Development of CAD System Based on Enhanced Clustering Based Segmentation Algorithm for Detection of Masses in Breast DCE-MRI

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Abstract

Breast cancer continues to be a significant public health problem in the world. Early detection is the key for improving breast cancer prognosis. Mammography is currently the primary method of early detection. But recent research has shown that many cases missed by mammography can be detected in Breast DCE-MRI. Magnetic Resonance (MR) imaging is emerging as the most sensitive modality that is currently available for the detection of primary or recurrent breast cancer. Breast DCE-MRI is more effective than mammography, because it generates much more data. Magnetic resonance imaging (MRI) is emerging as a powerful tool for the diagnosis of breast abnormalities. Computer Aided Detection (CAD) is of great help to this situation and image segmentation is most important process of computer Aided Detection, Magnetic Resonance Imaging data are a major challenge to any image processing software because of the huge amount of image voxels. Automatic approaches to breast cancer detection can help radiologists in this hard task and speed up the inspection process. To segment the mass of the breast region from 3D MRI set, a multistage image processing procedure was proposed. Data acquisition, processing and visualization techniques facilitate diagnosis. Image segmentation is an established necessity for an improved analysis of Magnetic Resonance (MR) images. Segmentation from MR images may aid in tumor treatment by tracking the progress of tumor growth and shrinkage. The advantages of Magnetic Resonance Imaging are that the spatial resolution is high and provides detailed images. The tumor segmentation in Breast MRI image is difficult due to the complicated galactophore structure. The work in this paper attempts to accurately segment the abnormal breast mass in DCE-MRI Images. The mass is segmented using a novel clustering algorithm based on unsupervised segmentation, through neural network techniques, of an optimized space in which to perform clustering. The effectiveness of the proposed technique is determined by the extent to which potential abnormalities can be extracted from corresponding breast MRI based on its analysis, this algorithm also proposes changes that could reduce this error, and help to give good results all around. Tests performed on both real and simulated MR images shows good result.

Keywords: *Image Voxels, Neural Networks, Clustering, Thresholding, Image Segmentation, Mass Detection.*

1. Introduction

Breast cancer happens to over 8% women during their lifetime, and is the leading cause of death of women [6]. Currently the most effective method for early detection and screening of breast cancers is MRI [7]. Microcalcifications and masses are two important early signs of the diseases [15]. It is more difficult to detect masses than microcalcifications because their features can be obscured or similar to normal breast parenchyma. Masses are quite subtle and often occurred in the dense areas of the breast tissue, have smoother boundaries than microcalcifications and have many shapes such as circumscribed, speculated (or stellate), lobulated or ill-defined. The circumscribed ones usually have a distinct boundaries, 2–30mm in diameters and are high-density radiopaque; the speculated ones have rough, star-shaped boundaries; and the lobulated ones have irregular shapes [8]. Masses must be classified as benign and malignant in order to improve the biopsy yield ratio. Generally speaking, masses with radiopaque and more irregular shapes are usually malignant, and those combined with radiolucent shapes are benign [14]. A DCE-MRI is basically distinct with four levels of the intensities: background, fat tissue, breast parenchyma and calcifications with increasing intensity. Masses develop from the epithelial and connective tissues of breasts and their densities on MRI's blend with parenchyma patterns. Several studies have revealed a positive association of tissue type with breast cancer risks [9, 10]. Women who have breast cancers can easily get ontralateral cancers in the other side breast [11, 12]. Distinguishing a new primary from metastasis was not always possible due to their similar features. Asymmetry of breast parenchyma between the two sides has been one of the most useful signs for detecting primary breast cancer [13].

Segmentation of medical images is a challenging and complex task. Medical image segmentation has been an active research area for a long time. There are many segmentation algorithms [28, 29, 30] but there is not a generic algorithm for totally successful segmentation of medical images. The Segmentation of images holds an important position in the area of image processing. It becomes more important while typically dealing with medical images where pre-surgery and post-surgery decisions are required for the purpose of initiating and speeding up the recovery process. Computer aided detection of abnormal growth of tissues is primarily motivated by the necessity of achieving maximum possible accuracy [5]. Manual segmentation of these abnormal tissues cannot be compared with modern day's high speed computing machines which enable us to visually observe the volume and location of unwanted tissues. In the proposed method the acquired DCE-MRI Image of the breast will be processed in 4 different stages,

1. Pre processing
2. Clustering
3. Edge enhancement
4. Extraction of mass.

The proposed algorithm effectively segments the mass region more accurately with high efficiency. The paper is organized as follows: Section 2, materials and methods are described; the proposed methodology explained in section 3 while results are reported in Section 4. Conclusions and possible further developments are illustrated in Section 5

2. Materials and methods

This paper presents the visual and statistical results of applying CAD System Based on Enhanced Clustering Based Segmentation Algorithm for Detection of Masses in Breast DCE-MRI over the simulated and real images of breast DCE-MRI images. Images used in this study were acquired with patients prone to 1.5T scanner with use of a dedicated surface breast coil array. The imaging protocol included bilateral fat suppressed T weighted images in the sagittal plane of 1mm slice thickness and a slab interleaved 3D fat suppressed spoiled gradient echo after the injection of contrast. One slice can contain 512×512 pixels.

2.1 Medical Imaging

The medical research has been quite receptive of image processing in applications like X-ray, Computer Aided Tomography, Ultrasound and Magnetic Resonance. The output of these techniques, an image of the patient's body, allows the physician to examine and diagnose without the need of surgery. Traditional imaging modalities, like X-Ray mammography, do not provide certain and reliable results on young women or in women who underwent surgical interventions. Three-dimensional breast MRI has proven to be a valuable tool for disambiguate uncertain mammographic findings and for the pre-operative planning. DCE-MRI has a statistically significant ability to diagnose malignancy in suspicious breast lesions detected using other diagnostic modalities. The sensitivity of breast MRI is relatively high (false negative rate is low). The reported specificities of MR have been variable ranging from 50% to 80.8%, and the sensitivity of MR will be 94.2% for even dense breast [35].

In recent years, Magnetic resonance imaging (MRI) of the breast has been increasingly used in the diagnosis of radiographically dense breasts, assessment of disease extent in the patient with newly diagnosed breast cancer, problem-solving applications for difficult diagnostic evaluations, for difficult diagnostic evaluations, for screening high risk women for early cancer detection, and on monitoring response to therapy. Magnetic Resonance Imaging is the most attractive alternative to Mammography. In order to be effective, breast MRI requires the use of a paramagnetic contrast agent. When used in combination with the contrast agent, the examination is called Dynamic-contrast-enhanced - MRI (DCE-MRI). The contrast-agent has no contraindications and is tolerated better than the radiations absorbed during a single mammography [42].

DCE-MRI is sensitive for detecting some cancers which could be missed by mammography. In addition, DCE-MRI can help radiologists and other specialists determine how to treat breast cancer patients by identifying the stage of the disease. It is highly effective to image breast after breast surgery or radiation therapy. DCE-MRI forms 3D uncompressed image. It can perform with all women including who are not suitable for mammography, such as young women with dense breast and women with silicone-filled breast implants. Since it uses magnetic fields, DCE-MRI has no harmful effects on human bodies. However, DCE- MRI takes rather long time to perform and has high cost which is more than ten times greater than mammography. Its low resolution limits its application to very small lesions or micro calcifications.

The promising potential of MRI in diagnosis of breast cancer, as a complementary modality to X-ray mammography, has been well recognized [1, 2, 3]. Despite its well-recognized utilities, however, the technique has not been introduced to routine clinical breast imaging. One of the most important obstacles has been the lack of standardization in terms of interpretation guidelines [2, 4]. The reproducibility, effectiveness and relative significance of interpretation criteria in the literature are far from being well evaluated. The purpose of the proposed research is to develop computerized methods to take full advantage of the wealth information that MRI offers to improve methods for the diagnosis and interpretation of breast MR images. The research involved investigation of automatic methods for image artifacts correction and tumor segmentation. Our hypothesis was that investigation of advanced image analysis algorithms would improve the performance of existing conventional methods in the task of detecting the tumors in the breast MR Images.

2.2 Image processing tools

Segmentation is a fundamental tool which aids in identification and quantitative evaluation. It conditions the quality of analysis. Computer based segmentation has reminded largely an experimental work many efforts have exploited MRI's multi-dimensional data capability through multi-spectral analysis. Segmentation as defined by Kapur [16] is "a labeling problem in which the goal is to assign to each voxel in an input gray-level image, a unique label that represents an anatomical structure". Many approaches to MRI segmentation both supervised and unsupervised have been proposed in literature [17, 22, 24, 25, 29]. Among the unsupervised segmentation techniques, the K-means algorithm is applied. Self-organizing feature maps (SOM) in a hierarchical manner is developed, with this approach using a certain degree of supervision. An acceptable classification is obtained when applied to test images.

In particular, Neural Networks try to simulate a structure similar to the one that is believed the human brain has. Two dimensional layers of cellular modules that are densely interconnected between them model most neural networks in the brain, especially in the cortex [28]. This area of the brain is organized into several sensory modalities such as speech or hearing. The engineering approach of neural networks develops hardware or software inspired by the brain's structure [27].

Neural network attracted more and more researchers for its abilities of parallel operation, self-learning, fault tolerance, associative memory, multifactorial optimization and extensibility [26]. Neural network based clustering has yielded good results [18, 19], yet the possibility of transforming the input space in order to facilitate segmentation has been largely unexplored [34]. This paper proposes a new unsupervised algorithm for MR image segmentation is implemented. In this method, classical Kohonen map-based clustering is enhanced through the search of an optimized space in which to operate the clustering [32, 33]. It allows for the ability to make the clustering methods able to retain more information from the original image than the crisp or hard segmentation methods [31].

3. Implementation of the proposed algorithm

The framework of the present work is the development of a novel algorithm acting as a support to the diagnosis process for those affections that require medical imaging. Such tools present to the clinician both a qualitative and a quantitative description of the disease. In this proposed algorithm each input is the image dataset, which undergoes a number of sequential processing steps: preprocessing, clustering, error back propagation, classification, enhancing edges of classification output and segmenting region of interest as shown in figure 1. Magnetic resonance imaging is a tomography technique, i.e. each image comprises of a number of slices, each corresponding to a given slice of tissue; following the pulse repetition period (TR) and parameters related to the applied radio-frequency magnetic field. It is possible to obtain images with different contrast, each reflecting a different parameter regulating the relaxation of the excited tissues. After the clustering process, each cluster is manually interpreted and assigned to a proper tissue class.

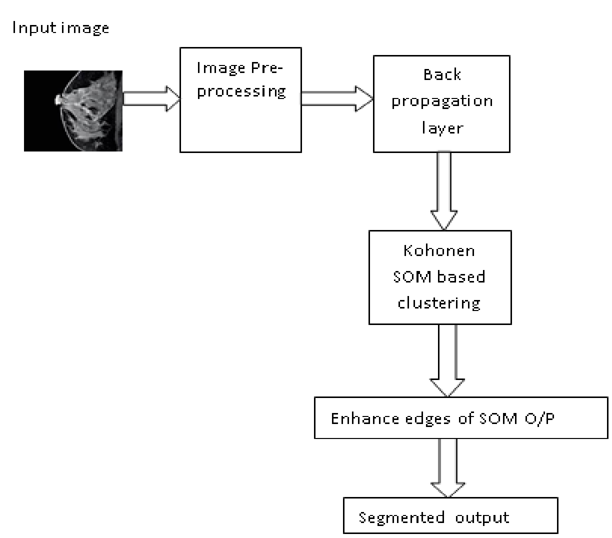

Fig. 1 Segmentation Process

3.1 Preprocessing

In segmenting DCE-MRI data, three main difficulties are considered namely: noise, partial volume effects (where more than one tissue is inside a voxel volume) and intensity in-homogeneity [30]. The majority of intensity in-homogeneities are caused by the irregularities of the scanner magnetic fields–static (B0), radio-frequency (B1) and gradient fields, which produce spatial changes in tissue static. Partial volume effects occur where multiple tissues contribute to a single voxel, making the distinction between tissues along boundaries more difficult. Noise in MR images can induce segmentation regions to become disconnection.
An important part of any image processing system is represented by the pre-processing phase. This phase could imply contrast enhancement techniques or methods for removing the noise. Preprocessing aims at improving the quality of each input image and reducing the computational burden for subsequent analysis steps, Each input voxel is formed as a feature vector as described by the preprocessing technique proposed in [30, 37]. This aims at compensating the effects of random noise, while minimizing the loss of resolution.

All feature vectors are normalized prior to segmentation by subtracting the mean and dividing by the standard deviation, where the mean and standard deviation are estimated independently for each slice.

3.2 Clustering

Clustering is a technique for finding similarity groups in data, called clusters. i.e., it groups data instances that are similar to (near) each other in one cluster and data instances that are very different (far away) from each other into different clusters. Clustering is often called an unsupervised learning task as no class values denoting an apriori grouping of the data instances are given, which is the case in supervised learning [33]. Unsupervised methods, on the other hand, do not require any human interference and can segment the breast with high precision. For this reason, unsupervised methods are preferred over conventional methods. Many unsupervised methods such as Fuzzy c-means, Self-Organizing map, etc. exist but Kohonen's Competitive Learning Algorithms yields good results [32, 34, 37].

The proposed network architecture consists of two fully interconnected layers; the first layer, composed of computing elements of order zero with linear activation function, followed by a second layer of computing elements of order two, with gaussian activation function. Let X be the input pattern, H the output of the hidden layer and Y the output of the network. W and Z are the weight vectors of the first and second layer, respectively. In order to jointly optimize both layers, training is carried out in two steps. In the first step, the second layer is trained using the standard Kohonen rule for unsupervised learning at each iteration, the winning neuron's centers are adjusted according to equation 1Footnotes should be typed in singled-line spacing at the bottom of the page and column where it is cited. Footnotes should be rare

$$\Delta Z_{ji} = \eta_z.(H_i - Z_{ji}) \tag{1}$$

Where

ΔZ_{ji} = Change in weight vector

η_z = learning rate of the Kohonen layer

H_i = Out put of the ith neuron of the hidden layer

Z_{ji} = The weight vector of the Winning neuron

The weights of the neighboring neurons are updated according to equation 2

$$\Delta Z_{ji} = \eta_z.f_{neigh}(H_i - Z_{ji}) \tag{2}$$

Where

f_{neigh} = Gaussian activation function

Contrarily to the second layer, the first layer is trained using Enhanced version of error back-propagation with the linear activation function, search of feature space. In supervised learning schemes, the error is given by.

$$E = \sum_P \left\| Y^P - T^P \right\|^2 \tag{3}$$

Where $\mathbf{T^P}$ is the user-supplied target associated to the $\mathbf{P^{th}}$ training pattern. Here the target is determined by associating each input pattern with the winning neuron. Intuitively, this corresponds to searching a linear transformation of the feature space, requiring that input patterns be as close as possible to the associated centroids. The hidden layer is then trained using the classical delta rule for training and is derived from equation (3)

$$\frac{\partial E}{\partial W_{li}} = \sum_{p} \eta_p \sum_{j} (\delta_j^{lp} . x_i^p) \qquad (4)$$

Where p denotes the p[th] input pattern and

$$\delta_j^{lp} = y_j^p - t_j^p$$

.

The weights of the first layer are then updated according to equation 5

$$\Delta W_{ij}(t+1) = -\eta_w . \frac{\partial E}{\partial W_{ij}} + \mu \Delta W_{ij}(t) \qquad (5)$$

$$\Delta W_{ij}(t) = \eta_w \delta_p H_j$$

Where

μ = momentum factor

η_w = learning rate of the Back propagation layer

The momentum term introduces the old weight change as a parameter for the computation of the new weight change. This avoids oscillation problems common with the regular back propagation algorithm when the error surface has a very narrow minimum area. Momentum allows the net to make reasonably large weight adjustments as long as the corrections are in the same general direction for several patterns. Using smaller learning rate prevents a large response to the error from any training pattern.

The first layer consists of 5computing elements with linear activation function. Thus, not only the hidden layer performs a linear transformation of the input space, but it also reduces the dimensionality of the feature space. This allows obtaining, in average, better experimental results than when all features are retained in the clustering step. The second layer has 5 computing elements. Five clusters are sufficient to discriminate between adipose tissue, glandular tissue, ducts, benign and malignant masses.

The network is separately trained for each image to account for inhomogeneities in intensity across different images by randomly selecting pixels per image as the training set. A Gaussian neighborhood function f_{neigh} is used for unsupervised training. An adaptive learning coefficient is initially selected for the first layer as η_w and for the second one as η_z. If the error increases, η is decreased and weight values are set to those of the previous iteration, whereas if the error decreases below a predefined threshold, η is increased. Finally, training is stopped when a predetermined level of error is reached.

3.3 Edge Enhancement

Digital image enhancement techniques are concerned with improving the quality of the digital image. The principal objective of enhancement techniques is to produce an image which is better and more suitable than the original image for a specific application. This process detects boundaries between objects and background in the image.

Many characteristics are used to segment an image into regions e.g. colour, brightness, texture and edge detection. Usually, the obtained edges need some additional improvement for the satisfactory segmentation. Linear filters have been used to solve many image enhancement problems. The unsharp filter is a simple sharpening operator which derives its name from the fact that it enhances edges through a procedure which subtracts an unsharp, or smoothed, version of an image from the original image. The unsharp filtering technique is commonly used in the photographic and printing industries for crispening edges.

Unsharp masking produces an edge image $g(x, y)$ from an input image $f(x, y)$ via

$$g(x, y) = f(x, y) - f_{smooth}(x, y) \qquad (6)$$

where $f_{smooth}(x, y)$ is a smoothed version of $f(x, y)$ as illustrated in Figure 2.

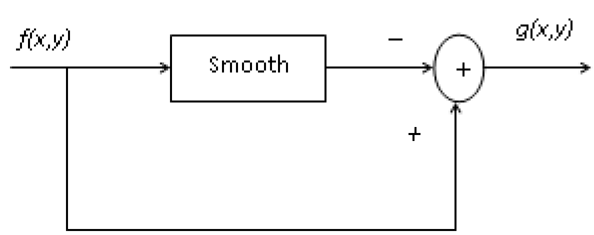

Fig. 2 Unsharp filter

Then the enhanced SOM based k-means clustered output image is then edge enhanced by unsharp filter as illustrated in [43] which is used to extract the edges of the tumour very efficiently in MRI images. The unsharp filter can be implemented using an appropriately defined lowpass filter to produce the smoothed version of an image which is then pixel subtracted from the original image in order to produce a description of image edges, i.e. a high passed image.

3.4 Segmentation

The segmentation used for extraction of masses in MR images is the region based segmentation. In region-based techniques, segmentation of an object is achieved by identifying all pixels that belong to the object based on the intensity of pixels. They are looking for the regions satisfying a given homogeneity criterion. Since in MR images masses mostly have high contrast and ill-defined edges, it is difficult to determine their boundary with edge-based techniques. Region-based techniques are more suitable for MR images since suspicious regions are brighter than the surrounding tissues. There are many region-based techniques such as Region growing [38], Watershed algorithm [39], and Thresholding [40].

In this work utilizes region segmentation based-thresholding. Thresholding is based on the image histogram; or local statistics such as mean value and standard deviation, or the local gradient. When only one threshold is selected for the entire image, based on the image histogram, it is called global thresholding. If the threshold depends on local properties, it called local thresholding. If the thresholds are selected independently for each pixel, it called dynamic or adaptive thresholding. The selection of threshold value is determined by experimenting with various threshold values and the best threshold value has been selected for breast DCE-MRI images. The thresholded image g (x, y) is defined as,

$$g(x,y)=\begin{cases}1 if\ (x,y)>T\\0 if\ (x,y)\le T\end{cases}$$

4. Experimental Results and Discussion

In this section, the results obtained using real and simulated DCE- MR Images are illustrated. Ultimately, the effectiveness of the proposed technique is determined by the extent to which potential abnormalities can be extracted from corresponding breast MRI based on its analysis.

4.1 Testing on Breast DCE- MR Images

The use of simulated images simplifies the task of validating a segmentation method as a reproducible. Moreover, it allows to separately testing the proposed segmentation method stability against intensity inhomogeneities and random noise [31]. But in this paper both real and simulated images are used for segmentation procedure, Since the real images obviously contains the noise induced during the imaging process, when the real image is used for validating the algorithm then we can find how efficiently the algorithm works for the image with noise, so no need to introduce or add noise to simulated image for testing the algorithm efficiency. The reference image is selected. With each cluster is associated with the most probable tissue class using maximum likelihood estimation.

A set of original and simulated breast DCE-MR images representative slice are considered for estimating the validation of the algorithm is shown in figure 3 to figure 7. To evaluate the results, trainings for each reference slice were performed with different random initial conditions for the centers of the neurons in the second layer. It is well-known that the training speed depends on the choice of the learning rate. If the learning rate is small, the learning process is stable but at the expense of computation time [26]. If the learning rate is too large, the estimation of the weights may diverge. Because of fast convergence in using SOM with adaptive learning rate, it can be applied in online applications. The lower learning rate provides better convergence and better quality than higher learning rates.

The abnormal image pairs were used to measure performance. The true positive detection rate and the number of false positive detection rate at various thresholds of the images are used to measure the algorithm's performance. These rates are represented using Receiver Operating Characteristic (ROC) curves. True Positive (TP) and False Positive (FP) rates are calculated at different thresholds selected on image pixels to generate an ROC curve and the best solution has been plotted as illustrated in figure 9. A region extracted in the asymmetry image, which overlaps with a true abnormality as provided in the ground truth of the image, is called a true positive detection. An overlap means that at least 80% of the region extracted lies within the circle indicating a true abnormality as determined using SOM with adaptive learning rate; it can be applied in online applications. The lower learning rate provides better convergence and better quality than higher learning rates as illustrated in [37].

The preliminary results of the proposed algorithm illustrated in figures 3and figure 4 shows a reasonable match between manual division and that of automatic method. In the best case, there is an average difference of only 20-30 pixels. This was not always seen, as in the worst case the difference was as great as 150 pixels. This algorithm also proposes changes that could reduce this error, and help to give good results all around.

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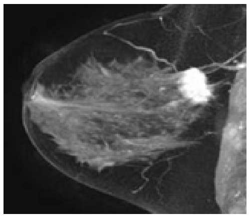
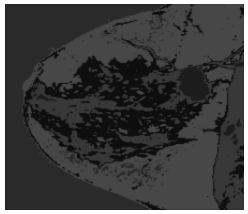
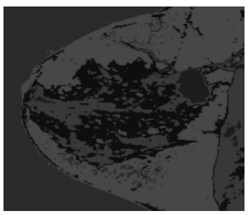


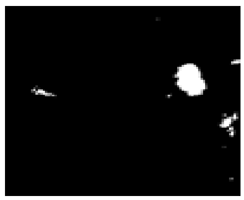
(a) Original image



(b) clustering output

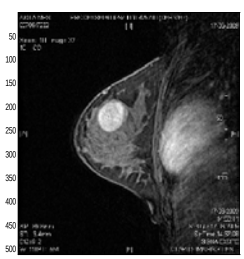


(c) Edge enhanced output

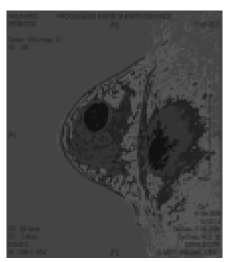


(d) mass segmented separately

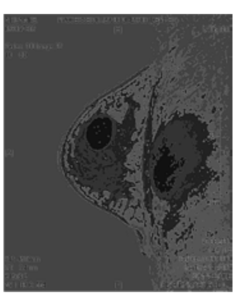
Fig. 3 A representative simulated breast image with mass and the corresponding segmentation of the mass separately



(a) Original image



(b) clustering output



(c) Edge enhanced output

(d) mass segmented separately

Fig. 4 A representative original breast image with tumor obtained from 1.5Telsa MRI and the corresponding segmentation of the mass separately

4.2 Performance evaluation of the algorithm

An objective method is needed to evaluate the performance of the new proposed image segmentation algorithm. The most important performance criterion is accuracy that is the degree to which an algorithm's segmentation matches some reference standard segmentation [36]. A number of similarity coefficients are used to specify how well a given segmentation matches a reference and the performance of the segmentation depends upon the learning rate factor. The performance of clustering output for different learning rate is illustrated in figure 5. In general, it is expected that the true positive detection rate in an ROC curve will continue to increase or remain constant as the number of false positives increase. The figure 6 illustrates the ROC curve performance of the algorithm for good values of the learning rate and the threshold value; if the threshold value is low true detections may become merged with false positive regions. The Table 1 shows the comparison of sensitivity and specificity rates of Breast Cancer using Clinical examination, mammography and MRI for disease diagnosis [35]. Evaluating the results obtained, it's found that the best results obtained when using K-NN classifier especially with using feature vector and enhanced images.

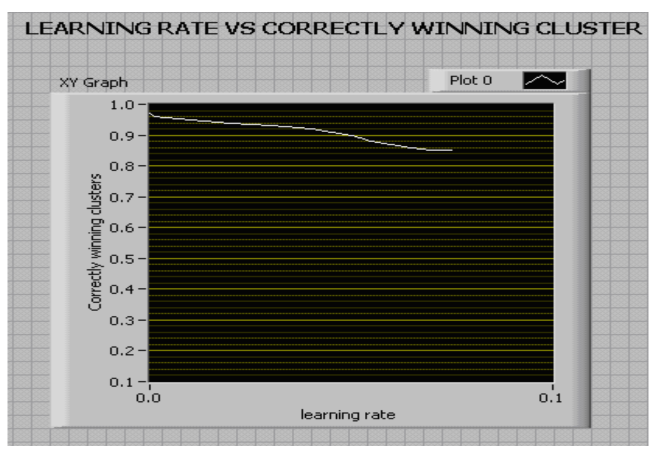


Figure 5 The performance of Clustering results with varying levels of learning rate

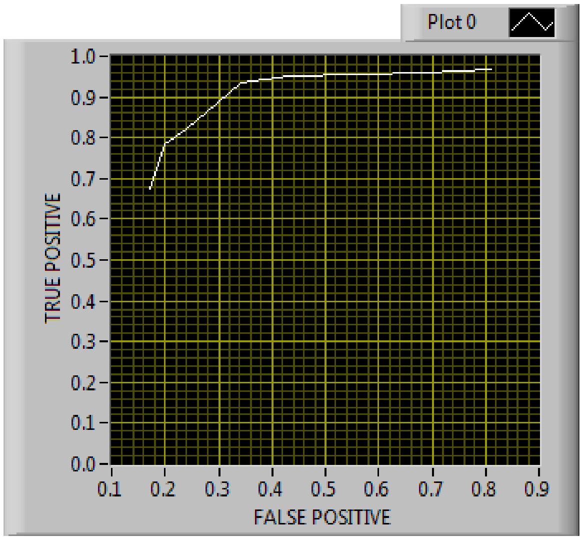


Figure 6 ROC Curve of Proposed Algorithm

5. Conclusions

Breast cancer is one of the major causes of death among women. So early diagnosis through regular screening and timely treatment has been shown to prevent cancer. In this paper we have presented a novel segmentation approach to identify the presence of breast cancer mass in breast DCE-MRI images. The proposed work utilizes the unsupervised clustering capabilities of a Kohonen self-organizing map with a linear transformation of the input space. Enhanced back propagation based Neural network is employed for clear identification of clusters.

The accurate and effective algorithm for segmenting image is very useful in many fields, especially in medical image. The training set originally had large dimension of data matrix, so the program used to reduce the dimension of training set and the new algorithm method is applied to show the ability of the method. A Self-Organizing Map network was programmed to receive images, as input signal regions. For this work, breast MRI images were used and segmentation of tumor is obtained. The proposed technique was evaluated on real and simulated DCE-MR images, showing promising performances from a qualitative point of view. Furthermore, being the proposed technique fully unsupervised, and the results substantially independent of the initial network conditions, Future efforts will be devoted to the further testing of the proposed technique, both from a qualitative and quantitative point of view, and to its application to the study of breast pathologies, in particular to breast tumor diagnosis and follow-up. The software's used for this algorithm development are MATLAB 7.5 and LABVIEW 10.0.

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