

# Review on Detection of Multiple Sclerosis in Brain MR Images

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**ABSTRACT:** Multiple Sclerosis (MS) is the most common demyelinating disease of the Central Nervous System (CNS) in humans characterized by a wide scope of neurological deficits. Magnetic Resonance Imaging (MRI) plays an important role in MS diagnosis, often for determining size and location of affected tissue. Research to this disease is highly important for better understanding of causes and progression of the disease, and improvement of treatment. Automatic detection and segmentation of MS lesions can help to improve diagnostic accuracy leading to proper treatment planning. It offers an attractive alternative to manual detection which remains a time-consuming task and suffers from intra- and inter-expert variability. The objective of this paper is to review the main approaches to automated MS lesion detection in human brain MRI. It is about MS lesions and effectiveness of MRI in detection of it. Paper covers review of different image processing algorithms and techniques used and comparison of results which will enable researchers in the field to understand the scope and challenges involved towards automatic detection of MS lesions from normal brain MRI scans.

**KEYWORDS:** Multiple Sclerosis (MS), Magnetic Resonance Imaging (MRI), Segmentation, Feature extractions, Classification, Computer-Aided Detection (CAD).

## I. INTRODUCTION

Multiple sclerosis (MS) is a chronic neurological disorder and the most common cause of neurological disability in young adults. MS is characterized by the destruction of proteins in the myelin surrounding nerve fibers. As a result lesions may appear, leading to a progressive decline of motor, vision, sensory, and cognitive function [14]. Early detection of the MS is very important for treatment planning. The radiological criteria for MS include the number of lesion on the MRI, their locations and their sizes, and this quantitative information is also crucial for studying the progression of MS lesions and the effect of drug treatments [15]. MRI is the primary complementary examination for the monitoring and diagnosis of MS. MRI is a noninvasive method for imaging internal tissues and organs. MRI is increasingly being used to assess the progression of the disease and to evaluate the effect of drug therapy, supplementing traditional neurological disability scales such as the Extended Disability Status Scale (EDSS). Segmentation of MS lesions from MR brain images is important in the diagnosis of the disease. However, manual detection and analysis of these lesions from MR brain images are usually time consuming, expensive and can produce unacceptably high intra-observer and inter-observer variability [8]. Manual segmentation is also impractical for large clinical data sets that may contain thousands of images, and can be less sensitive than automated methods, especially for smaller lesions [2].

Computer-Aided Detection (CAD) analysis can assist in identifying brain structures, extract quantitative and qualitative properties of these structures, and evaluate their progress over time [14]. The main idea of CAD is to assist radiologists in interpreting medical images by using dedicated computer systems to provide 'second opinions'. Studies on CAD systems and technology show that CAD will help to improve diagnostic accuracy of radiologists, lighten the burden of increasing workload, databases overloaded and improve inter and intra-reader variability. The final diagnostic decision is made by the radiologists can be improved with the CAD system bringing to his/her notice missed lesions, if any. Therefore, the CAD systems ought to have skills kind of like the radiologists in terms of learning and recognition of

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brain diseases. To create a CAD system, the integration of various image processing operations such as image segmentation, feature extraction and selection, and classification are essential.

The rest of this paper is organized as follows: Section II presents comprehensive survey of the existing MRI CAD systems with comparative study on the recent segmentation and classification techniques for MS. Section III presents the feature extraction for MR images. Section IV presents segmentation and classification for MS. Section V presents the evaluation and validation for MS detection. Section VI presents the conclusion.

## II. LITERATURE SURVEY

Automated MS diagnosis with MR images is becoming increasingly important in the medical field. The accuracy of this MS detection technique must be significantly high since the treatment planning is based on this identification. Many research papers with different approaches for image segmentation and classification are reported in the literature. Table 1 gives extensive survey of existing methods for MS detection in brain images. Xavier et al. [1] proposed augmenting the imaging data used to identify lesions to include both an intensity model of the patient under consideration and a collection of intensity and segmentation templates that provide a model of normal tissue. They call this combination as Model of Population and Subject (MOPS) intensities. Ahmad Bijar et al. [8] in this paper brain image is partitioned into three parts, including dark (CSF), gray (normal tissues) and white part (MS lesions), whose member functions of the fuzzy region are Z-function, P-function and S-function, respectively. Then the fuzzy regions of their member functions are determined by maximizing fuzzy entropy through the Genetic algorithm. Finally, MS lesions and CSF areas are determined by applying a localized weighted filter to the Bright and Dark membership images. Alex Zijdenbos et al. [25] developed an automatic pipeline image analysis framework and had successfully applied it to a number of large scale, multicenter studies (>1000 MRI scans). Akselrod-Ballin et al. [14] provide experiments on two types of real MRIs: a multichannel PD, T2, and T1-w and a single-channel FLAIR dataset.

Colm Elliott et al. [2] proposed method uses a two-stage classification process: 1) A Bayesian classifier provides a probabilistic brain tissue classification at each voxel of reference and follow-up scans, and 2) A random-forest based lesion-level classification provides a final identification of new lesions. Daniel Lorenzo et al. [11] used the FAST-TLE to estimate the NABT tissues with a fixed and proposed a hierarchical initialization based on random initializations to avoid its convergence to a local maximum and to provide an accurate initialization. Jundong et al. [15] presented a method treats MS lesions as outliers to the normal brain tissue distribution, and the separation is achieved by minimizing a statistically robust L2E measure, which is defined as the squared difference between the true density and the assumed Gaussian mixture. Mark Horsfield et al. [21] presented a method for incorporating prior knowledge into the fuzzy connectedness image segmentation framework. The method was tested by using it to segment brain lesions in patients with MS and the results compared to an established method for lesion outlining based on edge detection and contour following. Fitsum Admasu et al. [24] used the fuzzy connectedness algorithm to extract segments which are parts of CSF, WM or GM. Then trained ANN decides whether a segment was a part of a lesion or not.

Pallab Roy et al. [5] proposed automated segmentation method to identify MS related WM lesions from brain MRI data. SVM used to classify lesion pixels and level set based active contour and morphological filtering to achieve higher accuracy on lesion pixel identification. S. Bricq et al. [19] in this work, neighborhood information is taken into account during the inference process by using a Hidden Markov Chain model and outliers are detected using the TLE. Zahra Karimaghloo et al. [7] presented an automatic, probabilistic framework for segmentation of gadolinium-enhancing lesions in MS using THAT-CRF. Ezequiel Geremia et al. [12] presented segmentation of MS lesions in 3D MRI. It builds on a discriminative random decision forest framework to provide a voxel-wise probabilistic classification of the volume. Martijn Steenwijk et al. [4] presented method improved KNN classification of WM lesions by optimizing intensity normalization and using spatial TTPs. Volumetric agreement was evaluated using Intra-Class Coefficient (ICC), and voxelwise spatial agreement was evaluated using DSI. Rasoul Khayati et al. [18] proposed method based on a Bayesian classifier, utilizes the Adaptive Mixtures Method (AMM) and MRF model to obtain and upgrade the class conditional probability density function (CCPDF) and the a priori probability of each class.

Renske Boer et al. [16] in this method, the resulting GM segmentation was used to automatically find a White Matter Lesion (WML) threshold in a FLAIR scan. False positive lesions were removed by ensuring that the lesions are within the WM. Sushmita Datta et al. [6] used the ICBM (International Consortium for Brain Mapping) template to minimize

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the false lesion classifications. The EM-HMRF algorithm was applied to the T1 and T2 images to classify GM, WM, and CSF. , the classification of the dGM structures was further improved using the ICBM template. Ying Wu et al. [23] presented automated segmentation of MS lesions into three subtypes (i.e., enhancing lesions, T1 ‘black holes’, T2 hyperintense lesions). Intensity-based statistical KNN classification was combined with template-driven segmentation and partial volume artifact correction for segmentation of MS lesions and brain tissue compartments. Jason Corso et al. [20] proposed an extended graph-shifts algorithm for image segmentation and labeling. This algorithm performs energy minimization by manipulating a dynamic hierarchical representation of the image. It consists of a set of moves occurring at different levels of the hierarchy where the types of move, and the level of the hierarchy, were chosen automatically so as to maximally decrease the energy. Mariano Cabezas et al. [3] proposed a pipeline for MS lesion segmentation that combines prior knowledge and contextual information into a boosting classifier. The prior knowledge is introduced in terms of atlas distribution of the main brain tissues while the contextual information was based on a large set of features describing the spatial context in the lesion neighbourhood.

Ziming Zeng et al. [13] their workflow was composed of three steps: locate the MS lesion region in the joint histogram, segment MS lesions, and false positive reduction. The advantage of their approach was that it can segment small lesions, does not require prior skull segmentation, and was robust with regard to noisy and inhomogeneous data. Balasrinivasa Sajja et al. [22] proposed strategy that involves CSF and lesion classification using the Parzen window classifier. Contextual information is exploited for minimizing the false negative lesion classifications using HMRF-EM algorithm. Lesions are delineated using fuzzy connectivity. Petronella et al. [17] gives method which used voxel location and signal intensity information for determining the probability being a lesion per voxel, that generate probabilistic segmentation images. Sergi Valverde [28] approach exhibits a significant increase in the accuracy segmenting of WM lesions when compared with the rest of evaluated methods, highly correlating ( $r \geq 0.97$ ) also with the expected lesion volume on clinical MS data.

Table 1 gives comprehensive survey on types of MR Images, databases, segmentation and classification methods, and results which is used for MS detection in brain MRI as follows:

Table 1: Review for Detection of MS in brain MRI.

| Author                            | MR Images                   | Database                                      | Detection method                              | Results  |                          |                        |      |     |       |     |
|-----------------------------------|-----------------------------|---|---|--|--------------------------|------------------------|------|-----|-------|-----|
|                                   |                             |   |   | PPV  | combined intensity model | global intensity model | TP   | FP  | Sens. | FDR |
| Xavier Fernandez (IEEE) 2015 [1]  | T1w, T2w and FLAIR          | BrainWeb and MS Grand Challenge               | Graph-Cuts algorithm                          |  |                          |                        |      |     |       |     |
| Colm Elliott (IEEE) 2013 [2]      | T1, T2, FLAIR, T1c          | NA  | Bayesian classifier+ Random Forest Classifier | Sensitivity (at FD rate=0.1) : $0.83 \pm 0.08$<br>Sensitivity (at FD rate=0.2) : $0.89 \pm 0.05$ |                          |                        |      |     |       |     |
| Zahra Karimaghloo (IEEE) 2013 [7] | T1p, T1c, T2, PD and FLAIR. | multi-center clinical data sets               | (THAT-CRF)                                    | Overall  | 223                      | 55                     | 0.95 | 0.2 |       |     |
| PallabKanti Roy (IEEE) 2013 [5]   | T1-w, T2-w, FLAIR           | MS Lesion Segmentation Challenge 2008 dataset | Support Vector Machine (SVM)                  | mean F1 score = 0.5<br>number of win, drawn and loss (W; D; L)= 20;0;4                           |                          |                        |      |     |       |     |
| Ahmad                             | FLAIR                       | NA  | Maximum Fuzzy                                 | Patient category   | SI                       | OF                     | EF   |     |       |     |

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|--|-------------------|---|--|---|------------|------------|----------------|-----------|
| Bijar (IEEE) 2012 [8]                  |                   |   | Entropy+Genetic algorithm (MFE+GA)                               | Small lesion  | 0.7731     | 0.7728     | 0.2451         |           |
|  |                   |   |  | Moderate lesion   | 0.8194     | 0.8059     | 0.2058         |           |
|  |                   |   |  | Large lesion  | 0.8669     | 0.8425     | 0.1759         |           |
| Daniel Lorenzo(IEEE) 2011 [11]         | PD, T1, T2        | BrainWeb Clinical data                                  | Trimmed Likelihood Estimator (TLE)                               | DSC (Avg.) for Clinical data: 0.65 and BrainWebdata: 0.72                                     |            |            |                |           |
| AyeletAkseelrod (IEEE) 2009 [14]       | PD, T1, T2, FLAIR | Scientific Institute Ospedale San Raffaele              | Decision Forest + Fisher Linear Discriminant(FLD)                |   | DSC        | Sens.      | Spec.          | Accuracy  |
|  |                   |   |  | Multi-channel   | 0.53±.1    | 0.55±.13   | 0.98 ± 0.01    | 0.97±.01  |
|  |                   |   |  | FLAIR   | 0.55±.9    | 0.57±.14   | 0.99 ± 0.01    | 0.98±.01  |
| Jundong Liu (IEEE) 2009 [15]           | T2 and FLAIR      | University of Kentucky Hospital.                        | Integrated Squared Estimation (L2E)                              | Volume Difference= 19.38, Dice Coefficient= 0.6989<br>Sensitivity= 0.6667, Specificity=0.9997 |            |            |                |           |
| S. Bricq (IEEE) 2008 [19]              | T1 and FLAIR      | NA  | Hidden Markov Chain + TLE  | Images  | C1         | C2         | C3             | C4        |
|  |                   |   |  | Kappa Index   | 49         | 68         | 61.1           | 55        |
| Mark Horsfield (IEEE) 2007 [21]        | PD, T2            | Clinical data from Italy or the USA                     | fuzzy connections (FC)   |   | Observer 1 | Observer 2 | Intra-Observer |           |
|  |                   |   |  | Concordance   | 60.60%     | 63.10%     | 80.80%         |           |
| FitsumAdmasu (IEEE) 2003 [24]          | T2, T1, and PD    | NA  | fuzzy connectedness (FC) + ANN                                   | false positive = 7%,<br>false negative = 2.70%  |            |            |                |           |
| AlexZijdenbos (IEEE) 2002 [25]         | T2, T1, and PD    | clinical data from North America                        | Artificial Neural Networks (ANN)                                 | DSI= 0.83, TLL= 0.93,<br>average kappa value= 0.6   |            |            |                |           |
| J. Dehmeshki (IEEE) 2002 [26]          | NA                | Clinical data   | LDA and PCA+ nearest mean classifier                             | The success rate of binary classification was 86%–92%   |            |            |                |           |
| EzequielG eremia(NeuroImage) 2011 [12] | T1, T2, FLAIR     | MS Lesion Segmentation Challenge 2008                   | random decision forests  |   | VD         | SD         | TPR            | FPR       |
|  |                   |   |  | CHB   | 52.9±28.6  | 5.27±9.54  | 58.0±20.0      | 70.0±16.3 |
|  |                   |   |  | UNC   | 50.5±41.4  | 5.6 ± 6.67 | 51.3±19.9      | 76.8±11.7 |
| SergiValverde (Elsevier) 2017 [28]     | T1-w and FLAIR    | MS lesion segmentation challenge 2008 and clinical data | cascade of two 3D patch-wise convolutional neural networks (CNN) |   | VD         | TPR        | FPR            |           |
|  |                   |   |  | UNC Rater   | 62.5       | 55.5       | 46.8           |           |
|  |                   |   |  | CHB Rater   | 40.8       | 68.7       | 46             |           |

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| MartijnSteenwijk (Elsevier) 2013 [4] | FLAIR and T1                 | Clinical data from USA                      | k nearest neighbor (KNN)   | ICC= 0.96, DER= 0.07±0.06, OER= 0.25 ± 0.16, SI= 0.84 ± 0.10, Sensitivity= 0.86±0.14                             |  |                      |                   |           |
| SushmitaDatta (Elsevier) 2013 [6]    | T1, T2, FLAIR                | MS lesion segmentation grand challenge 2008 | expectation-maximization(EM)+ hidden Markov-random field (HMRF)    | Volume Difference = 36.18 ± 34.90<br>average distance (mm) = 1.64±1.30<br>TPR= 84.75±12.69, FPR= 34.10±16.00     |  |                      |                   |           |
| Renske Boer (Elsevier) 2009 [16]     | T1, PD, FLAIR                | Rotterdam Scan Study                        | k nearest neighbor (KNN)   |  | CSF                                    | GM                   | WM                | WML       |
|                                      |                              |   |  | TPF  | 0.9                                    | 0.87                 | 0.97              | 0.79      |
|                                      |                              |   |  | EF   | 0.13                                   | 0.057                | 0.13              | 0.5       |
|                                      |                              |   |  | SI   | 0.89                                   | 0.9                  | 0.92              | 0.72      |
| RasoulKhayati (Elsevier) 2008 [18]   | FLAIR                        | NA  | Bayesian classifier + adaptive mixtures method (AMM) and MRF model | Patient category   | Small lesion load                      | Moderate lesion load | Large lesion load |           |
|                                      |                              |   |  | SI   | 0.7253                                 | 0.752                | 0.8096            |           |
|                                      |                              |   |  | OF   | 0.7267                                 | 0.7388               | 0.7857            |           |
|                                      |                              |   |  | EF   | 0.2755                                 | 0.2206               | 0.1541            |           |
| Ying Wu (Elsevier) 2006 [23]         | PD, T2, contrast-enhanced T1 | clinical data from Germany                  | KNN + template-driven segmentation (TDS)                           | Types of lesions   | Sensitivity                            | Specificity          | Accuracy          |           |
|                                      |                              |   |  | T2 lesions   | 70%                                    | 98.70%               | 98.50%            |           |
|                                      |                              |   |  | Enhancing lesions  | 75.20%                                 | 99.90%               | 99.90%            |           |
|                                      |                              |   |  | Black holes  | 62.30%                                 | 99.70%               | 99.70%            |           |
| Mariano Cabezas (Springer) 2013 [3]  | PD-w and T2-w                | JosepTrueta and Valld'Hebron Hospital       | Gentleboost algorithm  | mean true positive fraction value = 53% (Valld'Hebron hospital) and 63% (JosepTrueta hospital)<br>DSC (Mean)=0.5 |  |                      |                   |           |
| ZimingZeng (Springer) 2011 [13]      | T1 and T2                    | Brainweb and clinical data                  | class-adaptive Gaussian Markov modelling approach (CAGMRF)         |  | 3 % noise                              | 5 % noise            | 7 % noise         | 9 % noise |
|                                      |                              |   |  | DSC  | 0.81                                   | 0.79                 | 0.77              | 0.74      |
| Jason Corso (Springer) 2007 [20]     | T1                           | NA  | Extended Graph-Shifts  | Lesion Detection Rate = 86% (Training Set) and 81% (Testing Set)   |  |                      |                   |           |
| Balasrinivasasajja(NIH) 2006 [22]    | PD, T2 and FLAIR             | Clinical Data                               | hidden Markov-random field(HMRF) + expectation-maximization (EM)   | Patient category   | percentage of correct estimation (PCE) |                      | SI                |           |
|                                      |                              |   |  | Small lesion load  | 80%                                    |                      | 0.67              |           |
|                                      |                              |   |  | High lesion load   | 93%                                    |                      | 0.84              |           |
| Petronella Anbeek (MICCAI) 2008 [17] | T1 and FLAIR                 | MS Lesion Segmentation Challenge 2008       | KNN  |  | All Average                            | All UNC              | All CHB           |           |
|                                      |                              |   |  | Sensitivity  | 50.92%                                 | 45.19%               | 55.01%            |           |
|                                      |                              |   |  | Specificity  | 97.39%                                 | 99.70%               | 95.73%            |           |
|                                      |                              |   |  | PPV  | 67.26%                                 | 91.43%               | 49.99%            |           |

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|----------------------------------|----------------|--|--------------------------------|---|------------------|---------------------|----------|
| C. P. Loizou (IEEE) 2011 [10]    | T2             | AyiosTherisos Medical Diagnostic Center  | Support Vector Machine (SVM)   | correct rate = 86%<br>Sensitivity = 79%<br>Specificity= 90%   |                  |                     |          |
| MelikaMal eki (JMPR) 2012 [9]    | FLAIR          | NA   | Multilayer Perceptron (MLP)    |   | Accuracy         | Sens.               | Spec.    |
|                                  |                |  |                                | CNN+MLP   | 92.93%           | 96.12%              | 97.58%   |
|                                  |                |  |                                | GLCM+MLP  | 79.66%           | 84.38%              | 83.95%   |
| Saba Gheshlghi (IJAIA) 2018 [33] | NA             | Laboratory of Health at the University of Cyprus                                     | edge detection + Fuzzy C-means | In this paper first edge detection method for finding edges has been used and then Fuzzy C-means has been applied for increasing diagnostic accuracy. Canny edge detection has a better result. |                  |                     |          |
| RupaliKamathe (JMIP) 2016 [29]   | T2             | MS lesion segmentation challenge 2008, Harvard Medical School data and clinical data | KNN, SVM and Adaboost          | Accuracy (%)  |                  |                     |          |
|                                  |                |  |                                | Classes   | KNN              | SVM                 | Adaboost |
|                                  |                |  |                                | MS and Normal   | 98.25 (k-fold=9) | 100 (Linear Kernel) | 100      |
| MS and Tumor                     | 100 (k-fold=5) | 100 (Polynomial order =5)  | 100                            |   |                  |                     |          |

SI=Similarity Index, OF= Overlap Fraction, EF=Extra Fraction, DSC=Dice Similarity Coefficient, VD= volume difference, DC= surface distance, PPV=Positive Predictive Value, FDR=False Discovery Rate, TP=True Positive, FP=False Positive, FN=False Negative, ICC = Intra-Class Coefficient, DER=Detection Error Ratio, OER= Outline Error Ratio, NA= Not Available, MRF =Markov random field, THAT-CRF= Temporal Hierarchical Adaptive Texture-Conditional Random Field, LDALinear Discriminant analysis, PCA=Principal Components Analysis, sens.=Sensitivity, spec.= Specificity

### III. FEATURE EXTRACTION

One of the most common problems of pattern recognition in medical image analysis is the classification of a set of features into the proper class. Feature extraction and selection are important steps in brain MS detection and classification. An optimum feature set should have effective and discriminating features, whereas largely reduce the redundancy of feature space to avoid 'curse of dimensionality' problem. A key stage of classification by CAD schemes is feature analysis and extraction. The transformation of an image into its set of features is known as feature extraction. Useful features of the image are extracted from the image for classification purpose. It is a challenging task to extract good feature set for classification. Principal Components Analysis (PCA), Linear Discriminant analysis (LDA) and Independent Components Analysis (ICA) are used to reduce the dimension of data. The integration between the feature extraction and the feature reduction algorithms led to developing a CAD technique which is capable of classifying human brain with clinically acceptable accuracy using less number of features that can be extracted with less computational cost [27]. J. Dehmeshki et al. [26] used two data reduction schemes LDA and PCA. LDA is good for the classification of MTR histograms because it takes into consideration the between class variation. By using LDA, the space of MTR histograms is transformed to the optimal discriminant space for a nearest mean classifier. In contrast, PCA is useful for correlation with current disability as it takes into consideration the variation within each subgroup in its process.

Independent on the segmentation technique, the brain MRI voxels are represented by set of features. Good features are those which are most discriminative between the normal brain tissues and MS lesions tissues. The features commonly used in the literature techniques may be categorized into intensity [1, 2, 11, 17, 21, 23], spatial [17], neighborhood [14,

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11], shape [14], size [2, 11], texture [5, 7, 29], atlas based priors [14] and context defined [2, 3, 12] features. Most of the techniques are using combination of features from the different categories [32].

## IV. SEGMENTATION AND CLASSIFICATION

### A. Segmentation:

The principal goal of the segmentation process is to partition an image into regions (also called classes or subsets) that are homogeneous with respect to one or more characteristics or features. In medical imaging, segmentation is important for feature extraction, image measurements, and image display. In some applications it may be useful to classify image pixels into anatomical regions, such as bones, muscles, and blood vessels, while in others into pathological regions, such as cancer, tissue deformities, and multiple sclerosis lesions. A wide variety of segmentation techniques have been proposed shown in table 1. However, there is no one standard segmentation technique that can produce satisfactory results for all imaging applications [31]. Automatic segmentation of abnormal brain structures, and particularly MS lesions, is difficult. Abnormal structures exhibit extreme variability. Their shapes are deformable, their location across patients may differ significantly, and their intensity and texture characteristics may vary. Existing systems commonly approach this problem by applying classification algorithms that rely on a voxel-by-voxel analysis, utilizing primarily image intensities and atlas probability values [14]. There are many proposed approaches [1, 2, 6, 8, 11, 15, 16, 18, 21, 24] for segmentation of brain into different tissues, including MS lesions.

### B. Classification:

Classification is the technique for classifying the input patterns into analogous classes. Selection of a suitable classifier requires consideration of many factors: (a) classification accuracy, (b) algorithm performance, (c) computational resources [27]. For the MS Segmentation, any of the pattern recognition algorithms is adapted to fit the binary classification of the voxels into two classes: voxel which is part of MS lesion and non-MS voxel. The pattern recognition technique is used to perform training with the training data sets' voxels labelled by the experts to get a discriminative model. The pattern recognition algorithm is again used by the model to perform the binary classification of the testing data sets' voxels [32]. Table 1 shows a survey on the classification techniques for brain MRI.

C. P. Loizou et al. [10], suggest that AM-FM method characteristics succeed in differentiating 1) between NWM and lesions; 2) between NAWM and lesions; and 3) between NWM and NAWM. A SVM classifier succeeded in differentiating between patients that, two years after the initial MRI scan, acquired an Expanded Disability Status Scale (EDSS)  $\leq 2$  from those with EDSS  $> 2$ . The best classification results were obtained from including the combination of the features: low-scale IA and IF magnitude with the medium-scale IA. J. Dehmeshki et al. [26] presents a new approach to characterize subtle diffuse changes in MS using histograms derived from Magnetization Transfer Ratio (MTR) images. Two major parts dominate our histogram analysis; 1) Classification of MTR histograms into control and MS subgroups; 2) Correlation with current disability, as measured by the EDSS scale. MelikaMaleki et al. [9] presents hybrid method uses CNN for features extraction and a multilayer neural network for classification into two classes normal and MS. CNN due to lack of sensitivity to noise is good for performance diagnosis. The result shows that CNN provides high detection rates without using any lesion segmentation. R. Kamathe et al. [29] developed CAD system is giving 100% accuracy for all three learning algorithms; with SVM outperforming the K-NN and Ada-boost.

## V. EVALUATION AND VALIDATION

The validity of MS lesions segmentation is an important issue in medical image analysis. Calculating the overlap with the ground truth has become the most common way to quantitatively evaluate segmentation results. In the field of MS segmentation, the Similarity Index (SI) and the Dice Similarity Coefficient (DSC) are the most commonly used evaluation standards. They can range from 0 to 1 with 0 indicating no overlap and 1 indicating perfect overlap. Other different metrics are used to evaluate the performance for detection of MS such as accuracy, sensitivity, specificity, Extra Fraction (EF) and positive predictive value (PPV). Besides, the automated evaluation system used by the MS

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Lesion Challenge uses the volume difference (Volume diff.), average distance (Avg. Dist.), true positive rate (True Pos.) and false positive rate (False Pos.) to evaluate the segmentation.

The majority of researchers validated their algorithms on a limited number of cases from their own data due to the lack of MS database with ground-truth segmentations that is available to a broad community of clinicians and researchers. This makes it difficult to compare the performance of different methods against each other in a standard way. Therefore, the accuracy, validity, and robustness of the individual methods cannot be directly compared with each other because the different metrics were used. Until recently, a synthetic data was presented to realize a purpose of consistent comparison, but so far only few groups tested their methods on these images.

## VI. CONCLUSION

With the advance of computational intelligence and machine learning techniques, computer-aided detection attracts more attention for MS detection. It has become one of the major research subjects in medical imaging and diagnostic radiology. Early detection of the MS is very important and the motivation for further studies. Therefore our research is based on the different segmentation and classification algorithms for detection of MS in brain MRI. However, the performance of most of the algorithms still falls far below expert expectations. The review reveals the CAD systems of human brain MRI images are still an open problem.

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