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Prognosis of prostate cancer by artificial neural networks

Ismail Saritas [a,*], Ilker Ali Ozkan [a], Ibrahim Unal Sert [b]

[a] Department of Electronic and Computer Education, Technical Education Faculty, Selcuk University, Konya, Turkey
[b] Department of Urology, Meram Medicine Faculty, Selcuk University, Konya, Turkey

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ABSTRACT

In this study, an artificial neural network has been devised that yields a prognostic result indicating whether patients have cancer or not using their free prostate-specific antigen, total prostate-specific antigen and age data. Though this system does not diagnose cancer conclusively, it helps the doctor in deciding whether a biopsy is necessary by providing information about whether the patient has prostate cancer or not. Data from 121 patients who were definitively diagnosed with cancer after biopsy were used in devising the system. The results of the definitive diagnoses of the patients and the results of the ANN that was performed were analysed using confusion matrix and ROC analyses. As a result of ANN, which was implemented on the basis of these analyses, success rates of 94.11% and 94.44% were achieved for prognosis of disease and validity, respectively. The ANN, which yielded these high rates of reliability, will help doctors make quick and reliable diagnoses without any risks and make it a better option to monitor patients with low prostate cancer risk on whom biopsies must not be carried out through a policy of wait and see.

1. Introduction

Prostate cancer is one of the most common types of cancer found in men. Risk factors for prostate cancer include age, the family's cancer history and ethnic background. The definitive diagnosis of prostate cancer can be made through a biopsy. An initial diagnosis is made after patients' transrectal ultrasonography, rectal examination results and the amount of prostate-specific antigen (PSA) are assessed by a specialist doctor. The PSA level in blood has become one of the most common methods as a result of the studies conducted in recent years for early diagnosis of prostate cancer (Catalona et al., 1998; Shin Egawa et al., 1997; Van Cangh et al., 1996a).

PSA levels below 4 ng/ml in blood are considered normal, while levels between 4 and 10 ng/ml are considered limit values and levels above 10 ng/ml are high. It is stated that the higher the PSA level is, the higher the prostate cancer risk is (Catalona et al., 1998; Metlin, Lee, & Drago, 1991; Nguyen & Kreinovich, 2001; Seker, Odetayo, Petrovic, & Naguib, 2003; Van Shin Egawa et al., 1997; Van Cangh et al., 1996a,b). However, PSA values may not yield conclusive results about existence of prostate cancer because PSA levels can be increased by inflammation of prostate and benign prostate hyperplasia (BPH). Therefore, patients are also given rectal examination. If anomalies are observed at the end of the rectal examination, even if PSA results may seem normal, it is recommended that a prostate biopsy be performed and definitive diagnosis be made.

In general, prostate cancer is a disease that can be diagnosed with prostate biopsy in accordance with the suspicions that arose as a result of PSA test, rectal examination, and transrectal findings (Metlin et al., 1991; Nguyen & Kreinovich, 2001; Seker et al., 2003).

The studies that were conducted in this regard established that prostate cancer is related to age and the age–PSA relationship obtained in these studies has been given in Table 1 (Brawer & Kirby, 1999; Prostate Cancer Symptoms, 2009).

There is a need for biopsy and definitive diagnosis besides transrectal ultrasonography and rectal examination for diagnosis of prostate cancer. Despite the need for biopsy for conclusive diagnosis, patients with low cancer risk avoid this process due to possible complications that may arise, the risk of rectal mucosa being damaged and its high costs. Therefore, before they agree to biopsy, patients may prefer a different optimum method that may yield a more accurate result. To attain this goal, a prediction method has been developed that determines patients' cancer risk on the basis of their age, ethnic background, history of cancer in the family and PSA levels (Prostate Online Calculator, 2009); besides, various logical models and ANN have been devised since 1998 (Cınar et al., 2009). These models, which use clinical and laboratory data, prevent patients with benign prostate hyperplasia from undergoing unnecessary biopsy operation as well as providing satisfactory information about diagnosis of prostate cancer. For this purpose,

* Corresponding author. Address: Selcuk University, Technical Education Faculty, Campus 42075, Selcuklu-Konya, Turkey. Tel.: +90 3322233354; fax: +90 3322412179.
E-mail addresses: isaritas@selcuk.edu.tr, ismail@selcuk.edu.tr (I. Saritas).

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Table 1
The normal PSA values that depend on age.

Age (year)	PSA (ng/ml)
40–49	<2.5
50–59	<3.5
60–69	<4.5
>70	<6.5

studies are underway on different fields of artificial intelligence such as fuzzy expert system that can identify cancer risk by using relationships between prostate volume (PV), PSA level and age (Abbod, Keyserlingk, Linkens, & Mahfouf, 2001; Allahverdi, 2002; Allahverdi & Yaldiz, 1998; Boegla, Adlassniga, Hayashic, Rothenfluhd, & Leiticha, 2002; Saritas, 2003; Saritas, Allahverdi, & Sert, 2003) and ANN that can detect prostate cancer risk at an early phase (Cınar et al., 2009; Lorenz, Blum, Ermert, & Senge, 1997; Ronco & Fernandez, 1999).

ANN is better able to predict patients' prostate biopsy results than traditional statistics and assess large numbers of variables ranging from non-linear relationships to logical regression.

The purpose of this study is to develop a model that can determine whether patients have prostate cancer or not on the basis of data about their tPSA, fPSA and age prior to prostate biopsy.

2. Materials and method

The present study used only a small portion of the biopsies performed in the urology clinic at Meram Faculty of Medicine of Selcuk University and the laboratory data belonging to 121 male patients who were diagnosed and treated in the urology clinic of the Faculty of Medicine of Ankara University between the years of 2002 and 2004. The tPSA (0.28–150 ng/ml), fPSA (0.04–25 ng/ml), and age (44–89) data belonging to these patients and the results of the definitive diagnosis after the biopsy indicating whether they had cancer or not were used in the study.

MATLAB Neural Network Toolbox software was used in order to devise an ANN and conduct analyses.

2.1. Artificial neural network

ANN are computer systems that have been devised to automatically perform abilities such as deriving new information through learning, forming new information and discovering, all of which are characteristics of the human brain.

Generally, it consists of three layers, i.e. an input layer, one or more hidden layers and an output layer. Each layer has a certain number of components attached to one another called neurons or nodes. Each of the neurons is connected to the other with weights and accompanying communication networks. Signals move through neurons over weights. Each neuron receives multiple inputs from other neurons depending on their weights and generates an output signal that may also be generated by other neurons (Cınar et al., 2009; Lorenz et al., 1997; Ronco & Fernandez, 1999).

In order to devise an ANN, the network is processed in two levels, i.e. training and testing. In the level of training, the network is trained for an output prediction on the basis of input data. In the testing level, on the other hand, it is tested to stop or save the training and is used to predict an output.

When the tested error reaches the desired tolerance value, the training of the network is stopped (Lorenz et al., 1997; Ronco & Fernandez, 1999).

The back propagation (BP) algorithm is the most popular algorithm that has the widest area of use. BP is composed of two phases, namely procedures of feed forward and back propagation.

During feed forward, information that is processed from the input layer to the output layer is generated. In the case of back propagation, on the other hand, the difference between the network output value obtained from the feed forward procedure and the desired output value is compared to the desired difference tolerance and the error in the output layer is calculated. The error thus obtained is propagated backward in order to update the links in the input layer (Cınar et al., 2009; Ronco & Fernandez, 1999).

The BP training algorithm is a gradient descent. The BP algorithm functions to improve the performance of the network by reducing the total error through changing weights along its gradient. When the tested mean squared errors (MSE) stop decreasing and they begin to increase, which is a sign of over-training, the training is stopped (Lorenz et al., 1997; Ronco & Fernandez, 1999).

$$\mathrm{MSE}\% = \frac{1}{n}\sum_{i=1}^{n}(d_i - O_i)^2 \tag{1}$$

Here d_i is targeted or real value, O_i is network output or predicted value, and n is the output data number.

2.2. Application of artificial neural network to patient data

The purpose of this devised ANN is to determine existence of prostate cancer (PCa) on the basis of the tPSA, fPSA and age data. Data belonging to the 121 patients were divided into two, namely a training set and a test set. Ninety two data (70% of the total data) selected randomly from these data were used for the training data set of the ANN and the remaining 29 data (30% of the total data) were used for the test set.

In this study, a feed forward network structure that contains an input layer, a hidden layer and an output layer (Fig. 1) was used. After the ANN structure was designed, the data obtained in the experimental study were normalized in the 0–1 value set using Eq. (2) in order to improve the characteristics of the training. The back propagation algorithm was used in the training procedure. Different transfer functions (Purelin, Tansig, Logsig, etc.) were used and tried in the neurons in the hidden and output layers and Logarithmic-Sigmoid (Logsig) was selected as the transfer function that yielded the best result.

$$x_{\mathrm{norm}} = \frac{x - x_{\min}}{x_{\max} - x_{\min}} \tag{2}$$

The training data set was used to determine ANN neuron and bias weight values. Training was repeated to obtain the lowest level of error by changing the number of neurons and the epoch number. Then, the trained algorithm was applied on the test data set.

First, ANN was trained by changing the number of neurons in the hidden layer (2–100) in order to determine the artificial neural

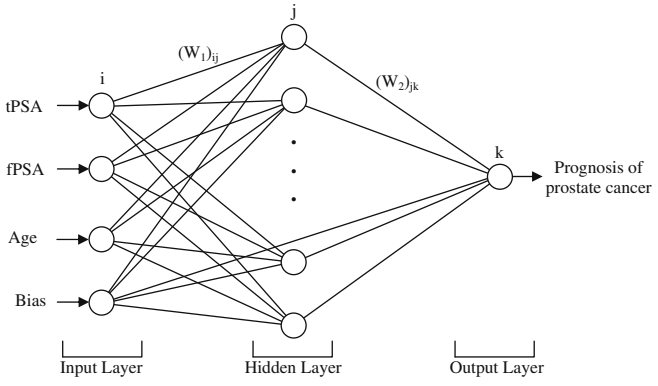

Fig. 1. The structure of ANN.