DOI: 10.36719/2707-1146/03/25-29

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PREDICTION OF PATHOLOGICAL STAGE IN PROSTATE CANCER PATIENTS BY PROSTATE MRI: ARTIFICIAL NEURAL NETWORKS METHODS

Summary

Prostate cancer is a disease that is most common in males and causes death in the second frequency in the world. If prostate cancer is diagnosed in the early stages, surgery can be performed and the disease can be cured.

The aim of this study is to design an expert system to catch prostate cancer as early as possible with the chance of surgical treatment by being diagnosed in the limited phase of the organ. The most accurate diagnosis is to use risk factors such as Age, PSA (prostate Specific antigen), Clinical Stage, Tumor Size, Prostate Size and ISUP (International Society of Urological Pathology). In other words, it is aimed to biopsy the minimum number of patients and to diagnose the largest number of cancers.

For better detection both sets of characteristics are used in our research. In this study, as a diagnostic model, we use a system based on multiple-layer (deep) feed-forward neural networks. The networks are trained with Differential Evolution training algorithm using in parallel a pair of data sets (training and validation sets) to avoid overfitting and improve model's generalization ability (performance on untrained data). The applied DE algorithm has allowed avoiding local minima of error function during the training. A third data set is used for testing trained network performance. According to the obtained results, this method demonstrated better results than other existing approaches.

Key words: *Prostate Cancer, Artificial Neural Network, Differential Evolution Optimization Computational Intelligence Methods*

Prostat MRT tərəfindən prostat xərçəngi xəstələrində patoloji mərhələnin proqnozlaşdırılması: Süni sinir şəbəkələri metodları

Xülasə

Prostat xərçəngi, kişilərdə ən çox yayılan və dünyada ikinci yerdə olan bir xəstəlikdir. Prostat xərçəngi erkən mərhələlərdə diaqnoz qoyulsa, əməliyyat edilə bilər və xəstəlik sağalda bilər.

Bu araşdırmanın məqsədi orqanizmin məhdud fazasında diaqnoz qoyularaq cərrahi müalicə şansı ilə prostat xərçəngini mümkün qədər erkən tutmaq üçün mütəxəssis sistem hazırlamaqdır. Ən doğru diaqnoz Yaş, PSA (prostata xüsusi antigen), Klinik Mərhələ, Şiş Ölçüsüsü, Prostat Ölçüsü və ISUP (Beynəlxalq Uroloji Patologiyası Cəmiyyəti) kimi risk faktorlarından istifadə etməkdir. Başqa sözlə, xəstələrin minimum sayını biopsiya etmək və ən çox xərçəng diaqnozu qoymaq məqsədi daşıyır.

Daha yaxşı aşkarlanması üçün tədqiqatımızda hər iki xüsusiyyət dəsti istifadə olunur. Bu araşdırmada, diaqnostik bir model olaraq çox qatlı (dərin) qidalandırıcı sinir şəbəkələrinə əsaslanan bir sistem istifadə edirik. Şəbəkələr, həddindən artıq uyğunlaşmamaq və modelin ümumiləşdirmə qabiliyyətini artırmaq üçün (öyrətilməmiş məlumatlar üzərində işləmək) paralel olaraq bir cüt məlumat dəsti (təlim və qiymətləndirmə dəsti) istifadə edərək Differensial Evolution təlim alqoritmləri ilə təlimləndirilir. Tətbiq olunan DE alqoritmi təlim əsnasında səhv funksiyalarının yerli minimumlarından qaçmağa imkan verdi. Üçüncü bir məlumat dəsti təlim keçmiş şəbəkə performansını yoxlamaq üçün istifadə olunur. Əldə edilmiş nəticələrə görə, bu üsul digər mövcud yanaşmalardan daha yaxşı nəticələr göstərdi.

Açar sözlər: *Prostat xərçəngi, süni neyron şəbəkəsi, diferensial təkamül optimallaşdırma hesablama intellekt metodları*

Introduction

The "prostate", which means preservatives in Greek (prostates), is an organ similar to the chestnut found between the bladder and the external urinary tract at the end of the discharge system. The prostate is not a disease, it is an organ found in all men. Prostate inflammation growth complaints to old age or cancer. Generally they are; Frequent urination, urinating, burning, urine is not a complete feeling, complaints such as urinating. Early diagnosis is vital for patients, as one of every 12 males is considered to have prostate cancer. In order to diagnose early prostate cancer, the most PSA test is applied [1].

Since cancer experts do not have a device such as prostate cancer, mammography, it is noted that the tissue sample was randomly taken in the biopsy and that the tumor could easily be overlooked. The definitive diagnosis of cancer is possible only by examining the samples taken by a pathologist under the microscope. Pathologist, the information obtained from the examination, with the diagnosis is transmitted to the doctor responsible for the treatment. The doctor decides the most appropriate treatment method by analyzing this information. The importance of the correct diagnosis for a successful treatment is enormous [2]. In some cases, definitive diagnosis is a very difficult problem and may vary by 30%-40% among the expert opinions. In such cases, auxiliary methods that use objective measurements will help the expert in improving the performance of the diagnosis.

For the physician to diagnose, the decision-making process through a variety of data from patients and the need to develop expert systems to help eliminate the difficulties in pre-diagnosis [3]. In this way, both the early diagnosis and the tests for the disease can be prevented due to the psychological problems that may occur in patients. In this study;

In this study among all possible methods to create required model, we have chosen multi-layer deep feed-forward neural networks for a number of reasons [4]. First, because they are indeed universal approximators and can be used to reveal any complex relationships in large data sets. Second, because recent developments in the theory and technology have significantly increased efficiency of neural networks. For instance, increased processing power and parallel processing abilities of modern computers allow efficient use of new evolutionary training approaches to effectively battle such bottleneck of large multi-layer neural networks as time-consuming parameter adaptation. The global parameter search, which avoids local minima trapping, is now much faster than ever. Third, because, neuron models are not now required to be constrained by smooth differentiable transfer functions, connection weights by simple numerical values, and network architecture for large input/output systems by single hidden layer of neurons.

Methods

The data of 84 male patients (mean age 63.5 and age range 52-75) who applied to the Urology Department of Hacettepe University were collected in the period from X to Y. 6 different attribute vectors were formed from the data obtained from 84 different patients for classification. According to the pathological results of these patients diagnosed with prostate cancer. Age, PSA (Prostate Specific Antigen), Clinical Stage, Tumor Size, Prostate Size and ISUP (International Society of Urological Pathology) score parameters were used to diagnose patients.

PSA (Prostate Specific Antigen) is a substance produced only in the prostate. The Normal value is below 4 ng/ml. However, when there is a problem with the prostate, the blood is more and more proportion, and the rise of the PSA level is noticeable. The only reason for the PSA height is the prostate it's not cancer. Benign prostate enlargement and prostate inflammation also elevates PSA.

The used detection model is multi-layer feed-forward neural network with non-linear transfer function based neurons in hidden layers and linear neurons in input and output layers.

Given particular values for the neural network parameters, and given values for the inputs, a neural network generates a value for each output:

$$y_i = NN_W \ \mathbf{x} \ ,$$

The operation of an L-layer feed-forward perceptron neural network at each layer $l\,(l = 1,...,L-1)$ can be described by the following equation:

$$y_i^{(l)} = f^{(l)}\left(\left(\sum w_{i,j}^{(l)} x_j^{(l)}\right) + \theta_i^{(l)}\right),$$

where $f^{(l)}(.)$ is the activation function used at network layer l.

In the vector form this can be written more compactly:

$$\mathbf{y}^{(l)} = f^{(l)} \ \mathbf{w}^{(l)}\mathbf{x}^{(l)}$$

Or, based on only the network activations as:

$$\mathbf{y}^{(l)} = f^{(l)} \ \mathbf{w}^{(l)}\mathbf{y}^{(l-1)}$$

Matrix $\mathbf{w}^{(l)}$ will denote weights connecting all neurons of layer l with all neurons of layer $(l+1)$. Thus for an L-layered NN set W will contain matrixes

$$\mathbf{w}^{(0)}, \mathbf{w}^{(1)}, ..., \mathbf{w}^{(L-1)}$$

$w_{i,j}^{(l)}$ is the weight of connection to neuron i at layer l from neuron j at the previous layer $(l-1)$, $\theta_i^{(l)}$ is the threshold parameter of neuron i at layer l

The total number of connection weights and thresholds (i.e. number of elements in the set W) for a feed-forward neural network is

$$N = \ n_0 + 1 \ n_1 + \ n_1 + 1 \ n_2 + ... + (n_{L-2} + 1)n_{L-1}$$

The evolutionary algorithm used for training is Differential Evolution [5], which is one of the fastest population based algorithms for global search in multi-dimensional vector space.
The DE algorithm in a basic form can be described in **Figure 1**.

Step 0. Initialize DE
Step 0.1. Set algorithm parameters: *f* (mutation rate), *cr* (crossover rate), and *ps* (size of population)
Step 0.2. Define the cost function as function of error function of current RFNN parameters

Step 1. Randomly generate ps vectors (potential network parameter sets) from respective parameter spaces (e.g. in the range [-1, 1]) and form a population $P=\{X_1, X_2, ..., X_{ps}\}$

Step 2. While Termination condition is not met generate new parameter sets:
Step 2.1. Choose a next vector X_i (i=1,...,ps)
Step 2.2. Choose randomly different 3 vectors from P: X_{r1}, X_{r2}, X_{r3} each of which is different from current X_i
Step 2.3. Generate trial vector $X_t=X_{r1}+f^*(X_{r2}-X_{r3})$
Step 2.4. Generate new vector from trial vector X_t. Individual vector parameters of X_t are inherited with probability *cr* into the new vector X_{new}. If the cost function from X_{new} is better (lower) than the cost function from X_i, current X_i is replaced in population P by X_{new} Next i

Step 3. Select the vector (RFNN parameter set) with best cost (training error E) function from population P

Figure 1. DE Algorithm for training NNs

The suggested Prostate Cancer Detection System is based on neural network based model is detection on the basis of patient's risk factors. The results from this system is combined to provide a quality detection of the disease.

The data to train the systems and test the system's performance are taken from real patients suffering the decease and taking treatment.

Input Data for accepts the following patient characteristics as its inputs:

- Age
- PSA
- Clinical Stage
- Tumor Size
- Prostate Size
- ISUP

Output Data for is the variable evaluating the severity (degree) of the disease:

- Pathologic Stage

The presents a Fragment of data used for training the neural network based in **Table 1**.

Inpu Data						Output Data
Age	**PSA**	**Clinical Stage**	**Tumor Size**	**Prostate Size**	**ISUP**	**Patologic Stage**
59	4,59	4	17	83,73	1	2
58	10,5	4	19	52,93	5	4
69	15	4	25	29,91	1	3
74	14,7	3	25	109,9	4	3
59	16,3	3	19	31,4	4	3
61	20,3	3	17	28,97	1	3
52	6,6	2	10	75,36	1	2
64	6,67	2	4	35,06	2	2
70	3,26	2	9	55,85	1	2
58	6,7	2	8	43,57	1	2
...	...	...	...	...	...	...

Table 1. A Fragment of data used for training Model 1 NN.

3. Results

Several architectures for networks have been used for experimenting. The parameters for a successful network are as follows:

4 Layered Feed-Forward NN with non-linear hidden and linear input and output layer neurons
Number of inputs (Layer 1): 6
Number of hidden neurons (Layer 2): 3
Number of hidden neurons (Layer 3): 6
Number of outputs (Layer 4): 1
Number of training/validation input-output data pairs: 84/10
Number of test input-output data pairs: 16
Training based on Differential Evolution algorithm
About 25 training experiments have been performed.
Best network RMSE after training (on training/validation data) obtained after 1000 iterations (generations of DE): 0.65
RMSE of trained network on test data was 0.82

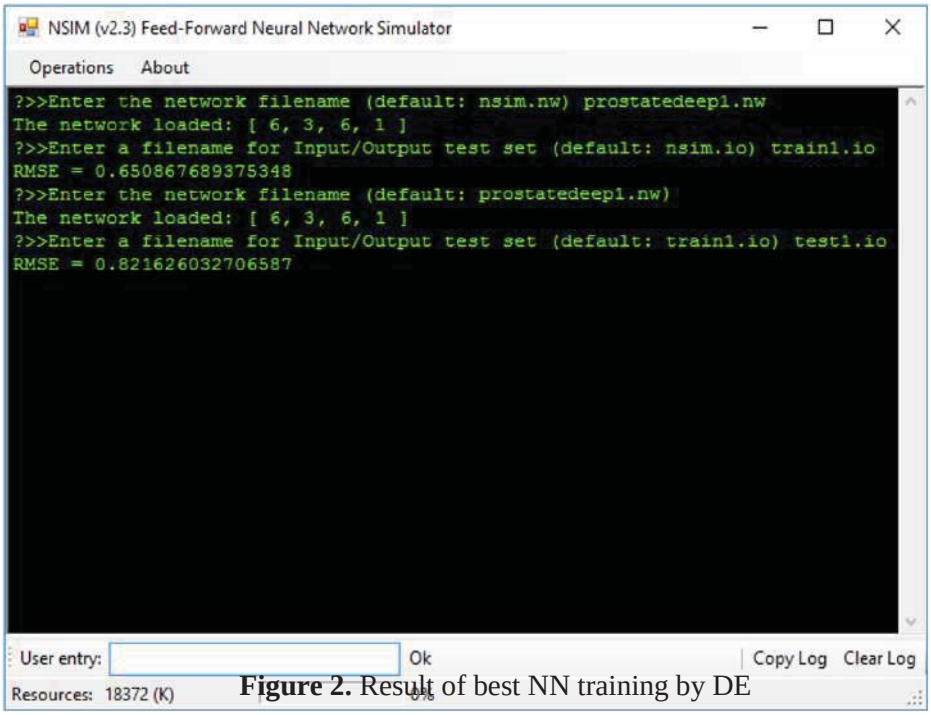

Figure 2. Result of best NN training by DE

In the future work we intend to apply other computational intelligence methods as well including Neuro-Fuzzy IS, Type-2 FIS, and Z-FIS to detect Prostate Cancer in patients on the basis of a number of stage.

Conclusion

Deep feed-forward neural network based approach is used for detection of Prostate Cancer. Two network models trained on separate sets of real patients' characteristics are used for better detection. The networks are trained with Differential Evolution training algorithm on a pair of data sets (training and validation sets) to avoid overfitting and improve model's generalization ability. Results of the experiments has proven the efficiency of the suggested method over the existing approaches.

Since prostate cancer causes fatal results, it is of great importance that the experts identify early and accurate diagnosis on the patient. In the diagnosis of the disease, the implementation of ancillary expert systems is an effective factor in order to prevent a malfunction due to human factor to have bad results.

With this study, it was aimed to create a system that would help the physician in early diagnosis and unnecessary biopsy of the patients. Therefore, ANN models were used as an auxiliary system. The Four Forward Layer Feed-Forward NN with non-linear hidden and linear input and output layer neurons which has the greatest success of ANN models, showed a performance of 0.82%.

Increasing the data used in future studies and increasing the classifier type will produce positive results for diagnosis. However, it will be possible to reduce the time spent on evaluations and the time spent on evaluations.

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Göndərilib: 13.07.2020 Qəbul edilib: 15.07.2020