Neural Network-Based Learning Kernel for Automatic Segmentation of Multiple Sclerosis Lesions on Magnetic Resonance Images

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ABSTRACT

Background: Multiple Sclerosis (MS) is a degenerative disease of central nervous system. MS patients have some dead tissues in their brains called MS lesions. MRI is an imaging technique sensitive to soft tissues such as brain that shows MS lesions as hyper-intense or hypo-intense signals. Since manual segmentation of these lesions is a laborious and time consuming task, automatic segmentation is a need.

Materials and Methods: In order to segment MS lesions, a method based on learning kernels has been proposed. The proposed method has three main steps namely; pre-processing, sub-region extraction and segmentation. The segmentation is performed by a kernel. This kernel is trained using a modified version of a special type of Artificial Neural Networks (ANN) called Massive Training ANN (MTANN). The kernel incorporates surrounding pixel information as features for classification of middle pixel of kernel. The materials of this study include a part of MICCAI 2008 MS lesion segmentation grand challenge data-set.

Results: Both qualitative and quantitative results show promising results. Similarity index of 70 percent in some cases is considered convincing. These results are obtained from information of only one MRI channel rather than multi-channel MRIs.

Conclusion: This study shows the potential of surrounding pixel information to be incorporated in segmentation by learning kernels. The performance of proposed method will be improved using a special pre-processing pipeline and also a post-processing step for reducing false positives/negatives. An important advantage of proposed model is that it uses just FLAIR MRI that reduces computational time and brings comfort to patients.

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Introduction

Multiple Sclerosis (MS) is a degenerative disease of Central Nervous System (CNS) such as brain and spinal cord. MS causes problems including vision, coordination and body weakness. MS patients have some dead tissues in their brain and spinal cord called MS lesions. Accurate measurement of number and volume of these lesions is important for both diagnostic and clinical trials. Magnetic Resonance Imaging (MRI) is a medical imaging technique sensitive to soft

tissues like brain and spinal cord. As Figure 1 shows, different normal and dead tissues are captured with different intensities in different MRI modalities. Since manual segmentation of MS lesions is time consuming, error prone and cumbersome, automatic segmentation of these lesions is preferred.

Automatic segmentation of MS lesions is a complex task. This complexity threatens the accuracy of automatic segmentation methods. The first source of complexity is inherent characteristics of MS lesions so that MS lesions appear with different shapes in different regions of brain. They also do not share a common intensity and texture characteristics. Partial Volume (PV) Effect that causes some pixels to have properties of more than one tissue type, is another reason for complexity of MS lesion segmentation. Image artifacts and noises also lead the segmentation techniques to come up with high false positive/negative rates.

As it is illustrated in Figure 2, a typical Computer Aided Detection (CAD) system for automatic segmentation of MS lesions has three main phases namely; pre-processing, classification and post- processing. In pre-processing phase, common tasks are inhomogeneity correction, noise reduction and skull striping.

Classification phase distinguishes dead tissues from normal tissues. Classification phase demands feature extraction, feature transformation and normalization. In order to reduce false positive/negatives, a post-processing method is applied on the output of segmentation phase [1].

In order to perform automatic segmentation of MS lesions, numerous methods have been proposed. These methods can be simple such as region growing and thresholding as data-driven techniques or sophisticated and intelligent such as Support Vector Machines [3], K-Means, Decision Tree [4], K-Nearest Neighborhood [5], Artificial Neural Network [6], Bayesian network and other statistical ones [2].

Massive Training Artificial Neural Network (MTANN) is actually a method for training an Artificial Neural Network (ANN) in context of medical imaging. In this training method, overlapped sub-regions of training image are extracted and used as input of ANN. The overlapped sub-region pixel sets are paired with a likelihood distribution map as teacher images. Determining network error by comparing the network output and teacher image leads the network parameters to be set. All output corresponding to sub-regions form a likeli-
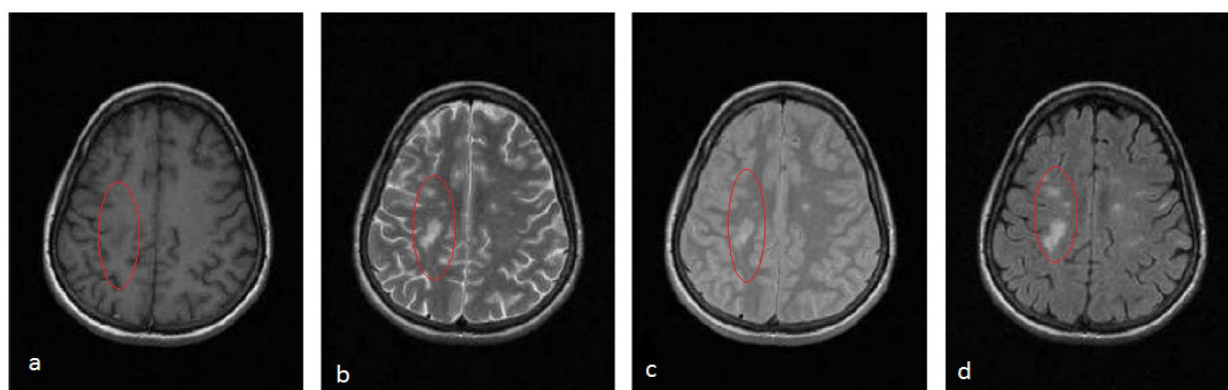
Figure 1: (a) T1-w image, lesions appear as hypo-intense signals; (b) T2-w image, lesions appear as hyper-intense signals; (c) PD-w image, lesions appear as hyper-intense signals; (d) FLAIR image, lesions appear as hyper-intense signals.
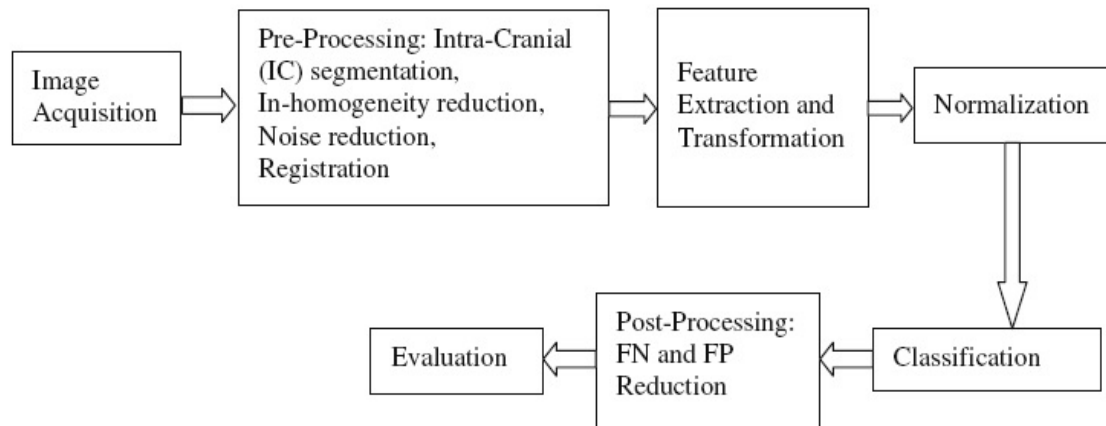
Figure 2: General framework of a typical CAD system for MS lesion segmentation [2].

hood distribution map that could determine abnormalities [7-10]. MTANN was broadly applied on lung and colon Computed Tomography (CT) images for detecting abnormalities such as nodules. The reason for using the term massive training is that ANN can be trained using small number of images with a lot of overlapped sub-regions. A modified MTANN will be used for training a kernel as core component of segmentation phase in the proposed method.

In this paper, a method for automatic segmentation of MS lesions based on learning kernels that incorporates surrounding pixel information is proposed. In the next section, materials and methods are discussed. Results section will show the qualitative and quantitative results. And finally, the results are discussed in the discussion section.

Material And Methods

In this section, materials and methods of the research will be explained. This method is a pixel- based segmentation method which tries to segment MS lesions as accurately as possible by incorporating surrounding pixel information. In this method, the task of extract-

ing features is delivered to a trained Artificial Neural Network (ANN). Unlike the majority of current methods that combine different MRI modalities to increase accuracy, in this method only FLAIR MRI is used. Sole use of FLAIR modalities increases patient's comfort and reduces processing time required for segmentation.

The data-set which is used in this study is a part of MICCAI Grand Challenge 2008 dataset. It is the largest publicly available data-set in the area of MS lesion segmentation. Although there are T1, T2, FLAIR, FA and MD images for each dataset, only the FLAIR modalities will be used. All cases come up with their corresponding ground truth created by the expert. The ground truth is used for evaluation purposes. Each MRI volume is sampled to fit isotropic $0.5 \times 0.5 \times 0.5$ resolution.

In order to automatically segment MS lesions, a method based on Massive Training Artificial Neural Network is proposed. Input of the proposed method is a raw FLAIR MRI image and its output is a lesion mask from which lesion load including number and volume of lesions can be computed. As figure 3 shows, the proposed method has three main
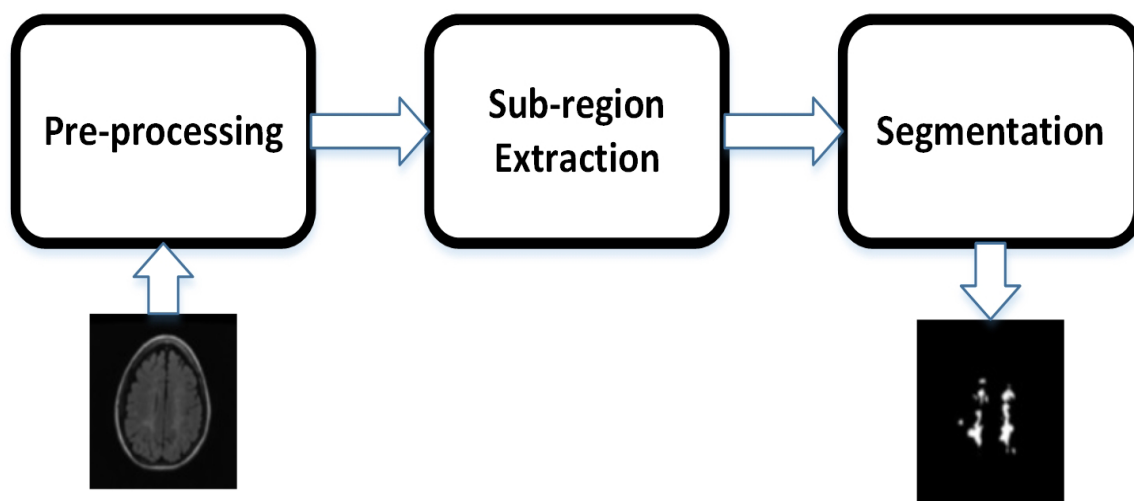
Figure 3: Main steps of proposed segmentation method.

steps namely; Pre-processing, Sub-region Extraction and Segmentation.

The goal of pre-processing step is to prepare images for precise segmentation. This step undertakes three tasks namely; Brain Tissue Extraction [11], Intensity Inhomogeneity/Bias Correction [12] and Intensity Range Modification which have been done using conventional methods. Existence of non-brain tissues changes the statistics of normal brain tissues and also lesions, brain tissue extraction is

**Figure 4:** Process of overlapped sub-region extraction [6].

needed to remove non-brain tissues from raw images. Inhomogeneities on the magnetic field cause a smooth inhomogeneity field across MRIs. These artifacts are also known as bias field and could be corrected using different techniques to increase the accuracy of segmentation. The aim of intensity range modification is to modify the intensity range of test images, the same as training images to make the segmentation of different image sets from different acquisition devices possible.
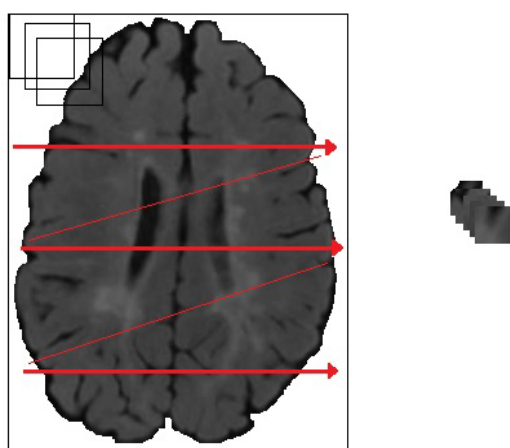
The purpose of sub-region extraction step is to extract overlapped sub-regions of MRI image. In order to extract overlapped sub-regions, a local kernel is moving across the image. Size of the local square kernel must be odd such as 13×13, 15×15, 17×17, 19×19 and so forth. The reason for choosing odd size sub-region is that these sub-regions are passed to the next step to decide whether their middle pixel belongs to lesion class or not. Figure 4 shows this process and the arrows in the figure show the movement of local window for extracting sub-regions.

In the segmentation step, the middle pixel of each sub-region is judged to be lesion or not thanks to trained kernel. After the application
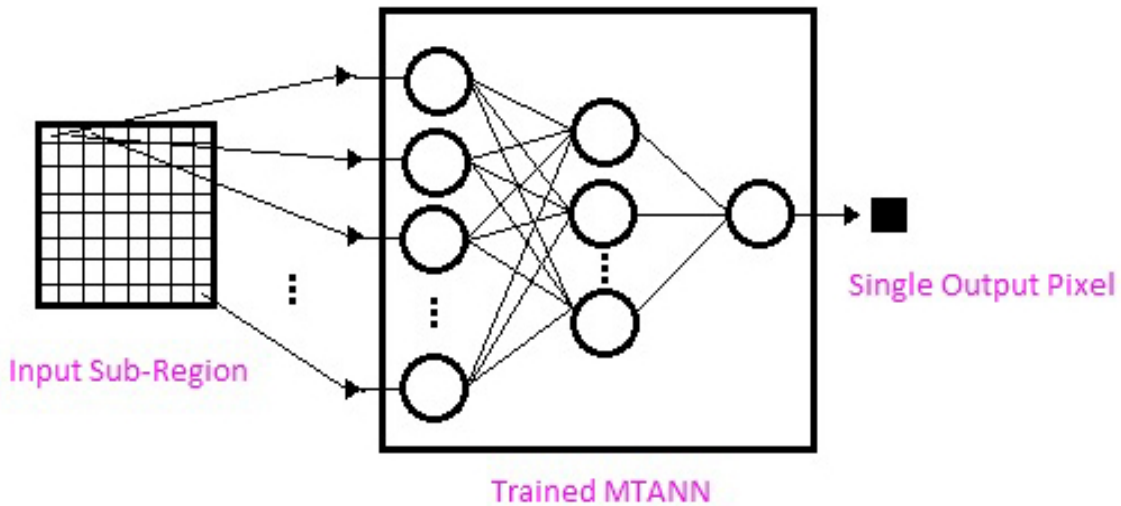
Figure 5: Architecture of Massive Training Artificial Neural Network (MTANN) for MS lesion segmentation [6].

of trained kernel on all of the overlapped sub-region final lesion mask is created. Main burden of segmentation is carried out by segmentation kernel which is actually a MTANN. As figure 5 shows, the architecture of our modified MTANN, it is a multi-layer ANN with one binary output cell. If the value of output cell is 1, the middle pixel of sub-region is considered as lesion otherwise it is considered as normal brain tissue. MTANN (kernel) is trained by manually segmented images. The training set consists of pairs of (X, y) that X belongs to a pixel set coming from a sub-region and y that belongs to {0, 1}; y shows whether middle pixel of sub-region have abnormal structure or not. In this method, a single pixel is judged using its intensity and support of its surrounding pixels. The responsibility of MTANN is to learn the features hid in the surrounding pixels and make decision based on learned features for new cases.

Results

The proposed method has been implemented

(a)   (b)   (c)

Figure 6: Segmentation results (a) FLAIR MRI Slice; (b) GT; (c) Automatic Segmentation.

Table 1: Different performance measure metrics for evaluation of MS lesion segmentation techniques and methods.

Metric	Definition	Unit	Best Value	Worst Value
Sensitivity; Overlap Function (OF); True Positive Rate (TPR)	TP/(TP+FN)	%	100	0
Specificity; True Negative Rate (TNR)	TN/(TN+FP)	%	100	0
False Positive Rate (FPR)	FP/(FP+TN)	%	0	100
False Negative Rate (FNR); Under Estimation Fraction (UEF)	FN/(FN+TN)	%	0	100
Similarity Index (SI); Percentage agreement Dice Similarity Coefficient (DSC)	2TP/(2TP+FN+FP)	%	100	0

Table 2: Quantitative Results of 8 Cases.

Test Case	Sensitivity	Specificity	FPR	FNR	SI
Case 1	0.890	0.993	0.006	0.001	0.727
Case 2	0.929	0.980	0.011	2.670	0.379
Case 3	0.810	0.993	0.006	7.310	0.470
Case 4	0.920	0.990	0.005	2.460	0.510
Case 5	0.990	0.980	0.010	1.540	0.300
Case 6	0.282	0.997	0.002	0.005	0.363
Case 7	0.670	0.990	0.001	0.001	0.643
Case 8	0.721	0.996	0.003	0.002	0.694
Average	0.776	0.989	0.005	1.725	0.510

and applied on 8 cases of previously mentioned data-set. The results of experiment have been captured both qualitatively and quantitatively. Purpose of qualitative analysis is to determine how much automatic lesion mask is close to the ground truth. The ground truth is created by a trained human expert. As Figure 6 shows, the quality of segmentation is near Ground Truth and very promising.

In order to quantify the performance of the proposed method, some performance measure metrics such as True Positive Rate (TPR)/Sensitivity, False Positive Rate (FPR), True Negative Rate (TNR)/Specificity, False Negative Rate (FNR) and similarity are calculated. Table 1 lists the associated definition for each of the mentioned metrics and also their alternate names. The mentioned metrics have been calculated for each case individually and summarized in Table 2. As reported by literature, the similarly index above 70 percent for a method is considered a convenient segmentation method. The similarity measure of proposed method for some cases are around 70 percent.

The average true positive rate (sensitivity) is high which shows most of the lesion pixels are segmented.

Discussion

In this paper, a method for automatic segmentation of MS lesions based on learning kernels has been proposed. Learning kernels incorporate surrounding pixel information as features for classification. These features are extracted by middle layer of ANN. The average true positive rate is high which shows most of the lesion pixels are segmented. Kernel size directly affects the true positive rate and also other metrics. So, a proper kernel size must be set to make tradeoff between sensitivity and specificity.

This study shows the potential of surrounding pixel information to be incorporated in segmentation by learning kernels. Although the results can be considered convenient, the performance of proposed method will be improved by using a special pre-processing pipeline and also a post-processing step for reducing false positives/negatives. Pre-processing and post-processing have direct effects on the accuracy of segmentation. In general, when the gray level variation between lesion voxels and normal voxels is high, the segmentation accuracy will also be high. Maximizing this gray variation increases the accuracy of segmentation. An important advantage of proposed model is that it uses just FLAIR MRI that reduces computational time and brings comfort to patients.

Conflict of Interest

None

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