Neural-association of microcalcification patterns for their reliable classification in digital mammography

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Abstract

Breast cancer continues to be the most common cause of cancer deaths in women. Early detection of breast cancer is significant for better prognosis. Digital Mammography currently offers the best control strategy for the early detection of breast cancer. The research work in this paper investigates the significance of neural-association of microcalcification patterns for their reliable classification in digital mammograms. The proposed technique explores the auto-associative abilities of a neural network approach to regenerate the composite of its learned patterns most consistent with the new information, thus the regenerated patterns can uniquely signify each input class and improve the overall classification. Two types of features: computer extracted (grey level based statistical) features and human extracted (radiologists' interpretation) features are used for the classification of calcification type of breast abnormalities. The proposed technique attained the highest 90.5% classification rate on the calcification testing dataset.

1. Introduction

Every year around a million women develop breast cancer world-wide [1]. It accounts for one in three cancer diagnosis in women [2]. Primary prevention is not yet possible as the causes of the disease are still unknown. The stage of development depends upon the detection time. Early detection of cancer saves patients from the more aggressive radical treatments and increases the overall survival rate.

At present digital mammography is the most reliable technique for early detection of breast cancer tumours. Microcalcifications are one of the mammographic hallmarks of early breast cancer [3]. Current image processing techniques make the primitive breast abnormalities detection easier; however their classification as malignant or benign still remains difficult for researchers. The key reason is a lack of individuality in microcalcification class patterns. In many cases of the screening database, microcalcifications exhibit both classes (malignant and benign) characteristics, i.e. size, shape and distribution of microcalcifications. Interpretation of such cases often produce screening errors; either to miss malignant cases (false negatives) or more benign biopsies (false positives). Advancement in computational intelligence has improved the performance of computerized classification of the breast abnormalities into malignant and benign classes in digital mammography. A computer-aided classification system can aid radiologists in the classification process serving as a 'vital second reader'.

The main objective of this research work is to investigate the significance of the neural-association of microcalcification patterns for their reliable classification into malignant and benign classes using computer-extracted and human-extracted features. The remainder of this paper is broken down into five sections. Section 2 reviews existing classification techniques. Section 3 discusses the proposed research technique. Section 4 presents the experimental results obtained with both types of features using the proposed research technique. Section 5 covers a brief discussion and analysis on the experimental results obtained with different feature vectors and the proposed technique. In section 6, conclusions are drawn and future research directions are addressed.

2. Related Work

Many research techniques have been proposed and investigated by researchers for the computerized detection and classification of microcalcification patterns [4]. Fuzzy logic [5-7], wavelet transforms [8, 9], statistical techniques [3, 10], and artificial neural networks [7, 11-22] are the most common techniques. The ability of neural networks to learn from the attributes of class patterns and to classify the unknown patterns of those classes into appropriate classes utilizing the acquired knowledge has shown its potential in the field of pattern recognition.

Performance of any classifier highly depends on the features used for classification. Selection and extraction of significant type(s) of features which characterize malignant and benign classes uniquely is another key issue to be considered in digital mammography. Shape features [10, 18], image structure features [7, 15, 21], texture features [11, 12, 18], wavelet features [8, 9] and BI-RADS lesion descriptor (radiologists' interpretation) features [15] have been explored by researchers in computerized classification of microcalcification patterns in digital mammography.

Chitre et al [21] compared three different classification techniques in their research: K-nearest neighbour (KNN) clustering technique; multivariate Baye's classifiers; and BPNN. They reported ANN appropriate for classification because of its effectiveness in portioning the multi-dimensional feature space into disjoint regions. With selection of best image structure features they achieved good result with ANN compared with statistical techniques. A comparative study of a radial basis function (RBF) and a multi layer perceptron (MLP) neural networks for the classification of breast abnormalities using the texture features was performed by Christoyianni et al [12] and Bovis et al [11]. Veldkamp et al. [23] have detected clustered microcalcifications using a Bayesian techniques and a Markov random field model. The novel aspect of the proposed technique was that the relative location and orientation of clusters inside the breast was taken into consideration in feature extraction. KNN was used to classify the detected clusters into malignant and benign types. Verma et al [7] used a back-propagation neural network for the classification of the microcalcifications extracted using a fuzzy rule based detection system. Their proposed technique could classify 88.9% of the 40 cases from the Nijmegen database. Edwards et al [22] used Bayesian neural network (BNN) to approximate the ideal observer variables for detection of microcalcification clusters in mammograms. The BNN differs from a conventional ANN in that the error function used in training includes a regularization term, equivalent to a Bayesian prior probability on the neural network weight values, to panellize solutions which are more complicated than the training data justify. They found that the regularization term makes BNN's performance less sensitive to the number of hidden neurons in the neural network than a conventional ANN.

Considering the vagueness of breast cancer data many researchers have researched and proposed various combined classifier schemes in an attempt to achieve a more accurate result. Foggia et al. [13] investigated a multiple classifier system (MCS) for detection of clustered microcalcification clusters from mammographic images. The system comprises two expert systems, to classify a cluster containing Nμ microcalcifications, each microcalcification being classified by the μC-Expert, while the cluster, considered as a whole, is classified by the Cluster Expert. The final classification decision is obtained using Weighted Voting rule. Similarly Santo et al. [16] have also developed a multiple classifier scheme to classify calcifications as malignant or benign. Some of the classifiers classified individual microcalcifications of a cluster, whereas others classified the entire cluster. Thus, they used features to characterize single calcifications and clusters. The final output was a weighted combination of the outputs of the various classifiers used. Lo et al. [15] evaluated the performance of local vs. ensemble model for classification of microcalcification clusters from mammograms of DDSM database. The local models were developed for each type of features; image processing, BI-RADS and patient age and the ensemble models developed combining different types of features performed better than the local models. The bi-model breast cancer microcalcification classification system was investigated by Khuwaja and Abu-Rezq [24].

3. Proposed Technique

Neural networks are used in many different applications because of their ability to generalize and describe non-linear processes. The proposed technique investigates two neural networks: auto-associator neural network (AANN) for neural-association of microcalcification patterns into malignant and benign class patterns, and the classifier neural network for the final classification of neural-associative patterns into malignant and benign classes. The proposed research technique comprises of four parts: acquisition of digital mammograms dataset, significant features extraction, neural-association of extracted features into malignant and benign classes, and final classification of neural-associative patterns into malignant and benign classes. Both neural networks of proposed technique have single hidden layer architecture and use a back-propagation learning algorithm.

3.1. Digital Mammograms

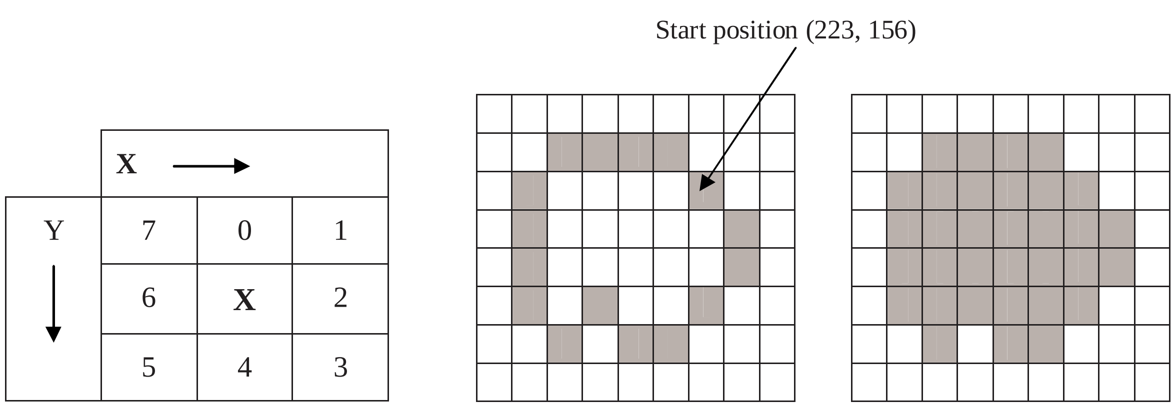
The experimental dataset of digital mammograms used in this research work is formed using the cases of the Digital Database for Screening Mammography (DDSM) benchmark database established by the University of South Florida (USF). This resource is established solely to aid researchers to evaluate and compare their research work with others in the area of computerized detection and classification of breast abnormalities via digital mammography [25]. DDSM cases can be downloaded freely from the USF's online digital mammography database website: httt://marathon.csee.usf.edu/Mammogrphy/Database.html. The DDSM provides mammograms with pixel level 'ground truth' information about the locations and types of suspicious regions, and associated patient information in interpretation report for each case study. Digital mammograms may have more than one suspicious area. The experimental dataset consist of total 106 digital mammograms of calcification type breast abnormality.

3.2. Feature Extraction

Two types of features discussed below are used in the proposed research technique.

3.2.1. Computer-extracted features

Computer extracted feature are extracted using a two-step process: 1) extract already marked suspicious areas from digital mammograms and 2) extract grey level based statistical features from extracted suspicious areas.



(a) Chain Code

(b) Suspicious area on Digital mammogram

BOUNDARY 223 156 3 4 5 5 6 7 5 7 0 0 0 1 2 2 2 #

Figure 1 Suspicious area extraction

Suspicious areas are already marked in all digital mammograms of the DDSM by expert radiologists. Suspicious areas are of uneven size on digital mammograms (Figure 1 (b)). For area extraction, first the boundary of each abnormality of the mammogram is defined by solving the chain code values given in the ".OVERLAY" file of each case. The *'.ics'* file gives the size of mammogram in terms of lines i.e. rows, and pixels per line i.e. columns. Figure 1 (a) shows chain code values and directions to be followed to solve chain code values to get adjacent pixel position on boundary of suspicious area. Figure 1 (b) shows a boundary of suspicious area defined solving an example chain code from start position to end. Using the boundary information each suspicious area is located on the mammogram. Grey level values of pixels of suspicious area and the respective surrounding boundary area are extracted to calculate the feature values using statistical formulas.

A total of 14 grey level based statistical features; number of pixels, histogram, average grey, average boundary grey, contrast, difference, energy, modified energy, entropy, modified entropy, standard deviation, modified standard deviation, skew, and modified skew are considered as computer-extracted features [7].

3.2.2. Human-extracted features

All DDSM cases are interpreted by expert radiologists and contain information such as the patient age, dates of mammogram study and digitization, ACR breast density, a subtlety value, and an abnormality description in terms of BI-RADS™ (ACR 1998) lexicon [25, 26]. The radiologist's interpretation is considered as a human-extracted features and is extracted from the associated patient information provided in the '.ics' file and the '.OVERLAY' file supplied along with the mammogram file of each DDSM case.

Patient age at the time the mammogram was taken, density rating of breast, an abnormality assessment rank, a subtlety of an abnormality and the morphological description of breast abnormality are considered as BI-RADS features. The morphological description features for calcification lesions are calcification type and calcification distribution. Like other features, morphological descriptions of breast abnormality are encoded into numeric values to yield real feature values. For example numeric value '1' is set for calcification type Punctate, '2' for Amorphous and so on. The numeric encoding is shown in Table 1.

Total 6 BI-RADS categorized features are patient age, density, calcification type, calcification distribution, assessment, and subtlety [15].

Table 1 BI-RADS categorized features and numeric encoding

Calcification Types							
Punctate	1	Lucent_Center	5	Coarse	9	Milk of Calcification	13
Amorphous	2	Fine_Linear_Branching	6	Large_Rodlike	10	Dystrophic	14
Pleomorphic	3	Skin_Calcification	7	Round	11	Suture	15
Round_And_Regular	4	Vascular	8	Egg Shell	12	Any	16

Calcification Distributions					
Clustered	1	Segmental	3	Diffusely_scattered	5
Linear	2	Regional	4	Any	6

3.3. Neural-association of Microcalcification Patterns

In pattern classification generally the feed forward networks are trained to approximate a function associating a set of input patterns with a set of output patterns. Auto-association discovers the redundancies in a set of input patterns which lead to more efficient featural representations of input patterns. It encourages the network to discover any structure present in the input so the input can be represented more abstractly and compactly. The pattern of hidden neuron activations must be efficient and concise if the hidden neurons are to successfully regenerate the input pattern on the output layer; they must discover some representation of the input which is reduced but which contains all the information necessary to recreate that input. A trained AANN returns a composite of its learned patterns most consistent with the new information. However training of AANN remains a complicated issue as AANN's ability to capture the distribution of training data is highly dependent on the size and structure of the AANN and the shape of activation function used for training [27].

In the proposed research technique, the basic concept behind the neural-association of microcalcification patterns was to regenerate the composite of its learned patterns most consistent with new information disregarding the compression of input data and thus the regenerated patterns are capable of signifying the oddity of each class patterns (malignant and benign) in a given feature set. A single hidden layer neural network is investigated for neural-association of microcalcification patterns. AANN takes as input and output the same feature vector. Network parameters such as number of hidden neurons and iterations, learning rate and momentum are adjusted during AANN training to obtain unique patterns for malignant and benign classes which enable the classifier to improve overall classification. Figure 2 shows the architecture of AANN used in the proposed technique.

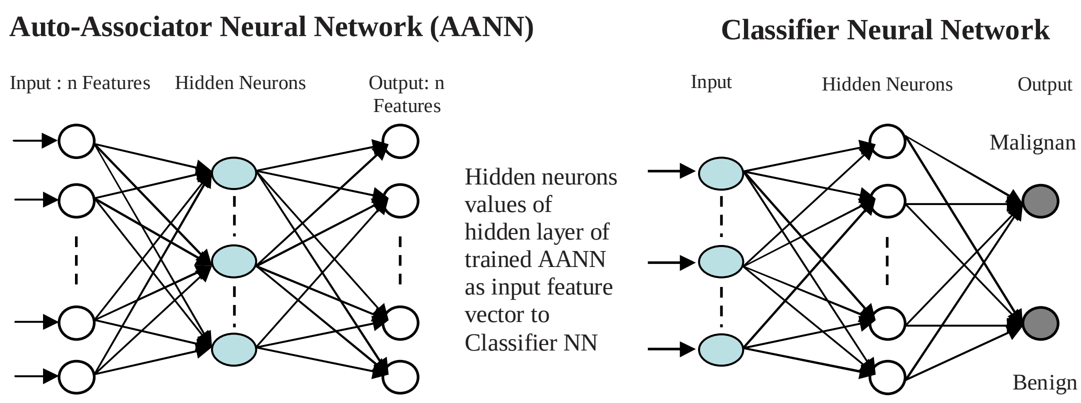


Figure 2 Architecture of two neural networks

3.4. Classifier Neural Network

A feed-forward neural network is incorporated and investigated in the proposed technique for final classification of neural-associative patterns into their appropriate classes. The neural-associative patterns (hidden neurons values) of the trained AANN are taken as input to the classifier neural network. Figure 2 shows the architecture of a classifier neural network. The number of hidden neurons in hidden layer is continuously adjusted in an attempt to achieve maximum classification on neural-associative microcalcification patterns. It has two output nodes in output layer, which represents each class; malignant and benign.

4. Experimental Results

A total of 126 calcification areas, contained 84 (43 benign, and 41 malignant) for training, and 42 (21 benign, and 21 malignant) for testing extracted from 106 digital mammograms were used for the experiments. All experiments were carried out using two sets of feature vectors.

- Feature vector 1 contains computer-extracted features (Dimension 14).
- Feature vector 2 contains both computer-extracted features and human-extracted features (Dimension 20).

Both networks were trained extensively using different numbers of hidden neurons (from 4 to 30 in even order) and iterations (from 0 to 100000) to attain the best and consistent classification on unknown test patterns. Learning rate 0.1 and momentum value 0.1 were set for both networks.

Tables 2 and 3 show the experimental results obtained with feature vectors 1 and 2 respectively on calcification dataset. The highest 100% training classification rate was achieved with both feature vectors. Feature vector 1 attained 85.7% testing classification rate with a corresponding 95.2% training classification rate. Neural-associative microcalcification patterns of feature vector 2 obtained from the AANN configured with 10 hidden neurons and 70000 iterations attained the highest 90.5% testing classification rate with a corresponding 100% training classification rate. The classifier network was configured with 6 hidden neurons for 10000 iterations (Table 3).

Table 2 Classification results with feature vector 1for Calcification cases

#	AANN		Classifier NN			
	Hidden Neurons	Iterations	Hidden Neurons	Iterations	Training (%)	Testing (%)
FV1_1	4	10000	14	20000	92.9	83.3
FV1_2	6	10000	20	30000	98.8	81
FV1_3	6	20000	14	40000	98.8	83.3
FV1_4	10	10000	18	20000	100	81
FV1_5	12	20000	6	5000	90.5	85.7
FV1_6	14	10000	16	5000	90.5	85.7
FV1_7	14	20000	6	10000	95.2	85.7

Table 3 Classification results with feature vector 2 for calcification cases

#	AANN		Classifier NN			
	Hidden Neurons	Iterations	Hidden Neurons	Iterations	Training (%)	Testing (%)
FV2_1	8	10000	6	20000	100	81
FV2_2	8	10000	8	20000	100	83.3
FV2_3	8	10000	8	40000	100	85.7
FV2_4	10	10000	6	5000	100	83.3
FV2_5	10	20000	14	30000	100	88.1
FV2_6	10	30000	10	5000	100	88.1
FV2_7	10	70000	6	10000	100	90.5

5. Discussion and Analysis

The results presented in the previous section demonstrate that the neural-associative patterns of feature vector 2 comprised of both types of features represented by 10 hidden neurons attained the highest classification rate 100% on training and 90.5% on the testing calcification dataset (Table 3). These results showed that the neural-association represents the input patterns more abstractly and compactly, i.e. 10 hidden neurons effectively represent total of 20 (14 computer extracted, and 6 human extracted) features. However the main aim of neural-association of microcalcification patterns in this research work was to regenerate the composite of its learned patterns most consistent with new information required to signify each class of input patterns effectively disregarding the compression of input data.

The dataset used in this research work was kept unbalanced. Different numbers of malignant and benign patterns were used however the difference in number of malignant and benign patterns was very little. The aim was to keep the number of malignant and benign patterns of training and testing sets as close as possible to avoid problems such as classifier becoming biased towards one particular class. Table 4 and Figure 3 shows the distribution of malignant and benign classification and misclassification (i.e. malignant classified as benign and vice versa) results of few experiments listed in Tables 2 and 3 attained with both feature vectors using the proposed research technique. The overall benign classification rate was higher than malignant classification rate in entire experimentation of both feature vectors. Improvement in overall classification accuracy was observed when human-extracted features were combined with computer-extracted features (feature vector 2) compared with only computer-extracted features (feature vector 1). The malignant classification rate improved significantly. The human-extracted features are derived from the interpretation results provided by at least two expert radiologists. This may be the reason for the improved classification rate. However the experimental results suggest that both types of features should be considered in computerised classification of calcification type of breast abnormalities.

Table 4 Distribution of malignant and benign classification and misclassification results (selected results from Tables 2 and 3)

#	Classification Rate (%)					Area under ROC curve Az value
	Total Test (%)	Malignant as Malignant (TPF)	Malignant as Benign (FNF)	Benign as Benign (TNF)	Benign as Malignant (FPF)	
FV1_3	83.3	81.0	19.0	85.7	14.3	0.803
FV1_7	85.7	76.2	23.8	95.2	4.8	0.812
FV2_6	88.1	85.7	14.3	90.5	9.5	0.880
FV2_7	90.5	85.7	14.3	95.2	4.8	0.912

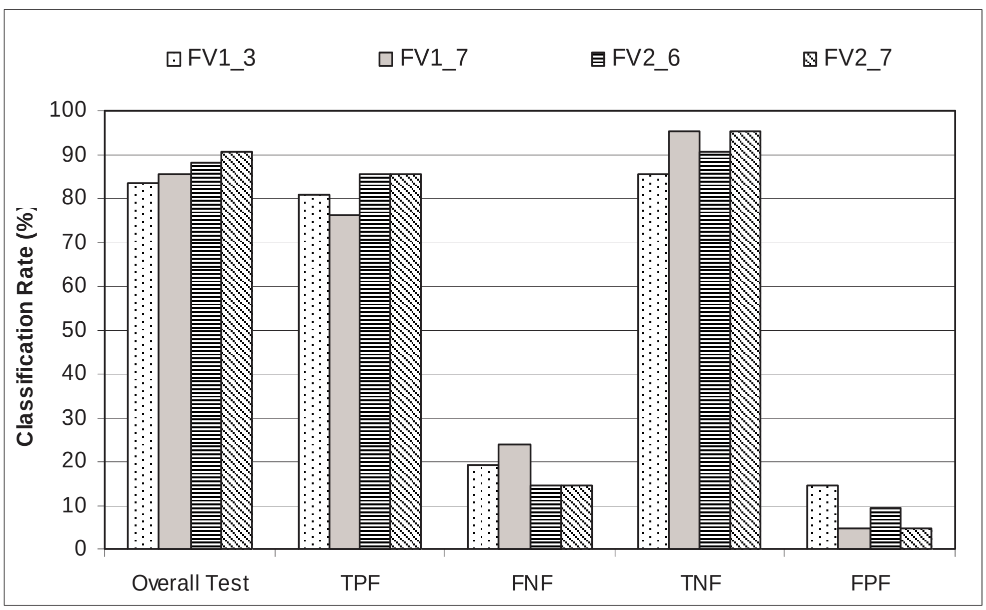


Figure 3 Classification results for feature vector 1 and 2

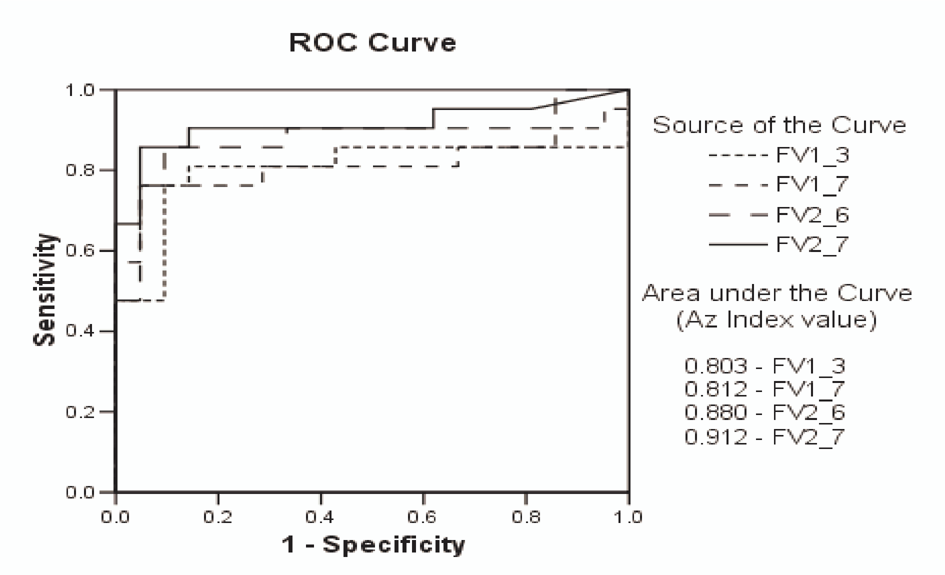


Figure 4 ROC Curve results for feature vector 1 and 2

Figure 4 shows the ROC curve analysis of experimental results listed in Table 4. The networks configuration listed under result FV2_7 (Table 3) attained the highest testing classification rate 90.5%, with high 90.5% malignant classification rate and 95.2% benign classification rate and yielded the highest Az index 0.912 area under the ROC curve.

Direct comparison of experimental results with previously reported results is difficult task due to use of different database, different types of features and classification techniques in the classification process. The proposed technique attained the comparative results over other previously proposed techniques listed in Table 5 except the approach proposed by Khuwaja & Abu-Rezq [24]. The ensemble model proposed by Khuwaja & Abu-Rezq [24] comprised two separately trained classifier models according to the mammogram view CC and MLO and are combined to achieve the final classification results. Whereas the proposed technique is developed on the dataset comprising only CC digital mammograms of DDSM database. The proposed technique attained better Az index value 0.912 area under the ROC curve using feature vector 2 over the 0.69 Az index value attained with ensemble model and similar features on dataset taken from DDSM in study of Lo et al. [15].

Wroblewska et al [18] have reported a 76% classification rate with their neural network based automated classification technique on the DDSM database. Their proposed system misclassified 64% malignant as benign (FNF) and 36% benign as malignant (FPF). The highest observed FNF is only 23.8% and FPF is 14.3% in experimental results attained with the proposed technique. Similar to our results the FNF was higher than FPF in their reported results.

Table 5 Distribution of malignant and benign classification and misclassification results

Technique	Classification rate (%)	Az Index value	Database
Proposed Technique	90.5%	0.912	DDSM
Ensemble model [24]	98.75%	-	DDSM
Neural Network [18]	76%	-	DDSM
LDA ensemble model [15]	-	0.69	DDSM
Bayesian techniques and a Markov random field model, KNN [23]	-	0.83	Nijmegen region, The Netherlands
EBPNN [28]	-	0.8749	-

6. Conclusions and Further Research

The proposed research work explores the auto-associative and classification abilities of neural networks for the classification of microcalcification patterns in digital mammograms. The proposed technique attained the highest testing classification rate of 90.5% on the calcification cases of DDSM benchmark database. The experimental results obtained with proposed technique show that neural-association of microcalcification patterns regenerates the new patterns most consistent with new information capturing the unique characteristics for both classes (malignant and benign) from input patterns which enables classifier network to produce consistent classification.

The proposed technique is a promising technique and performs comparatively with other previously proposed techniques to produce consistent classification of microcalcification patterns with selection of features in digital mammography. It motivates the exploration of AANN capabilities for experiments with different types of features, different network topologies and learning algorithms to produce unique patterns for malignant and benign classes. For such unique patterns a simple rule based classification system can be designed based on the rules extracted from the possible neural-associative patterns representation of input classes.

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