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Feature selection and classification of Breast Cancer on Dynamic Magnetic Resonance Imaging Using Genetic Algorithm and Artificial Neural Networks

Artificial neural networks (ANN) are frequently used in the development of computer-aide diagnosis systems for breast cancer detection. Although the ANN may work as an excellen predictor of malignancy, it may not be able to explain which findings are more relevant i reaching the diagnosis. A hybrid genetic-neural (GA-ANN) model was designed to differentiat malignant from benign in a group of patients with histopathologically proved breast lesions on th base of BI-RADS descriptors and data derived from time-intensity curve. We used a databas with 117 patients' records each of which consisted of 27 quantitative parameters mostly derive from time-intensity curve, 4 BI-RADS qualitative data which determined by expert radiologis and patient age. These findings were encoded as features for a genetic algorithm (GA) as preprocessor for feature selection and classified with a three-layered neural network to predict th outcome of biopsy. The network was trained and tested using the jackknife method and it performance was then compared to that of the experienced radiologist in terms of sensitivity specificity, accuracy and receiver operating characteristic curve (ROC) analysis. The networ was able to classify correctly 107 of 117 original cases and yielded a good diagnostic accurac (91%), sensitivity (95%) and specificity (78%) compared to that of the radiologist (92%), (96% and (78%). In this paper, GA and ANN techniques were combined for a particular classificatio problem: The Automatic Prediction of Mammary Biopsy Results from Dynamic MR Imaging.

KEYWORDS: Breast, Magnetic resonance Imaging, Neural network, Genetic algorithm.

1. Introduction

The accurate judgment and classification of diseases, especially on cancers, which are very important in the medical science, are difficult to achieve. Accurate classification allows doctors to select suitable therapies and treatments for diseases. Over last several decades, cancer classification has been advanced, but it still has limitations caused by the traditional method for morphological appearance analysis [1].

In the detection, evaluation and management of breast cancer, magnetic resonance imaging (MRI) is emerging as a powerful technique for the detection, diagnosis and monitoring of abnormalities. In particular, administration of a contrast agent can improve the diagnostic performance of the study [2]. Injection of a gadolinium-based contrast agent (e.g. Gd-DTPA) typically leads to rapid signal increase and early wash-out for malignant and therefore highly vascular tumors [3]. Previous studies have shown that contrast-enhanced MR mammography allows the distinction of benign from malignant breast lesions when the selected region of interest (ROI) is in the most enhancing part of the tumor [4,5]. Also the steepest slope of contrast medium uptake and the normalized slope of the SI enhancement profile evaluated at half the maximal signal intensity, has been reported to be highly correlated with malignancy and

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therefore offered improved discrimination between malignant and benign lesions [6, 7]. In this study we report an automated method in which 32 parameters consisted of 28 quantitative parameters mostly derived from time-intensity curve and 4 BI-RADS qualitative features, was used as input of the model. The most significant features were selected from these features by genetic algorithm optimization method.

2. Materials and methods

A. database

Our study group consisted of 117 patients whose ages ranged from 15 to 79 years (mean 50 years). The patients group included 94 malignant lesions and 23 benign entities. All patients underwent excisional biopsy (n= 117). Ninety-four patients in whom malignant lesions were diagnosed subsequently underwent mastectomy. Twenty-three patients had benign lesions. Table 1 shows the distribution of lesions at histopathologic analysis.

B. Data acquisition

The MRI images were performed at the Athari imaging center during the 2001-2004 using a Signa 1.5 Tesla unit (GE Medical Systems, Milwaukee, Wis) in the prone position with a specific breast coil. Initial sagittal or axial T1-weighted spin-echo images (T1W) were performed at 325/8 (repetition time (msec)/echo time (msec)) and axial or sagittal T2-weighted fast spin-echo images (T2W) were performed at 5,400/90. Other MR parameters used were 22 cm field of view, 3.6 mm section thickness, and 256×192 (T1-weighted) or 256 × 256 (T2-weighted) matrix. Dynamic study was performed after administration of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) over 10-15 seconds using a fast radio-frequency spoiled gradient-recalled-echo (SPGR) sequence (11.4/3.3; flip angle,10 degree; matrix, 256×192; section thickness, 3.6 mm; gap, 1.0-2.5 mm).

Data acquisition of the dynamic study was done in the time of the injection. Then the images were called back one by one and a free size ROI were drawn in the most enhancing part of the lesion (Fig. 1).

In some cases with specific patterns such as rim enhancement, two additional ROI were also drawn in the least-enhancing part of the tumor and/or adjacent uninvolved breast tissue to compare the relevant signal intensity. Similarly in some cases with mark inhomogeneous enhancement pattern multiple signal intensity profile were obtained from different ROI and the maximally enhancing signal intensity profile was considered. The obtained time-intensity values were used to generate the time intensity curve. A special computer program was then used to obtain quantitative parameters such as the steepest slope in the washin part, slope in washout part from 1-5 minute, the area under the time-intensity curve, area under the time-intensity up to the time of peak and the enhancement ratio and signal intensity ratio at the maximum point as well as at 1, 2 and 5 minutes. In order to compare the quantitative features with BI-RADS features, we used 4 BI-RADS parameters beside our quantitative features. Table 2 shows all the parameters in our database, which represented time-intensity curve findings and BI-RADS findings. Proposed criteria for extraction of BI-RADS parameters and time-intensity curve types, which used in this study, were shown in Table 3.

C. *GA feature selection*

The genetic algorithm (GA) has become increasingly popular in solving optimization and machine learning problems [8]. The fundamental principle underlying genetic algorithms is the mimicry of natural selection. Genetic algorithms are randomized search procedures inspired by the mechanics of genetics and natural selection [9].We used 32 parameters as

input of the ANN. A binary vector of dimension 32 represents the individual in the population. In other words, the chromosome defined contains 32 genes, one gene for each feature, which can take 2 values. A value of 0 indicates that the corresponding feature is not selected, and a value 1 means that the feature is selected. Therefore there are 2^{32} possible feature subsets. Genetic algorithm selects the best features from these possible feature subsets during different generations. In each generation, the population is probabilistically modified, generating new chromosomes that may have a better chance of solving the problem [10]. New characteristics are introduced into a chromosome by crossover and mutation. The probability of survival or reproduction of an individual depends more or less on its fitness to the environment. The population therefore evolves toward better-fit individuals. Each feature in a given feature space is treated as a gene and is encoded by a binary digit (bit) in a chromosome.

A chromosome therefore represents a possible solution to the feature selection problem. For every pair of selected parent chromosomes, a random decision is made to determine if crossover should take place. After crossover, another chance of introducing new features is obtained by mutation. Mutation is applied to each gene on every chromosome. For each bit, a uniform random number in (0, 1) is generated. If the random number is greater than *Pm*, the probability of mutation, then no mutation will occur; otherwise, the bit is complemented [3]. In our study, two point binary crossover and binary mutation are performed. The roulette wheel selection strategy is also used in the algorithm for parent selection. The relevant parameter settings which we used were: Population size: 30; Number of generation: 100; Probability of crossover: 0.8; Probability of mutation: 0.1. The fitness of the chromosome is calculated according to the multiplication of diagnostic sensitivity and specificity of the evolved subset of features. We used the equation (1) as evaluation function of the model and our purpose was to maximizing it in test cases:

$$F = Se * Sp \tag{1}$$

Where Se is the sensitivity of the model in test cases and Sp is the specificity of the model in test cases:

$$Se = \frac{TP}{TP + FN} \tag{2}$$

$$Sp = \frac{TN}{TN + FP} \tag{3}$$

In these equations, TP stands for true positive fraction, TN stands for true negative fraction, FP stands for false positive fraction and FN stands for false negative fraction of the model in test cases.

For the simulation of this hybrid model, the quantitative data were selected using genetic algorithm optimization method and normalized between 0 and 1 according to the maximum value of each feature in the data set. The normalized data was then fed into the network to map them with corresponding pathological findings and fitness calculation. This procedure is shown in Fig. 2.

D. Neural Classifier

We used a three-layered feed-forward artificial neural network with linear activation function in input layer and sigmoid activation function in hidden and output layers. The selected features from genetic algorithm were considered as inputs into the established neural network. Several training algorithms were implemented and tested: gradient descent methods, resilient back-propagation, conjugate gradient methods, and quasi Newton method [11]. The best results obtained using a resilient back-propagation method [12].

The number of the inputs is automatically optimized using GA processing. The values of the inputs normalized between 0 and 1. One hidden layer is used in neural network. The

numbers of nodes in this layer were adjusted in an attempt to achieve optimum diagnostic sensitivity and specificity on test cases. One node is used in the output layer which has been trained to represent 1 for malignant cases and 0 for the benign ones. In order to determine the best optimized structure for the neural network, we simulated a large number of neural networks by varying the number of hidden units (from 3 to 15), iterations and learning rates. The optimum learning rate, which adjusts the weight matrixes for all layers, was 0.1.

Finally, after the network had been trained perfectly in each simulation the testing case was presented to the trained network giving a diagnostic output vector in the range of (0-1). Our network was trained perfectly over 1000 iterations on an IBM compatible personal computer (Pentium 4, 2.8 GHz). The software used to construct the neural network was written locally in MATLAB programming language. Our network was trained and tested using the jackknife technique in which all cases were used in both the training and testing processes. In this method, all but one case in the database is used to train the network. The single case that is left out is then used to test the network. This procedure is repeated until each case in the database is used once as a testing case. It therefore provided 117 different simulations. Although, this method is extremely time consuming but it is useful especially for the small database such as ours. We used Resilient Back-propagation algorithm for training our ANN because of its fast and accurate operation on large number of input data such as ours (n=32). The algorithm Resilient Back-propagation is a local adaptive learning scheme, performing supervised batch learning in feed-forward neural networks.

E. ROC Analysis

Besides the diagnostic accuracy, sensitivity and specificity, the area under the ROC curve (AUC) was used to evaluate the performance of the established hybrid ANN model and that of radiologist. ROC curves can be used to show the trade-off in sensitivity and specificity achievable by a classifier by varying the threshold on the output decision variable. Sensitivity or the true positive fraction (TPF) is the fraction of positive cases that were classified correctly as positive. The specificity, or one minus the false positive fraction (FPF), is the fraction of negative cases that were correctly classified as negative. An ROC curve is generated by applying a threshold to the output of a classification scheme and then plotting the (FPF, TPF) pairs for each threshold. The performance of the hybrid ANN can be compared in terms of indices calculated from their curves. In particular, the area under the ROC curve (AUC) is often used as a measure of classifier performance. The values for AUC range from 0.5 for chance to 1.0 for a perfect classifier. We applied the ROCFIT software for Apple Macintosh based on the Charles E. Metz algorithm [13].

3. Results

A. Radiologist performance

An expert radiologist read the images and classified them into benign and malignant groups using a five-scale category with increasing likelihood of malignancy. The overall statistical results of sensitivity, specificity and accuracy of 96%, 78% and 92% was found for experienced radiologist.

B. Full ANN model performance

We initially trained the ANN with all 32 extracted features and tested it using the jackknife method. The obtained maximum diagnostic sensitivity, specificity and accuracy were 94%, 65% and 88% respectively on ANN with 4 hidden units. Also, we trained and tested this ANN with all 28 features extracted from time-intensity curve using jackknife method. These results have been gathered in Table 6 and Table 7.

C. Hybrid model performance

We randomly selected 40 cases from 117 cases for feature selection. We used these 40 cases (31 malignant and 9 benign) for testing and remaining 77 cases for training of ANN .We performed GA feature selection with different hidden units (from 3 to 15). Table 4 shows the results of the experiments using output threshold 0.5. The obtained maximum diagnostic sensitivity, specificity and accuracy in 40 randomly selected cases were 100%, 89% and 97.5% respectively on ANN with 7 hidden units and trained with 13 optimized features. When analyzing the results of the experiments from 3 hidden units to 15 hidden units, it is noticed that there are a few features which are more frequently selected than the others are. In every experiment, the feature sets that get the highest fitness function value $(Se*Sp)$ are selected from all the generations. Table 4 gathered all the feature combinations, which get the highest fitness value using different number of hidden units. We can see that in every selection, feature number 1 ($T_{\max}$) and feature number 29 (mass shape) are selected constantly. Fig. 3 indicates the frequency of every feature selected in the feature sets which gave the highest fitness function value for each number of hidden units from 3 to 15. We trained and tested our ANN model with optimized features using the jackknife method. The results of this section were listed in Table 5. The best result in this section obtained with 5 hidden units and 17 selected features. Fig. 4 shows the frequency of selection of each feature in 100 generations of genetic optimization of an ANN with 4 hidden units.

We finally selected 12 significant features that selected 4 times and more according to Fig. 3. We applied jackknife method for training and testing of a three layered feed-forward neural network with 3 hidden units. Table 6 shows the comparative performance of the participating radiologist, neural network full model (input units=32) and neural network reduced model (input units=12) with 3 hidden units in jackknife testing (n=117). Fig. 5 compares the ROC curves of the expert radiologist, full ANN model (input units=32) and hybrid ANN model (input units=12).

4. Discussion

Artificial neural networks (ANN) are frequently used in the development of computer-aided diagnosis systems for breast cancer detection. Although the ANN may work as an excellent predictor of malignancy, it may not be able to explain which findings are more relevant in reaching the diagnosis. In this study, GA was used to select the most significant features from a large variety of parameters that are input to the ANN. Applying GA to the feature selection problem is straightforward: The chromosome of the individuals contains one bit for each feature, and the value of the bit determines whether the feature will be used in the classification. The individuals are evaluated by training the networks (that have a predetermined structure) with the feature subset indicated by the chromosome. The resulting accuracy is used to calculate the fitness [14]. Our network was trained and tested by the conventional jackknife method on 117 proven cases. We used this method because it can show the degree of stability and random behavior of ANN model. The overall average results for sensitivity, specificity, and accuracy of 94%, 65%, and 88% for the full ANN model (hidden units = 4) were moderately lower than the radiologist: 96%, 78%, and 92%. We could increase the classification ability of ANN by applying GA for feature selection. The sensitivity, specificity, and accuracy for the hybrid ANN have been slightly improved (94%, 78% and 91%) using genetic algorithm compared with our previous report [7]. In a comprehensive glance several reasons can be suggested for the relative low specificity. One important reason for the lower specificity values obtained for the GA-ANN model may be related to the relatively small number of benign cases in our database (23 out of the 117 cases). Consequently misdiagnosis of one or two benign cases had an exaggerated effect on

specificity. Therefore preparing a balanced, comprehensive training data set is essential for the application of a neural network. This means that the neural network performs poorly if the number of one type of pattern is under-represented or over-represented in the training procedure.

Ultimately our results show that the application of a three layered feed-forward neural network with a back-propagation algorithm based on the quantitative data and selected by GA to optimize multiplication result of sensitivity and specificity , may lead to a more automated, objective and consistent diagnosis compared with the radiologists. Applying BI-RADS findings besides the time-intensity quantitative features, has improved the specificity of our model. We couldn't achieve a good classification performance in training and testing the ANN with all 28 quantitative features, because the presence of redundant features in this database can easily reduce the classification performance of the ANN (Table 7), but the presence of 4 BI-RADS descriptors besides these 28 features in training dataset, have improved the classification performance of the ANN (Table 6). These results can prove that BI-RADS findings play an important role in classification of breast lesions on dynamic MRI. Fig. 4 shows that mass shape and homogeneity are more significant than the other BI-RADS descriptors. Also the parameters TMAX, SIR1, Age, TPRIOR and Delay time are more selected parameters than the other quantitative features.

According to Fig. 3, TMAX is the most significant feature in time-intensity quantitative parameters and mass shape is the most significant feature in BI-RADS descriptors. By the way, the using of quantitative parameter directly extracted from time intensity profile, the output of the ANN would be more independent and therefore can be considered more supportive for the radiologist as an independent second computerized opinion.

Table 1. Demonstrating the distribution of lesions at histopathologic analysis.

Histopathologic diagnosis	No. of lesions
Malignant (n=94)	
Noninvasive intraductal carcinoma	3
Ductal invasive carcinoma	81
Mucinous	4
Lobular	1
Medullary	1
Squamous	1
Lymphoma	1
Malignant phyllodes tumor	2
Benign (n=23)	
Fibroadenoma	11
Fibrocytic disease	6
Fat necrosis	1
Benign phyllodes tumor	2
Intraductal papilloma	1
Granulomatous mastitis	2

Table 2. The extracted quantitative parameters from time-intensity profile which used as input into the model.

Indexes	Mean ± Std. deviation
1- Time at the maximum intensity	161.24 ± 82.923
2- Steepest slope in the washin part	4.42 ± 2.49
3- Curve type*	
4- SI** at 1 minute	190.48 ± 76.419
5- SI at 2 minute	207.38 ± 78.893
6- Enhancement ratio at 1 minute	98.2252 ± 60.3197
7- Enhancement ratio at 2 minute	115.8036 ± 55.9548
8- Enhancement ratio at the maximum point	130.4983 ± 55.9548
9- Signal intensity ratio at 1 minute	1.9823 ± 0.6032
10- Signal intensity ratio at 2 minute	2.1580 ± 0.5595
11- Signal intensity ratio at the maximum point	2.3050 ± 0.5242
12- Enhancement factor	1.4428 ± 0.6271
13- Signal intensity	139.0273 ± 67.3114
14- Tumor size	3.1479 ± 2.6754
15- Patient age	50.03 ± 12.413
16- SI before the injection of contrast medium	97.80 ± 32.530
17- SI at the Initial point to calculate the steepest slope	112.91 ± 41.264
18- SI at the end point to calculate the steepest slope	176.88 ± 71.861
19- Maximum SI	221.23 ± 78.584
20- Initial time to calculate the steepest slope	34.62 ± 12.373
21- Ending time to calculate the steepest slope	49.98 ± 13.701
22- Slope in washout part from 1-5 minute	-0.0567± 0.13043
23- Slope in washout part from 2-5 minute	-0.1694 ± 0.16979
24- Signal intensity ratio at 5 minute	202.2821± 69.0077
25- Enhancement ratio at 5 minute	111.5201 ± 47.5197
26- Delay time	34.4517 ± 10.4924
27- T1 value	0.0470 ± 0.1051
28- T2 value	0.0011 ± 0.0014

* The curve type was a semi-qualitative feature and its average has not meaning.
** Signal intensity

Table 3. Coding of the BI-RADS parameters of MR images and type of the time-intensity curve of 117 patients, which extracted with experienced radiologist.

Radiological Features	Findings	code
Mass Size	No mass	0
	Mass	Size(mm)
Mass Shape	No mass	0
	Round	1
	Oval	2
	Lobulated	3
	Irregular	4

Mass Margins	No mass	0
	Well-defined	1
	Microlobulated	2
	Ill-defined	3
	Speculated	4
Homogeneity	No mass	0
	Homogeneous	1
	Slightly inhomogeneous	2
	Inhomogeneous	3
	Markedly inhomogeneous	4
Associated features	None	0
	Internal septations	1
	Intracystic mass	2
	Cystic spaces	3
	Skin and/or nipple enhance	4
	Satellite nodules	5
	Ductlike enhancement	6
	Nipple retraction	7
	Peripheral enhancement	8
	Axillary adenopathy	9
Time intensity curve type	Type D	1
	Type C	2
	Type B	3
	Type A	4

Table 4. The highest sensitivity and specificity in testing set from experiments of different hidden units with threshold 0.5. These results obtained by 3 times repetitions on 40 test cases (HU stands for Hidden Units).

Best chromosomes	HU	SE	SP
10111110001100101000100000011010	3	0.93	0.89
10101100011111110001010000101011	5	0.93	0.89
11001100110101100000100001011000	7	1	0.89
10110100001101101000010100001011	9	0.93	0.89
11100000011111100001000000111001	12	0.97	0.89
10110100111011101101100100111011	15	0.97	0.89

Table 5. The highest sensitivity, specificity and accuracy obtained in jackknife training and testing method from experiments of different hidden units (n=117).

Hidden Units	SE. (%)	SP. (%)	ACC. (%)
3	94	78	91
5	95	78	91
7	93	70	88
9	95	74	91
12	93	70	88
15	95	74	91

Table 6. Comparative performance of the participating radiologist, neural network full model and neural network reduced model in jackknife testing (n=117).

Parameter	Expert Radiologist	ANN	
		Full Model	Hybrid ANN (H.U. =3)
SE. (%)	96	94	94
SP. (%)	78	65	78
ACC. (%)	92	88	91
FPF	5 of 23	8	5
FNF	4 of 94	6	6
AUC	0.9113 ± 0.037	0.8215 ± 0.064	0.9012 ± 0.04

Table 7. Comparative performance of the participating radiologist and ANN model trained with 28 features (time-intensity quantitative features + patient age) in jackknife testing (n=117).

Parameter	ANN (Hidden Units = 4)
	Time-intensity features + Age (n=28)
Sensitivity (%)	87
Specificity (%)	43
Accuracy (%)	79
False positive fraction	13
False negative fraction	12
Misclassified rate (%)	21

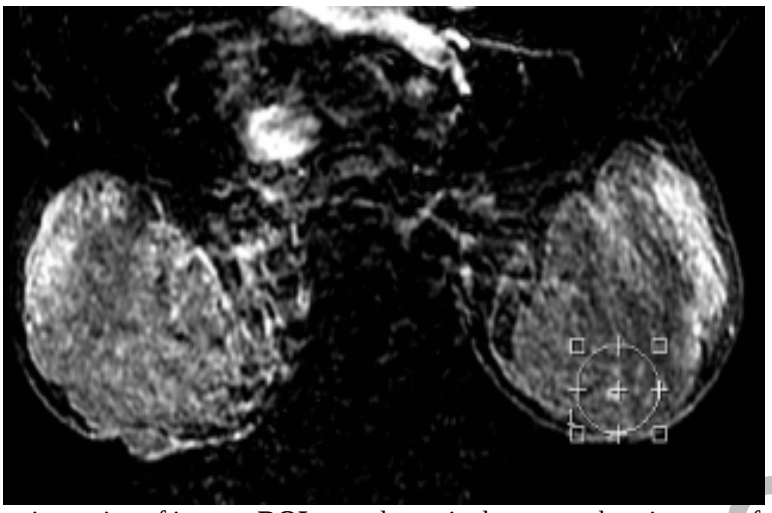

Fig. 1. Free size region of interest **ROI** were drown in the most enhancing part of the lesion.

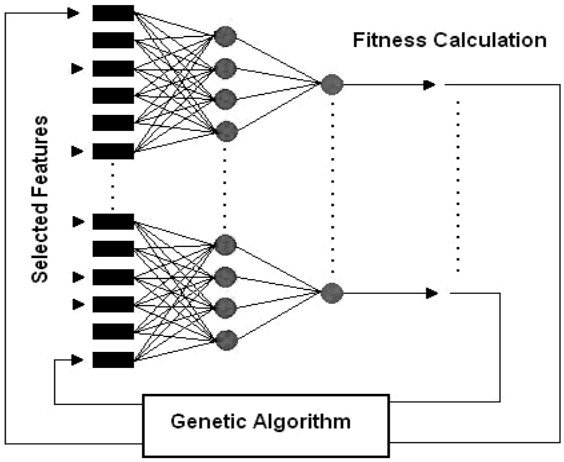

Fig. 2. Feature selection based on neural network classification.

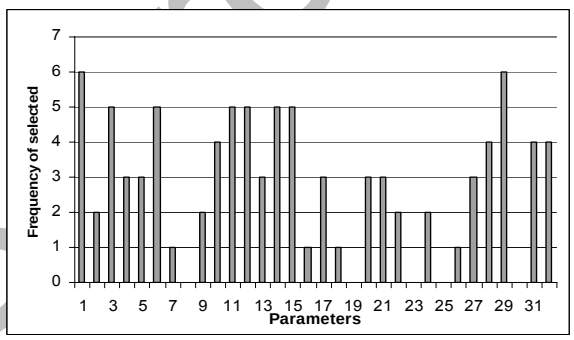

Fig. 3. The selection rate of every feature in the experiments with output threshold 0.5.

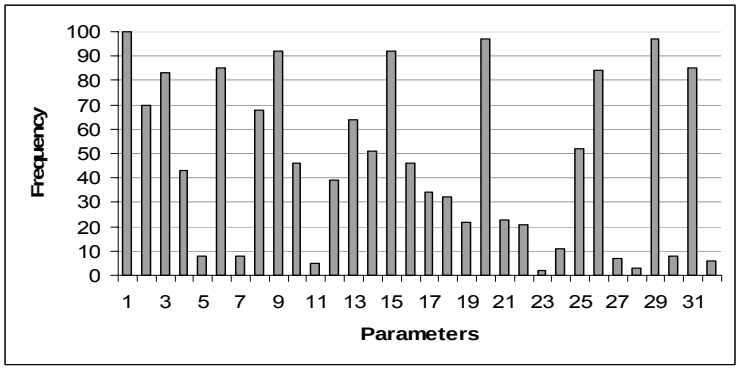

Fig. 4. The selection rate of every feature in 100 generations of genetic algorithm with 4 hidden units and output threshold 0.5.

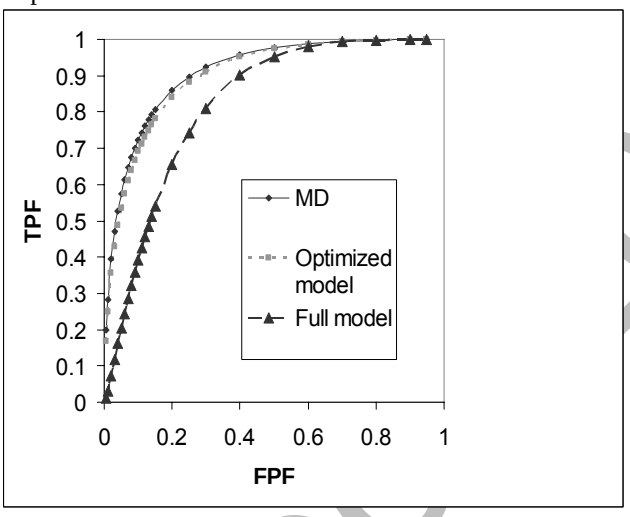

Fig. 5. ROC curves for comparing the performance of experienced radiologist, optimized ANN model and full ANN model.

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