A Computer-Aided Detection System for Automatic Classification of Prostate Cancer from Benign Hyperplasia of Prostate

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Abstract — *Intelligent computer programs were implemented to aid physicians and other medical professionals in making difficulty medical decisions. In this paper, a computer aided detection (CAD) system is designed that classifies prostate neoplasia into two classes (cancer and hyperplasia) for supporting urologist. Early detection of Prostate Cancer (PCa) is crucial for patient survival. Automated diagnostic method could reduce diagnostic complications, financial and human resources. In presented system, data from 360 patients were used who diagnosed after biopsy with cancer and benign hyperplasia of prostate. In order to design present CAD, we have used; Bayesian regulation Backpropagation Neural networks (BRBNN). Performance of selected algorithm in detection of prostate cancer was evaluated by calculating sensitivity, specificity indicators and areas under receiver-operating characteristics (ROC) curve. The result of present study shows that, CAD based on BRBNN could serve as a strong diagnostic tool with 92.88% specificity, 90.62% sensitivity, 91.67% accuracy for early automatic detection of prostate cancer from benign prostate hyperplasia*[1].

Keywords — decision support system, prostate cancer, benign hyperplasia of prostate, neural network .

I. Introduction

Medical diagnostic decision support systems have become an established component of medical technology. Computers could have a role in supplementing patient assessments, diagnosis and treatment in a variety of clinical settings. A number of software tools are being designed and are already in use. These tools are found useful in administrative, data management and in clinical experiments. These tools reduce time and minimize errors in medical practice. The clinical decision support system synthesizes and Integrates patient specific information, perform complex evaluations and present the results to clinicians in a timely fashion [1-3]. Computers may be of immense benefit to them. Decision support systems may enable the doctor to assess his performance and improve his diagnostic accuracy. Prostate Neoplasia problems including benign hyperplasia and cancer of prostate are very common and cause significant delay in recovery and often require costly investigations before coming to its diagnosis[4-6]. Adenocarcinoma of the prostate is now the most frequently diagnosed male malignancy with 1 in every 11 men developing the disease[7]. It is the second most common cause of cancer deaths in men. Each year in the UK more than 25,000 men are diagnosed with prostate cancer and approximately 10,000 die from the disease. The equivalent incidence and mortality numbers in the USA are approximately 239,900 and 32,400, whilst the world wide numbers are approximately 679,000 and 221,000, respectively [8-11]. Historically, DRE was the principle method of prostate cancer detection. The technique is limited and subject to inter-observer variation. The sensitivity of DRE in predicting organ-confined disease is approximately 50%. Since its introduction into clinical practice in 1987, PSA testing has become a mainstay in the management of cancer of the prostate[12]. There appears to be a linear relationship between increasing PSA levels and extra prostatic tumor spread; 64% of those with a PSA of <4 ng/ml had organ-confined disease, the proportion falling to 9% for those with a PSA of >50 ng/ml[13]. 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) and there are a grey area in the range 4–10 ng/ml, partly due to the overlapping between prostate and benign prostatic hypertrophy (BPH). About half the men with prostate cancer fall into this PSA group and serial measurements or supplementary investigations may be required. 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[14, 15]. 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[16, 17]. Prostate cancer diagnosis is complicated by the biological heterogeneity of the disease. There are a lot of treatment options, which has different short and long term risks and complications. These make difficult to choice the treatment for the individual. The patient dilemma has gained increased awareness among urologist. There is an obvious need for decision-making tools that individual patients and physicians can apply to the specific

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parameters of disease to reach an informed decision[4]. 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 biopsy are rectal mucosa being damaged, Hematuria and its high costs[14, 18, 19].Because there is need to Medical diagnostic systems to help doctors and patients.

The conventional approach to build medical diagnostic system requires the formulation of rules by which the input data can be analyzed. But the formulation of such rules is very difficult with large sets of input data. Realizing the difficulty, a number of quantitative mathematical and statistical models including pattern classification technique such as artificial neural networks (ANN), rolled based system, discriminant analysis and regression analysis has been applied as an alternative to conventional clinical and medical diagnostic. Among the mathematical and statistical modeling techniques used in medical decision support, artificial intelligence (AI) and artificial neural networks attract many attentions in recent studies and in the last decade, the use of neural networks has become widely accepted in medical applications. This is manifested by an increasing number of medical devices currently available on the market with embedded AI algorithms, together with an accelerating pace of publication in medical journals, with over 500 academic publications year featuring Artificial Neural Networks (ANNs). Neural networks are being used in medical diagnostic support systems to assist human decision-makers in disease diagnosis. ANN can be trained without encapsulating the knowledge derived from these rules. Hence ANN has been found to be more helpful than traditional medical expert system in the diagnosis of diseases [15, 20-26].

ANN is better for prediction of patients' prostate biopsy results than traditional statistics and assess large numbers of variables ranging from non-linear relationships to logical regression[14]. The purpose of this study is to develop a model that can detect and diagnosis whether patients have prostate cancer or benign prostate hyperplasia on the basis of data about their tPSA, fPSA, ratio (fPSA/tPSA) and age prior to prostate biopsy. In this study, we designed a medical decision support system in order to avoid unnecessary biopsy and reduce diagnostic costs.

II. Materials and Methods

Data

The data from 300 men were collected at the Urology Department of Imam Khomeini Hospital, Tehran, Iran since January 2008 to March 2011. The distribution of the patients into pathology classes was prostate Adenocarcinoma (100), chronic prostatism or benign prostatic hyperplasia (200).

The data set is a two-class problem either positive or negative for prostate cancer disease. Laboratory data belonging to 181 cancerous patients and other 179 patient were diagnostic to the BPH, their diseases found by biopsy performed in different urology clinic between years of 2008 and 2011 and the results of the definitive diagnosis after biopsy indicating whether they had cancer or not were used in the study. The Data including laboratory data like PSA, freePSA, result of disease and demographic data like Age. Thereafter, the ratio (fPSA/tPSA) calculated and database was formed. The above dataset 181 patients are having prostate cancer, which can be interpreted as "1" and the remaining patients are not having prostate cancer and can be interpreted as "0". MATLAB Neural Network Toolbox software version 2012 was used in order to devise an ANN and conduct analyses. The descriptive statistics of preoperative parameters are given in Table 1:

TABLE 1 Pro Disease Database description of attributes*

Num	Attribute description	Values of Attribute	Mean	Standard deviation
1	Age	45-91	69	9.89
2	Total PSA	0.1-100	13	17.15
3	Free PSA	0.07-49.9	2.84	4.74
4	Ratio	0.018-2.9	0.2549	0.2

* N = 360 observations including 181 malignant and 179 benign.

In order to observe the distribution Prostate neoplasia data set including prostate cancer and benign hyperplasia of prostate, the data has presented in two figures. Figure 1 presents the distribution of raw cancer and benign hyperplasia of prostate dataset according to the first three features (Age, PSA, and freePSA attributes).

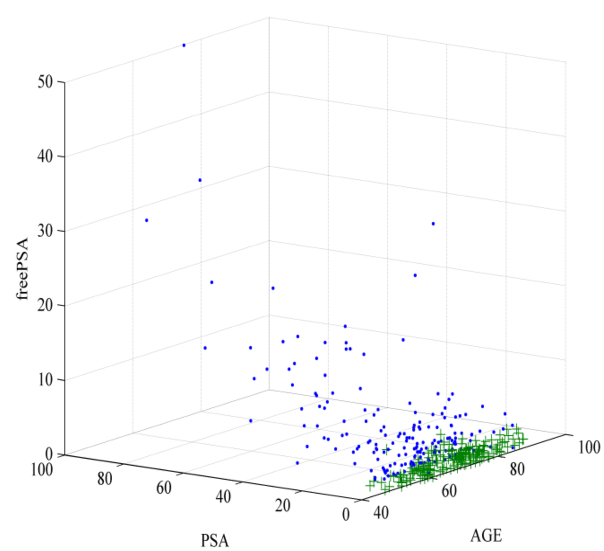

Fig1. Distribution of row prostate neoplasia dataset including prostate cancer '.' And benign hyperplasia of prostate '+', according to three feature

In addition figure 2 presents raw cancer and benign hyperplasia of prostate dataset according to main feature to detection of cancerous and benign prostate organ. It can from conclude figure 2 that there is much overlapping between benign and cancerous patient.

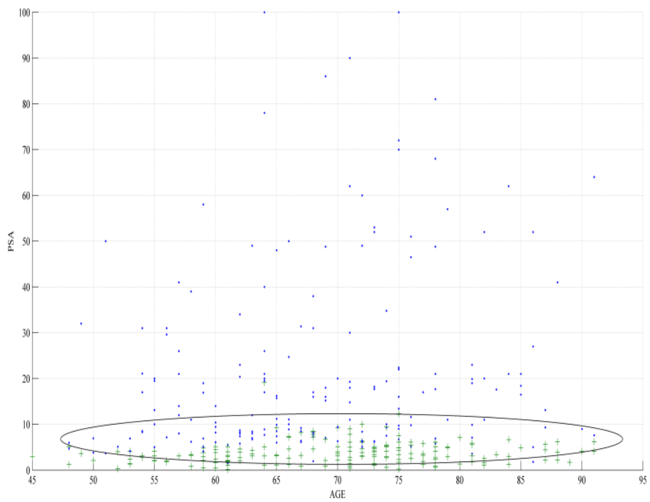

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Fig2. Distribution of row prostate neoplasia dataset including prostate cancer '.'And benign hyperplasia of prostate '+', and overlapping between two class according to two feature.

From 360 cases, 80% were randomly selected as training group and remaining 20% as validation group. Cases of training group (n=228) were used in development of the neural network model. The validation group (n=72) was used to test the performance of these models.

Many applications tried to help human experts, offering a solution. Artificial neural networks (ANNs) have been used in a great number of medical diagnostic decision support system applications because of the belief that they have greater predictive power. ANNs are computational architectures composed of interconnected units (neurons). Its name reflects its initial inspiration from biological neural systems, though the functioning of today's ANNs may be quite different from that of the biological ones. Sometimes the term neural network also refers to the corresponding mathematical model, but properly speaking a network is architecture. In modern medicine, artificial intelligence has been used for diagnosis, treatment selection, and prediction of outcome in many clinical scenarios[27, 28]. The ability to exploit nonlinear relationships between variables makes ANN suitable particularly for analysis of complex cancer data and for prediction of treatment outcome. It has been demonstrated that neural networks can predict survival in patients with breast, lung, prostate, and colorectal cancer [29-32]. There are many types of neural networks; the back propagation neural network (BPNN) is one of the most popular algorithms used for prediction. Back propagation training technique uses a gradient-descent approach for adjusting the weights of ANN. A multi-layer feed-forward neural network typically has an input layer, an output layer and one or more hidden layers. Feed-forward back propagation neural network is used as a classifier to distinguish between infected (cancerous tissue) and no infected (noncancerous tissue) person in both cases. In multilayer feed-forward networks, neurons are arranged in layers and there is a connection among the neuron of other layers. The feature as inputs are applied to the input layer and the output layer contributes to the output directly. Other layers between input and output layers are called hidden layers. Inputs are propagated in gradually, modified form in the forward direction, finally reaching the output layer[33, 34]. As algorithm's name implies, errors (and therefore learning) propagate backwards from output nodes to the inner nodes. So technically speaking, back-propagation is used to calculate error's gradient of network with respect to network's modifiable weights. Then, this gradient is almost always used in a simple stochastic gradient descent algorithm to find weights that minimizing the error. Often the term "back-propagation" is used in a more general sense, to refer to entire procedure encompassing both the calculation of the gradient and its use in stochastic gradient descent[35]. There are many algorithm based Backpropagation concept that have different convergence speed and is very difficult to know which training algorithm will be the fastest for a given problem[36]. In this study, back-propagation based multi-layer perceptron (MLP) network was used. Bayesian regulation back propagation algorithm was tested.

A. Bayesian regulation back propagation (BRBNN)

Bayesian regulation back propagations are composed of interconnecting artificial neurons (programming constructs that mimic the properties of biological neurons).Artificial bayesian regulation back propagations may either be used to gain an understanding of biological bayesian regulation back propagations, or for solving artificial intelligence problems without necessarily creating a model of a real biological system. The real, biological nervous system is highly complex: artificial bayesian regulation back propagation algorithms attempt to abstract this complexity and focus on what may hypothetically matter most from an information processing point of view. The original inspiration for the term Artificial Bayesian regulation back propagation came from examination of central nervous systems. In an artificial bayesian regulation back propagation, simple artificial nodes, variously called "neurons", "neurodes", "processing elements" (PEs) or "units", are connected together to form a network of nodes mimicking the biological bayesian regulation backpropagations hence the term "artificial Bayesian regulation back propagation". A Bayesian regulation back propagation (NN) is a computer software (and possibly hardware) that simulates a simple model of neural cells in animals and humans. The purpose of this simulation is to acquire the intelligent features of these cells. In this document, when terms like neuron, bayesian regulation back propagation, learning, or experience are mentioned, it should be understood that we are using them only in the context of a NN as computer system[37].

We used standard ANN package contained in the MATLAB 2012 Version 7.14 software for implementing Scaled conjugate gradient Back propagation Algorithms. The key design decisions for neural networks used in classification are architecture and training process[38]. Research has shown that the most important factor in MLP structure is the choice of hidden neurons number. In present study, after several trials it was seen that a single hidden layered network achieved the task in high accuracy. Different transfer functions (Purelin, Tansig, Logsig, etc.) were used and tried in the neurons in hidden and output layers and hyperbolic tangent sigmoid (Tansig) was selected as transfer function for hidden layer and output layers, that selection was yielded the best result. Research has shown that another parameter in success of neural network is number of nudes in hidden layers. It will significantly influence network's ability to generalize from the training data to unknown examples but there are no general rule for selection of appropriate number of hidden layers units[39-44]. The network with small number of neurons in hidden layers may not be sufficiently powerful to model a complex function. On the other hand, a neural network with too many neurons may lead to overfitting the training sets and lose its ability to generalize which is main desired characteristic of a neural network. The most popular approach to findings the optimal number of hidden layers is trial and error[39]. In this study the neural network was trained by changing the number of neurons among 1 and 100 in hidden layers for all algorithms in order to determine the artificial neural network algorithm that yielded the best result and optimum structure.

In applications, the number of nodes in input layers and in output layers change according to the number of samples and class labels in used dataset, respectively. Figure 2 shows the structure of ANN with Scaled conjugate gradient.

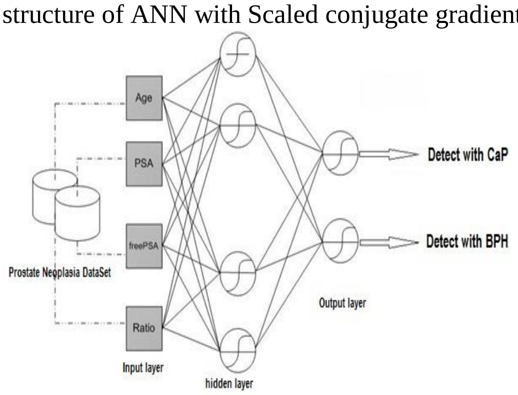

Fig2: The structure of ANN with Scaled conjugate gradient.

B. Result

In this section, the performance measure criteria to test the performance of proposed method have been given. Later, the subsection of results and discussion are explained.

After designing the ANN structure, diagnosis is an essential step in medical care. Usually this involves 'diagnostic tests' of some description. A health check is also a group of diagnostic tests. Decisions about medical treatment are made on the basis of test results. These tests are sensitivity, specificity, positive and negative predictive values[45]. In this research we use Confusion matrix and ROC analyses in order to calculate the success rate of DSS that was carried out.

C. Performance measurement criteria

In order to test the performance of proposed method, the classification accuracy and sensitivity specificity values were used on the predicting of prostate neoplasia of Urology department of Imam Khomeini hospital in Tehran, Iran. These measures were shortly explained on a confusion matrix. After constructing our model and testing it using 300–60 train–test samples, we build the confusion matrix for the dataset. Confusion matrix is shown in Table 2 (actual vs. predicted) and other parameters which are computed using confusion matrix are shown with the following equations. The entries in the confusion matrix have the following meaning in the context of our study:

TABLE 2 REPRESENTATION OF CONFUSION MATRIX

Actual	Predictive	
	Positive	Negative
Positive	TP = 29	FP =3
Negative	FN = 2	TN =26

When the diagnostic test conducted on all of data, the following results are obtained: For sensitivity and specificity analysis, we use the following expressions.

Sensitivity is the ability to distinguish the patient with Prostate Cancer from the true Cap's cases.

$$Sensitivity = \frac{TP}{TP+FN} \qquad (1)$$

From Eq. (1), sensitivity was found to be: 90.62%

Specificity is the ability to distinguish the patient with BPH from the true BPH cases.

$$Specificity = \frac{TN}{TN+FP} \qquad (2)$$

From Eq. (2), specificity was found to be: 92.85

Classification accuracy: accuracy is the likelihood of correctly predicted total number of modules and it is computed using Eq. (3) :

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \qquad (3)$$

From Eq. (3), accuracy was found to be: 91.67

III. CONCLUSION AND DISCUSSION

We have presented a medical decision-support system with purpose of aiding medical specialist in their classification and diagnosis of prostate neoplasia disorders. The decision support system contains a classification system, and this system can help doctors in making accurate decision about prostate cancer and benign hyperplasia of prostate. By using such system, doctors can remove unnecessary biopsy and reduces cost. In addition this system can speed up diagnostic time.

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