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An approach based on probabilistic neural network for diagnosis of Mesothelioma's disease ☆

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ABSTRACT

Malignant mesothelioma (MM) is an aggressive progress tumor that results from mesotel cells and pleura usually incurs. The two important causes, in MM etiologies are known as asbestos and erionite, both mineral fibers. Environmental asbestos exposure and MM are one of the major public health problems of Turkey. In this study, two different probabilistic neural network (PNN) structures were used for MM's disease diagnosis. The PNN results were compared with the results of the multilayer and learning vector quantization neural networks focusing on MM's disease diagnosis and using same database. It was observed the PNN is the best classification with 96.30% accuracy obtained via 3-fold cross-validation. The MM disease dataset were prepared from a faculty of medicine's database using new patient's hospital reports from south east region of Turkey.

1. Introduction

Malignant mesotheliomas (MM) are very aggressive tumors of the pleura. These tumors are connected to asbestos exposure, however it may also be related to previous simian virus 40 (SV40) infection and quite possible for genetic predisposition. Molecular mechanisms can also be implicated in the development of mesothelioma [1].

Rural living is associated with the development of mesothelioma [2–4]. Soil mixtures containing asbestos, known as 'white-soil' or 'corak' can be found in Anatolia, Turkey and 'Luto' in Greece [4–8].

MM is a rare disease with an incidence rate of 1–2 per million/year [9] in the general population. In industrialized countries, the rate ranges from 1 to 5 per million/year for women and 10–30 per million/year for men [10–12]. The higher incidence rates in industrialized countries may be due to asbestos exposure [8].

Diagnosis usually appears when a patient visits the doctor to have symptoms checked out. Patients may be met with shortness of breath, pain in the chest or back, painful, persistent coughing or any number of other symptoms, none of which immediately alert the doctor to a diagnosis of mesothelioma [13].

Several studies were carried out about MM epidemiology, clinics in south east of Turkey [14–16]. As we know, there is not any study on MM disease diagnosis using artificial neural networks (ANNs) with prognostic data.

MM disease diagnosis is an important classification issue. Classification is often a very important part of process in many different fields like medicine. The use of artificial intelligence methods in medical diagnosis have been increasing gradually. There is no doubt that evaluations of data taken from patients and decisions of experts are the most important factors in diagnosis. However, sometimes different artificial intelligence techniques need for classification disease [17].

The PNN structures provide a general solution to pattern classification problems by following an approach developed in statistics, called Bayesian classifiers. The PNN uses a supervised training set to develop distribution functions within a

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pattern layer. Training of the PNN is much simpler than other ANNs structures. However, the pattern layer can be quite huge if the distinction between categories is varied and at the same time quite similar in special areas [18]. Because of the PNN provides a general solution to pattern classification problems, it is suitable for the disease diagnosis systems [19,20,22].

Some advantages of the PNN are

1. Very fast learning and recalling process.
2. No iteration for weight regulations in learning process.
3. No predecision for the number of hidden layers and the number of hidden nodes in each layer. With the predetermined.
4. Training samples, the number of hidden nodes could be effectively determined.
5. Limit number of samples for training.
6. Adaptability for architectural changes.

The multilayer neural network (MLNN) structure is the most common neural network structure which has been successfully used for the disease diagnosis systems [22–24]. The back-propagation (BP) algorithm [25] is widely recognized as a powerful tool for training of the MLNN structures. However, BP algorithm suffers from a slow convergence rate and often yields suboptimal solutions [26,27]. A variety of related algorithms have been introduced to address that problem and a number of researchers have carried out comparative studies of MLNN training algorithms [28,29]. Levenberg–Marquardt (LM) algorithm [28] used in this study provides generally faster convergence and better estimation results than other training algorithms [30,31].

The classification of the learning vector quantization (LVQ) neural network structure is based on the similarity of the unknown data and these prototypes. An LVQ neural network has a competitive layer and linear output layer. The competitive layer learns to classify input vectors. The linear output layer transforms the competitive layer's classes into target classifications defined by the user. The classes learned by the competitive layer can be referred as subclasses and the classes of the linear output layer can be referred as target classes [32,33]. The LVQ network structures have been successfully used for the disease diagnosis systems [19,20,22].

Computer simulation shows that PNN-based disease diagnosis system could be very effective in processing the diagnosis information. And it can be seen easily that good performance was achieved by our previous studies [19,20,22] and other disease diagnosis problems with PNN performance [22,34,35]. Therefore in this paper, a study of PNN on MM disease diagnosis was realized. The MM disease dataset were prepared from a faculty of medicine's database using patient's hospital reports. Also, the PNN results were compared with the results of the MLNN and LVQ neural networks focusing on MM's disease diagnosis and using same database.

We aimed to investigate clinical, laboratory, radiological characteristics of MM cases in the region where there is an intensive environmental asbestos contact. This study offers an alternative approach that MM may be useful for a prospect of early diagnosis. Another focus of the study is providing machine learning based decision support system for contributing to the doctors in their diagnosis decisions.

2. Methods

2.1. Data source

In order to perform the research reported, the patient's hospital reports from Dicle University, Faculty of Medicine's were used in this work. One of the special characteristics of this diagnosis study is to use the real dataset taking from patient reports from this hospital. Three hundred and twenty-four MM patient data were diagnosed and treated. These data were investigated retrospectively and analysed files.

In the dataset, all samples have 34 features because it is more effective than other factors subsets by doctor's guidance. These features are; age, gender, city, asbestos exposure, type of MM, duration of asbestos exposure, diagnosis method, keep side, cytology, duration of symptoms, dyspnoea, ache on chest, weakness, habit of cigarette, performance status, White Blood cell count (WBC), hemoglobin (HGB), platelet count (PLT), sedimentation, blood lactic dehydrogenise (LDH), Alkaline phosphatise (ALP), total protein, albumin, glucose, pleural lactic dehydrogenise, pleural protein, pleural albumin, pleural glucose, dead or not, pleural effusion, pleural thickness on tomography, pleural level of acidity (pH), C-reactive protein (CRP), class of diagnosis. Diagnostic tests of each patient were recorded.

2.2. Diagnosis of the Mesothelioma's disease using probabilistic neural network

The PNN provides a general solution to pattern classification problems by following an approach developed in statistics, called Bayesian classifiers. The network paradigm also uses Parzen Estimators which were developed to construct the probability density estimation required by Bayes theory [18]. The PNN structure was used in this study has a multilayer structures consisting of an input layer, a single hidden layer (radial basis layer), and an output layer (competitive layer) as shown in Fig. 1 [19–22,34,35].

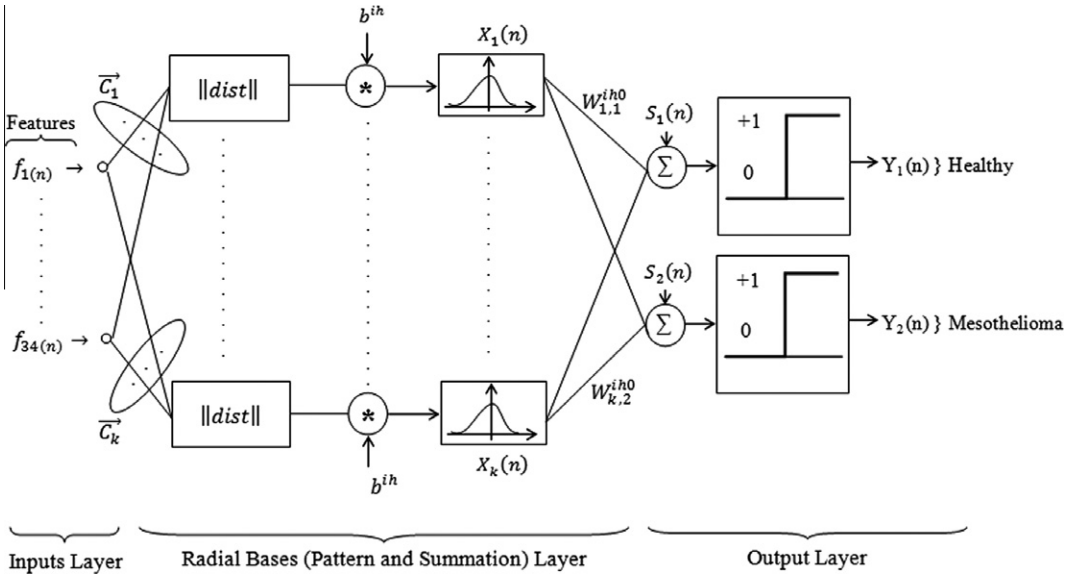

Fig. 1. Architecture of PNN.

In this system, real valued input vector is feature's vector and two outputs are index of two classes (healthy and mesothelioma). All hidden units simultaneously receive the 34-dimensional real valued input vector. The pattern layer consists of a set of radial basis functions. All of the radial basis functions are the same type (Gaussian) [18]. The architecture of PNN is shown as Fig. 1.

Equations which used in the neural network model are given as (1)–(5) [22].

$$X_j = \phi(\|\vec{f} - \vec{c}_j\| * b^{ih}) \tag{1}$$

$$\phi(x) = \exp(-x^2) \tag{2}$$

$$b^{ih} = 0.833/s \tag{3}$$

$$S_i = \sum_{j=1}^{h} W_{ji}^{ho} * X_j \tag{4}$$

$$Y_i = \begin{cases} 1, & \text{if } S_i \text{ is max of } \{S_1, S_2\} \\ 0, & \text{else} \end{cases} \tag{5}$$

where $i = 1,2$, $j = 1,2$, Y_i is the ith output (classification index), $\vec{f}$ is the 34-dimensional real valued input vector, W_{ji}^{ho} is the weight between the jth hidden node and the ith output node, $\vec{c}_j$ is the center vector of the jth hidden node, s is the real constant known as spread factor, b^{ih} is the biasing term of radial basis layer, and $\phi(\cdot)$ is the nonlinear radial basis function (Gaussian) [19,20,22].

Probabilistic neural network is a kind of radial basis network suitable for classification problems. PNN uses the supervised learning where the data is divided into two parts, the training and the testing part. The performance of PNN is related to two procedures: training procedure and recall procedure [36].

In the training procedure, the training data is given to the network and passes from the input layer through the pattern layer to the output layer. PNN uses training input data to set up the weights (W^i) between input and pattern layer as follows:

$$\begin{aligned} &\vec{C_{ij}} = \vec{f_j} \\ &\vec{f_j} = [f_1, f_2, f_3, \ldots, f_{34}] = W^i = [w_{ij}]_{ixj} \\ &i = 1,2,3,\ldots,34 \quad j = 1,2,3,\ldots,324 \end{aligned} \tag{6}$$

where w_{ij} is the jth weight value of weight (W^i). Then the network will define the weight (W^o) among the pattern layer and output layer as follows:

$$W_{ji}^{iho} = \begin{cases} 1, & \text{if the } j\text{ih sample and neuron belong to the same class} \\ 0, & \text{others} \end{cases} \tag{7}$$

If the jth sample is associated with class c, $c = 1,2$ the weight value is defined as 1 and others are 0.

In the recall procedure, the testing data is given to the network and the weights between the input and pattern layer calculates the Euclidean norm (Ed_j) of training and testing data. The Euclidean norm function can be described as:

$$Ed_j = \sqrt{\sum (w_{ij} - f_i)^2} \tag{8}$$

where w is the weight vector and f is the input vector. The pattern units generate the probabilistic vectors and after calculating the probabilities of each condition, the weight W^o transports these probabilities to the summation layer. The summation layer neurons sum the inputs from the pattern layer and transmit them to output layer. Output layer uses 'winner takes all' attitude to compare the probability density of each condition in the output layer [36].

2.3. Diagnosis of the Mesothelioma's disease using multilayer neural network

In the second stage of the study, the MLNN with two hidden layers was used for the MM's disease diagnosis. This MLNN structure (with one input layer, two hidden layers, and one output layer) is shown in Fig. 2. The hidden layer neurons (41 neurons for each hidden layer) and the output layer neurons use nonlinear sigmoid activation functions. In this system, 34 inputs are features, and two outputs are index of two classes (mesothelioma and normal). Equations used in the MLNN structure with two hidden layers are shown in (9)–(11).

Outputs of the first hidden layer neurons are,

$$\vec{X}^{ih1}(n) = 1 \Big/ \left(1 + \exp\left(W^{ih1}(n) * \vec{f}(n) + \vec{b}^{ih1}(n)\right)\right) \tag{9}$$

Outputs of the second hidden layer neurons are,

$$\vec{X}^{ih2}(n) = 1 \Big/ \left(1 + \exp\left(W^{ih2}(n) * \vec{X}^{ih1}(n) + \vec{b}^{ih2}(n)\right)\right) \tag{10}$$

Outputs of the network are,

$$\vec{Y}(n) = 1 \Big/ \left(1 + \exp\left(W^{ho}(n) * \vec{X}^{ih2}(n) + \vec{b}^{ho}(n)\right)\right) \tag{11}$$

where $W^{ih1}(n)$ are the weights from the input to the first hidden layer and $\vec{b}^{ih1}(n)$ are the biases of the first hidden layer, $W^{ih2}(n)$ are the weights from the first hidden layer to the second hidden layer and $\vec{b}^{ih2}(n)$ are the biases of the second hidden layer, $W^{ho}(n)$ are the weights from the second hidden layer to the output layer and $\vec{b}^{ho}(n)$ are the biases of the output layer, $\vec{f}(n)$ values are the features, $\vec{Y}(n)$ values are the outputs for the class index, and n is training pattern index.

The back-propagation (BP) algorithm [25] is widely recognized as a powerful tool for training of the MLNNs. But, since it applies the steepest descent method to update the weights, it suffers from a slow convergence rate and often yields suboptimal solutions [26,27]. A variety of related algorithms have been introduced to address that problem. A number of researchers have carried out comparative studies of MLNN training algorithms [28,29]. Levenberg–Marquardt (LM) algorithm [28] used in this study is one of the fastest types of these algorithms. Detailed computational issues about the application of the training algorithms to MLNN structures can be found in Refs. [30,31,37].

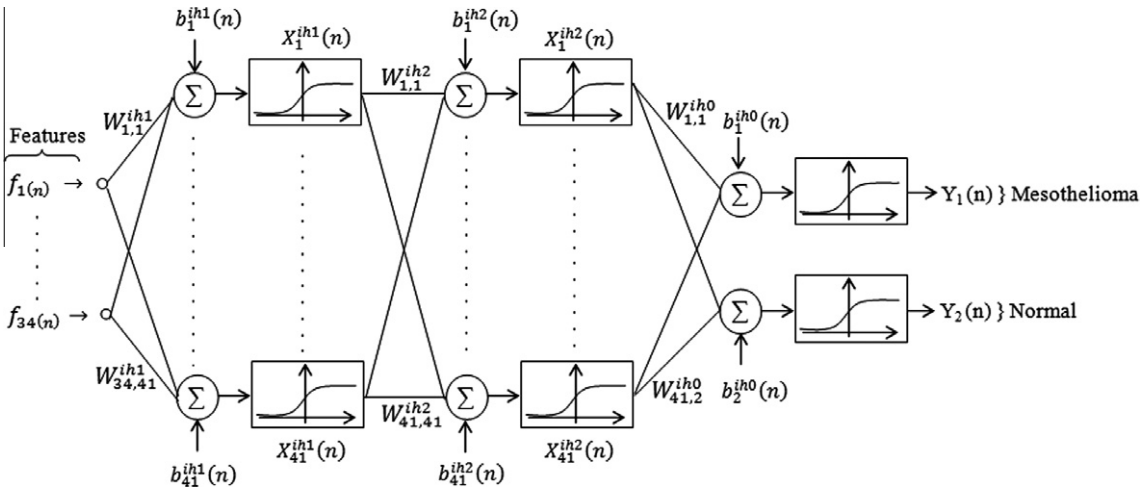

Fig. 2. Implementation of multilayer neural network for the MM's disease diagnosis.

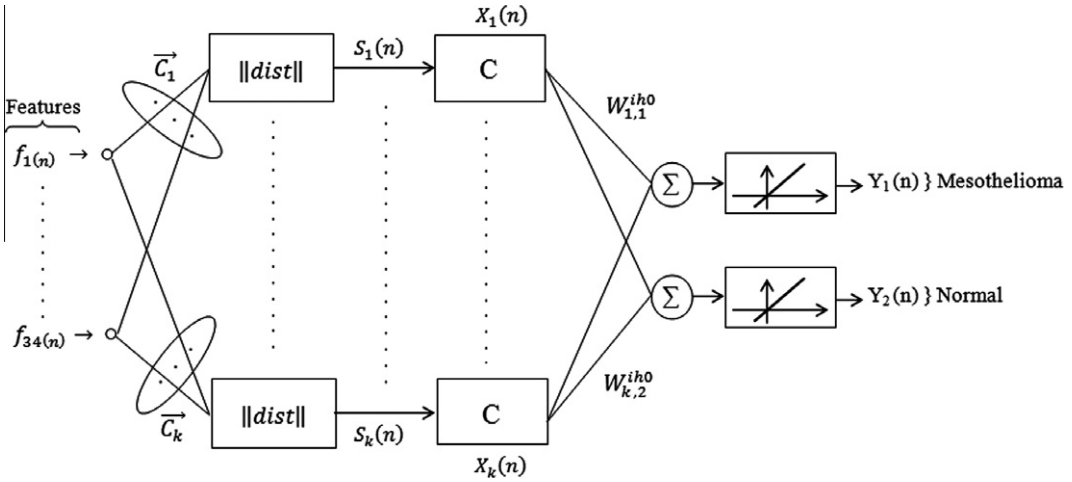

Fig. 3. Implementation of learning vector quantization neural network for the chest disease diagnosis.

2.4. Diagnosis of the Mesothelioma's disease using learning vector quantization neural network

At the third stage of this study, a learning vector quantization neural network was used for the MM's disease diagnosis. The network structure used for this purpose is shown in Fig. 3.

The LVQ structure [32] used in this study has a multilayer structures consisting of a single hidden layer (competitive layer) and an output layer (linear layer) of two units, as shown in Fig. 3. In this system, real valued input vector is feature's vector, and two outputs are index of two classes (has mesothelioma or not). The hidden layer consists of a set of competition functions. Equations which used in the neural network model are shown in (12)–(14) [19,20,22,34]

$$S_j = \|\vec{f} - \vec{c}_j\| \tag{12}$$

$$X_j = \begin{cases} 1, & \text{if } S_j \text{ is max of } \{S_1, \ldots, S_h\} \\ 0, & \text{else} \end{cases} \tag{13}$$

$$Y_i = \sum_{j=1}^{h} W_{ji}^{ho} * X_j \tag{14}$$

where $i = 1,2$, $j = 1,2,\ldots,h$, Y_i is the ith output (classification index), $\vec{f}$ is the 34-dimensional real valued input vector, W_{ji}^{ho} is the weight between the jth hidden node and the ith output node, $\vec{c}_j$ is the center vector of the jth hidden node. Detailed information about the realization of the LVQ structures can be found in Refs. [19,20,37].

2.5. Measures for performance evaluation

2.5.1. Classification accuracy

Classification accuracy [38] has been used for the study on MM disease diagnosis.

Equations used in the classification accuracies are shown in (15) and (16):

$$\text{Classification accuracy } (N) = \frac{\sum_{i=1}^{|N|} \text{assess}(n_i)}{|N|}, \quad n_i \in N \tag{15}$$

$$\text{assess } (n) = \begin{cases} 1 & \text{if classify}(n) = nc \\ 0 & \text{otherwise} \end{cases} \tag{16}$$

where N is the set of data items to be classified (the test set), $n \in N$, nc is the class of the item n, and classify(n) returns the classification of n by NNs [19–21].

2.5.2. Validation of the estimation results

The conventional (one training and one test) validation [35] and 3-fold cross-validation techniques were performed to compute the accuracy of the neural networks for MM's disease diagnosis. For the conventional validation (CV) method, the 227 cases where used as the training set and the remaining 97 cases were used as the test set. In k-fold cross-validation [19–22,30,34,35,39,24], whole data are randomly divided to k mutually exclusive and approximately equal size subsets. The

Table 1
Average of classification accuracies of test dataset for MM disease by 3-fold cross-validation (3xFC).

Methods	Experimental results Accuracy (%)			Average
	1.FC (108 samples)	2.FC (108 samples)	3.FC (108 samples)	
PNN (with 3xFC, RSM)	97.22	93.52	98.15	96.30
MLNN (with LM, 3xFC, two hidden layers)	95.37	92.59	95.37	94.41
LVQ (with 3xFC)	89.15	93.52	90.74	91.14
PNN (with CV)		93.81		93.81
MLNN (with CV)		91.75		91.75
LVQ (with CV)		89.69		89.69

classification algorithm trained and tested *k* times. In each case, one of the folds is taken as test data and the remaining folds are added to form training data. Thus *k* different test results exist for each training-test configuration [24]. The average of these results gives the test accuracy of the algorithm. If a neural network learns the training set of a problem, it makes generalization to that problem. So, this type trained neural network can give similar result for untrained test sets. But, if a neural network starts to memorize the training set, its generalization starts to decrease and its performance may not be improved for untrained test sets [31]. The *k*-fold cross-validation method shows how good generalization can be made using neural network structures [40].

3. Results

This work presents an application for PNN with random search (RMS) method (using 3xFC) on MM disease diagnosis. Also, the PNN results were compared with the results of the MLNN and LVQ neural networks focusing on MM's disease diagnosis and using same database. The classification accuracies obtained by PNN, MLNN and LVQ structures for MM disease were presented in Table 1.

In this study, the best result for the average classification accuracy was obtained using PNN (with 3xFC, RSM) structure by 96.30% as seen in the Table 1. This result is quite good for MM's disease diagnosis problem. The second best result for the classification accuracy was obtained using MLNN (with LM, 3xFC, two hidden layers) by 94.41%. The third best result for the classification accuracy was obtained using LVQ (with 3xFC) by 91.14%. The similar results were obtained for the neural network structures using conventional validation method. It is found that the neural network structures generally show good performances for MM's disease diagnosis problem.

4. Conclusions

These studies have applied three different ANNs structures to the MM's disease diagnosis problem using same dataset. As it can be seen from this study, a patient can be classified as having a MM's disease or not. According to overall results, it is seen that the most suitable neural network structure is PNN structure for classifying MM's data. The second best result for the classification accuracy was obtained using MLNN with LM for the diagnosis of MM's disease. It was seen that all ANN structures could be successfully used to help diagnosis of MM's disease. This classification accuracy is highly reliable for such a problem because only a few samples were misclassified by the system. 3-fold cross-validation technique is more suitable than conventional validation algorithm for PNN structures for the diagnosis of MM's disease. Finally, ANN structures can be helpful as learning based decision support system to contribute to the doctors in their diagnosis decisions.

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