzy clustering where the membership to clusters can be seen as a degree of typicality membership matrix U, $uih \in [0, 1]$. Possibilistic clustering algorithms prove the fact that it can be applied for one cluster at a time.

$$J_{GP}(U, v) = \sum_{i=1}^{N} \sum_{j=1}^{c} (u_{ij})^{m} [d(x_{i}, v_{j})]^{2} + \sum_{j=1}^{N} i/(e_{j})^{2} \sum_{i=1}^{N} (1 - u_{ij})^{m}$$
(3)

3.3.1 GPC Algorithm

S1 Randomly select 'c' cluster centers.

S2 Calculate the possibilistic membership.

S3 Calculate the spatial variability.

S4 Incorporate the spatial variability into objective function as in equation (3).

S5 Minimise the objective function (a small value of difference) then stop.

3.4 Region of Interest

ROIs can be defined either in terms of structural or functional features. Structural ROIs are generally defined based on macro anatomy whereas Functional ROIs are generally based on analysis of data from the same individual. ROIs can be defined either in terms of structural or functional features. The concept of an ROI is commonly used in medical imaging. Most image-related tasks can process a subset of the pixels in an input image. Careful selection of regions is an essential step in ROI analysis. A common approach to the analysis of MRI data involves the extraction of signal from specified regions of interest (or ROI's).ROI is defined by creating a binary mask, which is a binary image that is the same size as the image you want to process with pixels that define the ROI set to 1 and all other pixels set to 0. ROI is found by automatic threshold on the membership map. To differentiate white matter detected using GFCM a parametric

model is used. Although ROI analysis is most often considered for analysis of activations, it can sometimes be equally useful for determining the reasons for lack of activation. There are several strategies for selecting a ROI:

- based on the actual activation (select the region based on voxels above some threshold).
- drawing a sphere around some peak in the activation.
- based on anatomical labelling (requires a good brain mask or segmentation)

There are three fundamentally different means of encoding an ROI:

- burned in to the dataset, with a value that may or may not be outside the normal range of normally occurring values
- as separate purely graphic information, such as with vector or bitmap drawing elements, perhaps with some accompanying plain text annotation
- as separate structured semantic information with a set of spatial and/or temporal coordinates

3.4.1 ROI Steps

S1 Read the input image.

S2 Determine the ROI based on intensity.

S3 Calculate the difference between the value of original image and predicted region of original image.

S4 Calculate the unique value.

S5 Compare and match the unique value with the predicted region's value.

4 Experimental Results



Fig.5 MRI of FLAIR image

Fig. 5 shows white matter changes in the MRI scan of brain. The cerebrum is divided into the left and right hemispheres, each consists of four lobes: frontal, parietal, occipital, and temporal. The outer layer of the brain is known as the cerebral cortex or the grey matter, whereas tissues cover the nuclei deep within the cerebral hemisphere known. Fig. 6 and Fig.7 (a) shows the WML detections of using the FCM and GFCM methods, respectively. The results were over detected/segmented by both methods; particularly numerous small regions were falsely detected. The combined model of GFCM and GPC could further enhance the result, which was

close to that of the GFCM [15], where some false small spots were removed.

Fig. 7(b) and 8(b) shows the region of interest of the clustered FLAIR image of the brain. Thus the region of interest found by automatic threshold on the membership map differentiates the white matter detected using GFCM. GPC could better capture the largest loads of WML in the upper ventral horns as shown in Fig. 8 (a).



Fig.6 WML detection using FCM



Fig.7 (a) WML detection using GFCM



Fig.7 (b) ROI of Clustered Image (GFCM)



Fig.8 (a) WML detection using GPC



Fig.8 (b) ROI of clustered image (GPC)

Much more accurate detected results were obtained by GFCM and GPC, particularly the GFCM, which better localized the large regions of WMLs while suppressed small spots seeming to be changes of the white matter. As there are no analytical methods that can be generally agreed on the assessment of image segmentation results, particularly for the detection of white matter changes, a common practice is by the ranking of medical experts. All segmented scans obtained from different image segmentation models are manually ranked based on the values in Table 1 in terms of under detected, over detected, properly detected as shown in Fig. 9. FCM made equal errors on over detection and under detection, whereas the GFCM made relatively smallest errors only on under detection. In general, GFCM and GPC yield the best rate for detecting the white matter changes of the brain when compared to FCM.

Table I

WML Detection Rates (%) of

FCM, GFCM and GPC

Model	Over Detected	Under detected	Properly detected
FCM	22	20	44
GFCM	4	22	72
GPC	20	12	65



Fig.9 FCM Vs GFCM

4 Conclusion

The proposed Fuzzy c-means Clustering and Geostatistical Fuzzy *c*-means Clustering is used for detecting WML (white matter lesions) in brains of people. The incorporation of elderly the Geostatistical estimate variance into the objective functions of Fuzzy clustering algorithm is relatively a simple procedure for implementation and can be further explored using various advanced kriging systems in multivariate Geostatistics. Experimental results using the MRI data of the elderly individuals have shown advantages of the proposed methods for extracting white matter changes. More accurate results are obtained by Geostatistical Fuzzy cmeans, where false spots are removed.

Future work includes the implementation of Particle Swarm Optimization, Geostatistical

Possibilistic Clustering and Information Fusion of combined models for detecting White Matter Lesions in brain images. Particle Swarm Optimization (PSO) is a biologically inspired computational search and optimization method developed based on the social behaviors of birds flocking or fish schooling. The combined model of Geostatistical Fuzzy c-means and Geostatistical Possibilistic Clustering could further enhance the result.

References:

- L. O. Wahlund, F. Barkhof, F. Fazekas, L. Bronge, M. Augustin, M. Sj"ogren, A. Wallin, H. Ader, D. Leys, L. Pantoni, F. Pasquier, T. Erkinjuntti, and P. Scheltens, "A new rating scale for age-related white matter changes applicable to MRI and CT," *Stroke*, vol. 32, pp. 1318–1322, 2001.
- [2] E. Matsusue, S. Sugihara, S. Fujii, E. Ohama, T. Kinoshita, and T. Ogawa, "White matter changes in elderly people: MR-pathologic correlations," *Magn. Reson. Med. Sci.*, vol. 5, pp. 99–104, 2006.
- [3] F. Fazekas, "Pathological correlates of incidental MRI white matter signal hyper intensities," *Neurology*, vol. 43, pp. 1683–1689, 1993.
- [4] J. Udupa, L. Wei, S. Samarasekera, Y. Miki, M. A. van Buchem, and R. I. Grossman, "Multiple sclerosis lesion quantification using fuzzy connectedness principles," *IEEE Trans. Med. Imaging*, vol. 16, no. 5, pp. 598–609, Oct. 1997.
- [5] B. Alfano, A. Brunetti, M. Larobina, M. Quarantelli, E. Tedeschi, A. Ciarmiello, E. M. Covelli, and M. Salvatore, "Automated segmentation and measurement of global white matter lesion volume in patients with multiple sclerosis," *J. Magn. Reson. Imaging*, vol. 12, pp. 799–807, 2000.
- [6] Y. Wu, S. K. Warfield, I. L. Tan, W. M. Wells III, D. S. Meier, R. A. van Schijndel, F. Barkhof, and C. R. G. Guttmann, "Automated segmentation of multiple sclerosis lesion subtypes with multichannel MRI," *NeuroImage*, vol. 32, pp. 1205–1215, 2006.
- [7] P. Anbeek, K. L. Vincken, M. J. P. van Osch, R. H. C. Bisschops, and J. van der Grond, "Automatic segmentation of different-sized white matter lesions by voxel probability estimation," *Med. Image Anal.*, vol. 8, pp. 205– 215, 2004.
- [8] R. Khayati, M. Vafadust, F. Towhidkhah, and S. M. Nabavi, "Fully automatic segmentation

of multiple sclerosis lesions in brain MR FLAIR images using adaptive mixtures method and Markov random field model," *Comput. Biol. Med.*, vol. 38, pp. 379–390, 2008.

- [9] Z. Lao, D. Shen, D. Liu, A. F. Jawad, E. R. Melhem, L. J. Launer, R. N. Bryan, and C. Davatzikos, "Computer assisted segmentation of white matter lesions in 3D MR images using support vector machine," *Acad. Radiol.*, vol. 15, pp. 300–313, 2008.
- [10] M. L. Seghier, A. Ramlackhansingh, J. Crinion, A. P Leff, and C. J. Price, "Lesion identification using unified segmentationnormalisation models and fuzzy clustering," *NeuroImage*, vol. 41, pp. 1253–1266, 2008.
- [11] R. Beare, V. Srikanth, J. Chen, T. G. Phan, J. Stapleton, R. Lipshut, and D. Reutens, "Development and validation of morphological segmentation of age-related cerebral white matter hyper intensities," *NeuroImage*, vol. 47, pp.199–203, 2009.
- [12] R. de Boer, H. A. Vrooman, F. van der Lijn, M.W. Vernooij, M. A. Ikram, A. van der Lugt, M. M. B. Breteler, and W. J. Niessen, "White matter lesion extension to automatic brain tissue segmentation on MRI," *NeuroImage*, vol. 45, pp. 1151–1161, 2009.
- [13] M. delC .V. Hernendez, K. J. Ferguson, F. M. Chappell, and J. M. Wardlaw, "New multispectral MRI data fusion technique for white matter lesion segmentation: method and comparison with thresholding in FLAIR images,"*Eur. Radiol.*, Feb. 16, 2010.