

# ARTIFICIAL NEURAL NETWORKS. APPLICATIONS IN UROLOGY

**Razvan Bardan**

## REZUMAT

Retelele neuronale artificiale (RNA) sunt modele matematice complexe, inspirate de rețelele biologice de neuroni, ce pot efectua analize multifactoriale, fiind capabile să recunoască relații neliniare între diferiți parametri, având o precizie mai mare decât metodele convenționale de analiză statistică. RNA au fost utilizate cu succes în medicină, rezultate remarcabile fiind obținute în urologie, mai ales în depistarea, stadializarea și prognosticul cancerului de prostată. Scopul acestui articol este să prezinte teoriile actuale în domeniul RNA, cu descrierea rețelelor neuronale cel mai frecvent folosite în cercetarea urologică.

**Cuvinte cheie:** rețele neuronale artificiale, predicție statistică, urologie, cancer de prostată

## ABSTRACT

The Artificial Neural Networks (ANNs) are complex mathematical models, inspired by the biological networks of neurons, which can perform multifactorial analyses, being able to recognize nonlinear relationships between different parameters, providing better accuracy than conventional statistical analysis methods. ANNs have been successfully used in the field of medicine, remarkable results being obtained recently in urology, especially as useful tools for prostate cancer detection, staging or prognosis prediction. This review article intends to present the actual theories on ANNs and to describe the most common types of neural networks used in urological research.

**Key Words:** artificial neural networks, statistic prediction, urology, prostate cancer

## INTRODUCTION

In the new age of evidence-based medicine, disease diagnosis and prognosis is usually the result of a complex thinking process, synthesizing several types of clinical information. When the amount of the information becomes overwhelming, various mathematical and statistical analysis methods are used increasingly, to complement and sometimes replace the clinical evaluation.

Artificial Neural Networks (ANNs) are computational models, inspired by real-life networks of biological neurons, which can perform multifactorial analyses, being used in the clinical diagnosis process. Their major advantage over other conventional statistical analysis methods (e.g., linear regression analysis) consists in their ability to recognize complex (nonlinear) relationships inside the parameter

sets, providing better accuracy. The advantages and disadvantages of the conventional statistical methods and of the newer intelligent techniques are summarized in Table 1.

ANNs have been successfully used in medicine and remarkable results were obtained recently in the field of urology. This review intends to give an insight to the actual theories on ANNs, and to describe the most common types of neural networks used in medicine, focusing on the latest achievements in the urological research.

## NEURAL NETWORKS: AN OVERVIEW

### Short history

Artificial intelligence is not a new research field - ANNs have been in the attention of the scientists over the last 60 years. First studies on neural networks were done in 1943 by McCollough and Pitts. After a while, Rosenblatt conceived in 1959 the first learning algorithm, creating a model known as the perceptron, which was then only a solution to simple linear problems. The first non-linear processing capabilities of ANNs were reported in 1974 by Werbos, and afterwards the interest of the scientific community steadily increased, boosted in the last years by the

---

Department of Urology, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania

Correspondence to:

Razvan Bardan, Department Of Urology, Timisoara University Hospital, 156 Dr. I. Bulbuca Blvd., 300736 Timisoara, Tel: +40-256-306-115, Email: rbardan@yahoo.com

---

Received for publication: Jul. 22, 2004. Revised: Aug. 17, 2004.

**Table 1:** Comparison of statistical analysis techniques (after Snow et al.<sup>19</sup>)

Method	Advantages	Disadvantages
<b>Conventional statistical methods</b>		
Multivariate regression (linear, logistic, nonlinear, other)	Good accuracy Fast development time (except for nonlinear) Moderate decision insight	Must assume intervariable relations and in some applications the distribution of data within variables
<b>Intelligent techniques</b>		
1. Rule-based systems (expert systems, decision trees)	Highest decision insight	Less accurate because of rigid decision boundaries
2. Neural networks	Highest accuracy: makes no assumptions about variables	Lengthy development time for optimized networks Lowest decision insight Prone to overfitting
3. Fuzzy logic systems	Non-rigid decision boundaries Accuracy yet to be determined for medical decision making	Membership functions difficult to derive for complex problems

discovery of the backpropagation algorithm and by the increase in computational power, due to the exponential advances in computer technology.<sup>1</sup>

### Definition

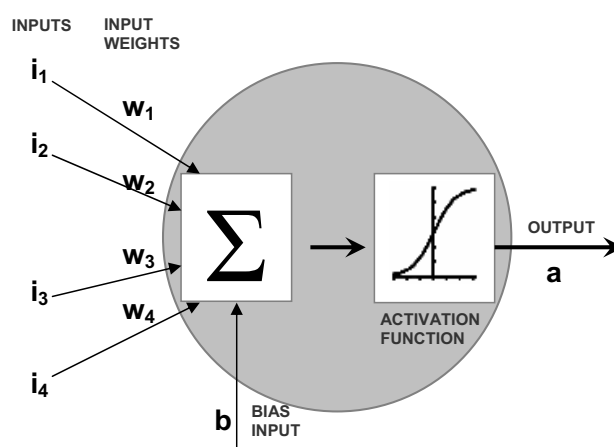
In biology, nervous networks are composed by a large number of neuron cells that are extensively interconnected to each other. Each neuron is in fact a specialized component, being able to propagate specific electrochemical signals; the axons of every neuron are connected to the dendrites of other neurons by synapses. The signals are transmitted by this complex mechanism, regulated primarily by synapses. Research conducted by Donald Hebb proved that the learning process consists primarily in altering the strength of various synaptic connections: every passing of a signal generates a response, with careful regulation of its transfer by the synapses.<sup>2</sup>

Like the biological nervous networks, ANNs also contain layers of simple processors (nodes) of data, which interact through carefully weighted connection lines, so that they may elaborate an outcome. The weight-balance of these lines is accomplished by a training session of input data, to be used by the network as the means for the adjustment of its interconnections (learning or training session). Of course, current ANNs have a much simpler architecture, with a lot fewer nodes or interconnections than the actual nervous system.

### The artificial neuron

The basic element of an ANN is the neuron, which is composed from a summator block and an activating block. (Figure 1) The input variables (*i*) are multiplied with the optimized weight parameters (*w*), and their products are summed. The neuron's output is achieved by the sum transformation, using an activation function. Usually, the perceptron networks utilize continuous sigmoidal activation functions, which

transform the output value into a range between 0 and 1. In this aspect, the artificial neuron is comparable with the traditional regression models. Also comparable to the regression models, a bias weight ("constant" - in statistical terminology) is utilized in order to optimize the final prediction. A common limitation of the traditional regression models and single-neuron networks is the fact that they are not able to detect complex relationships in the given dataset; additionally, the correlation type between the input and the output needs to be selected before the analysis start.<sup>3</sup>

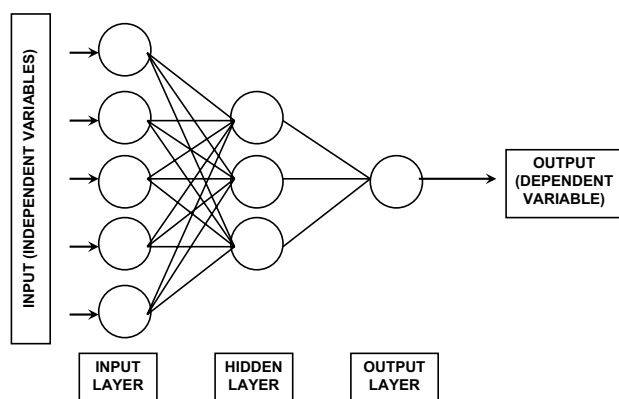


**Figure 1.** Representation of an artificial neuron. The inputs (*i*) are multiplied with the optimized weights (*w*) and thereafter summed. The sum is transformed by the neuron's activation function into the output value (*a*).

### The structure of a neural network

When a connection between several neurons is realized, more complex functions and interactions between the input data can be detected. The most usual network structure, the multilayer perceptron (MLP), consists in several layers of neurons, organized in such way that the neurons from the same level (layer) are not communicating with each other. (Figure 2) However, every neuron sends an output to all neurons in the next layer. The input variables compose the input layer, but in fact they are not a layer, because they are

not neurons. The layers situated inside the network, between the input and the output layers are called the hidden layers. The number of hidden layers and the number of neurons in each layer are important parameters, which influence the prediction results. The output layer produces the network response, consisting usually of one or two neurons.<sup>4</sup>



**Figure 2.** Representation of an artificial neural network

### The training process

The fundamental process of an ANN is the training, which uses both the input variables and known values of the output variables. During the training the input weights and the input bias are modified, in order to produce an output as close to the known values as possible.

The training process is usually regulated by three parameters: learning rate, momentum, and training tolerance.<sup>2</sup>

**Learning rate** is a parameter that narrows or expands the extension of the weight adjustments during a training cycle. If the learning rate is high, it can react fast to the input changes, even making the network unstable if the rate is too high. A high learning rate accelerates the learning process up to the moment when the weight adjustments draw closer to a plateau. To the other extreme, if the learning rate is too low, the training time is significantly longer.

**Momentum** quantifies the weight difference which is added to every consecutive weight adjustment. Low momentum is a factor of weight oscillation and instability, reducing the network's learning capacity, while high momentum influences network adaptability. Small momentum is useful in the middle of the training interval and high momentum is necessary at the end of the training.

**Training tolerance** represents the error margin allowed in the comparison between the output parameters obtained during the training and the target output parameters. Zero training tolerance means that the two sets of parameters match exactly, this being

the ideal situation; the error is usually minimized to a previously established value.

When should network training be stopped?

A disadvantage of the ANNs is the fact that they can suffer an over-optimization process, which will reduce their capacity for generalization, failing to recognize similar patterns that do not present in the exact same way, a phenomenon that can be considered as a memorization of the information (memory effect). This process can be avoided using the **early stopping method**, using a part of the training set as a separated validation set. Usually the training is stopped when the prediction accuracy suddenly decreases, due to over-training. Other methods to avoid over-training include the minimization of the prediction errors, by the reduction of the input parameters.<sup>1</sup>

The **validation set** is a segment of all training data which is used only for the validation of the training process, while the **test set** is the remaining data, used for the final testing process. There is no exact proportion between the two sets, but the validation set should be large enough for proper modeling.

In the moment when the training process is finished, the ANN results can be expressed as a mathematical formula, which may be inserted in a computer program, in order to be utilized on a desktop computer or on a handheld device.

## APPLICATIONS OF ANNS IN MEDICINE

### Why do we need artificial neural networks in medicine?

Evaluations of the key prognostic factors in different forms of cancer have shown that we must have more precise therapy guidelines and a more accurate prediction of the patients' outcome. Statistical analysis should be very useful for the clinician, as a tool providing more clarity to the complicated classification systems, risk group categories or therapeutic options.

The TNM system is a key tool in oncology, describing the anatomic extent of the different forms of cancer, being helpful to the clinician in the process of therapeutic choice. However, the system has its own limitations: although it has specifications for every organ location, it does not comprise many newer markers or pathological findings, which are necessary for specific diagnosis and therapy. This is the main reason why new prediction instruments are needed, which could adjust to every specific clinical parameter, giving results of great accuracy. ANNs are a possible solution, permitting to discover nonlinear relationships

between all the parameters (depending on each other or independent), being superior to the logistic regression, which need supplementary modeling in order to have a comparable flexibility.

With the power and speed of the actual computer hardware and dedicated software, ANNs can easily correlate different prediction factors, find hidden interactions among variables, predict an outcome for a group of patients, stratify patients in risk groups, or approximate a function and complete a known pattern.

Other possible (and already verified) applications of the ANNs in medicine include, but are not limited to the diagnosis, imaging, pathology and prognosis evaluation of appendicitis, back pain, dementia, myocardial infarction, arrhythmias, psychiatric disorders, acute pulmonary embolism or sexually transmitted diseases.<sup>1,5</sup>

## **APPLICATIONS IN UROLOGY**

The most extensively studied field in Urology is prostate cancer, where there is a great demand for the use of the ANNs. The necessity of an early diagnosis and of the exact timing of a prostate biopsy, along with the importance of an accurate staging, outcome prediction, therapy choice and the elimination of possible risk factors, represent elements that can benefit from the use of the ANNs.

### **Prostate cancer diagnosis**

The first application of an ANN in urology was the prediction of the prostatic biopsy results. The parameters used as input variables were: PSA, age, digital rectal examination (DRE) and the findings from transrectal ultrasound (TRUS). The ANN was a multilayer perceptron (MLP) and the training set included 1578 male patients, all with serum PSA higher than 4 mg/L. The test set results, using 209 patients, were very promising, with 88% specificity at 84% sensitivity.<sup>6</sup>

Gomari et al. have compared the capacity of a learning vector quantization (LVQ) ANN model, MLP and logistic regression to predict the outcome of prostate biopsy in screened men with a serum PSA of 3-10 mg/L. The used parameters were the age, total and free PSA, DRE result, TRUS result, symptoms and family history of prostate cancer. The LVQ model was more accurate than the MLP model, or the logistic regression model.<sup>7</sup>

Finne et al. have tested an MLP network on 656 men with a serum PSA of 4-10 mg/L in the Finnish prostate cancer screening trial. The input variables

included PSA, free PSA, DRE result and prostate volume. The results showed that the MLP performed better than logistic regression at sensitivities of 90% or higher, but was similar to logistic regression at lower sensitivity.<sup>8</sup>

Loch et al. have trained an MLP network to extract visual information from ultrasonographic images of the prostate, to predict the presence of prostate cancer, and the high or low Gleason score. The training set comprised only 53 pictures from 5 patients, but the results were very good on the test set, which included 500 pictures from 56 patients: the ANN identified 79% of the malignant lesions and 99% of the benign patterns.<sup>9</sup>

Ronco and Fernandez have also reported that an ANN which reunited clinical, biochemical and ultrasonographic parameters obtained 82% of positive predictive value and 97% of negative predictive value, compared with 67%, respectively 91%, obtained by logistic regression.<sup>10</sup>

Mattfeldt et al. have utilized MLP and LVQ networks on data obtained from a computerized image analysis system, trying to automate the process of histological diagnosis of prostate cancer. They used pathological specimens from 70 patients, analyzing four independent morphological parameters. The results were very promising: the accuracy of the LVQ model was 84%, very near to the accuracy of an experienced pathologist, while the MLP prediction was 77% and the logistic regression prediction was only 73%.<sup>11</sup>

Babaian et al. have developed an ANN based on retrospective data of 151 men (from three different institutions) with PSA values between 2.5 ng/ml and 4 ng/ml, who underwent multi-core prostatic biopsy. The training parameters were: age, total and free PSA, alkaline phosphatase and creatinine kinase. Prostate cancer detection rate was 24.5%, with a clear superiority of the ANN compared to the two PSA parameters in terms of specificity, at a sensitivity of 92%.<sup>12</sup>

### **Staging of prostate cancer**

The ANNs may have an important role in the staging process, because they use pathological findings from transrectal biopsy, along with other non-invasive parameters (especially lab findings) avoiding radical prostatectomies or lymph node dissections which are not correctly indicated.

Tewari et al. have developed a GENN to predict the positive margins or metastasis in a large group, of 1200 patients diagnosed with localized prostate cancer, using the following input parameters: age, race, DRE results, tumour size, Gleason score and the number

of positive biopsy cores. The results were very promising: the network had a specificity of 72-75%, at 81-100% sensitivity.<sup>13</sup>

Murphy et al. tested a MLP on a group of 275 patients with prostate cancer, trying to predict lymph node involvement, based on the following input parameters: prostatectomy history, total and free PSA, Prostate-specific Antigen score. They have found out that the most significant variable was prostatectomy history, probably as a consequence of the fact that only patients with low probability of nodal involvement underwent the prostatectomy.<sup>14</sup>

In a similar study, Batuello et al. used the Gleason score, PSA levels and clinical stage as input variables of an ANN, trying to predict the lymph node involvement. After training the network on 6135 patients, the authors obtained a sensitivity of 64%, at 81% specificity.<sup>15</sup>

Han et al. used clinical stage, Gleason score, preoperative PSA and age as input parameters for a MLP network, in order to predict lymph node status and organ confinement. At 90% specificity the ANN detected 34% of the patients with localized cancer and 59% of those with lymph node involvement, predictions which were much better than the ones obtained with the Partin nomograms (actual golden standard), based on regression analysis (29% and 52%, respectively).<sup>16</sup>

Borque et al. have developed an ANN to evaluate the preoperative pathological stage in prostate cancer, in order to decrease the understaging of the patients, which now still occurs in 40% to 60% of the cases, comparing the results with those obtained using multivariate logistic regression. The retrospective study comprised 468 men which underwent surgery for prostate cancer. Predictive study variables included patient age, clinical stage, biopsy Gleason score and preoperative prostate specific antigen (PSA). The predicted result included in analysis was organ confined or nonorgan confined disease. 6 neural network models were evaluated and the radial basis function model, which included age, clinical stage, Gleason biopsy score and preoperative PSA distributed in 5 categories, proved to be the most predictive. Similarly, from the 5 logistic regression models generated, the model created with clinical staging, Gleason biopsy score and PSA distributed in 5 proved to be most predictive of pathological stage. The difference in the area under the curves in the 2 chosen models was 0.042 ( $p=0.1$ ).<sup>17</sup>

Zlotta et al. used the European Prostate Cancer Detection Data Base to train an artificial neural network to predict pathological stage in 200 men with

serum prostate specific antigen 10 ng/ml or less who underwent radical prostatectomy. Variables included in the multilayer perceptron neural network were patient age, serum PSA, free-to-total PSA ratio, PSA velocity, transrectal ultrasound calculated total and transition zone volumes with their associated PSA parameters (transition zone PSA density and PSA density), digital rectal examination and Gleason score on biopsy. Overall classification accuracy of the artificial neural network was 92.7% and 84.2% for organ confined and advanced prostate cancer staging, respectively. For preoperatively predicting local versus advanced stage the area under the ROC curve for the artificial neural network was significantly larger (0.91) compared with logistic regression analysis (0.83).<sup>18</sup>

### Prognosis of prostate cancer

ANNs were designed also to be able to predict the eventual recurrence of prostate cancer.

Snow et al. used age, clinical stage, tumour grade, preoperative PSA level and race of 938 patients as input parameters in a MLP network, which was trained to predict postoperative cancer recurrence. The network performance was very good: at 67% sensitivity it indicated all the patients not going to develop a recurrence.<sup>19</sup>

Ragde et al. have compared the performance of a MLP with that of a regression model, trying to predict cancer recurrence after brachytherapy, on a group of 128 patients. The prediction, which used the age, clinical stage and Gleason score as input parameters, had a specificity of 90% at 55% sensitivity, an accuracy grade much higher than the regression model.<sup>20</sup>

Mattfeldt et al. have utilized a MLP network, a LVQ network and linear discriminant analysis, trying to predict tumor progression after radical prostatectomy, in 2 groups of 20 patients that were matched for age, preoperative PSA level and duration of follow-up. The results showed that LVQ was the most accurate method, followed by linear discriminant analysis and MLP prediction.<sup>21</sup>

Han et al. tried to predict the cancer recurrence (measured by the PSA level rise) three years after the radical prostatectomy, including in the data sets used for the training of a MLP only the patients with localized cancer and a Gleason score of 7. The input parameters were: age, race, preoperative PSA level, clinical stage and the type of Gleason score (4+3 or 3+4). The ANN outperformed the equivalent logistic regression model, having a specificity of 90% at 37% sensitivity.<sup>22</sup>

The main problem in the assessment of the different studies on prognosis is the fact that the

follow-up interval is generally too short, an aspect that is neglected by the designers of the ANNs.

One possible solution to this issue was the one tested by Zupan et al., who included the follow-up time into the input variables; the rationale for this was the fact that "patients with short follow-up times have a larger probability of eventually having a recurrence than those who have been recurrence-free for a longer period".<sup>23</sup>

Potter et al. have evaluated a group of patients with intermediate risk of progression ( $T_{1b}$ - $T_{2c}$   $N_0$   $M_0$ , Gleason scores 5-7), using a "genetically engineered" ANN (GENN), which is capable to develop its optimal architecture, in order to obtain the most accurate prediction. The input parameters were: pathological characterization after radical prostatectomy, age, DNA ploidy and quantitative nuclear grade (variations of 41 specific nuclear describing elements). The accuracy of the GENN model was close to 80%, significantly higher than the accuracy of the predictions made using logistic regression analysis.<sup>24</sup>

Finally, Naguib et al. have trained an ANN with eight input variables (six conventional factors - age, stage, bone-scan findings, grade, serum PSA, treatment, and two experimental markers - immunostaining for *bcl-2* and *p53*), trying to correctly classify patients' outcome (no response to treatment, relapse after initially successful treatment, or sustained response to treatment). The results were considered superior to linear discriminant analysis, with a reduction of the prediction after the exclusion of the *bcl-2* and *p53* immunoreactivity from the training process.<sup>25</sup>

### Other urological pathology

Baegli et al. have identified 242 input parameters (14 demographic, 35 radiographic, 23 surgical, 125 ultrasonographic and 45 of nuclear renography) and used them to train an MLP network on 84 retrospectively evaluated patients, with pyeloplasty for pyelo-ureteric junction obstruction. The outcome was divided into four categories, which reflected the hydronephrosis grade, evaluated by ultrasound. The accuracy was very close to 100%, when the model was tested on 16 patients.<sup>26</sup>

Sonke et al. have compared in 1999 the performance of a three layered backpropagation ANN with that of a linear regression model, both models being used to predict the bladder outlet obstruction in men with lower urinary tract symptoms, quantified by the Abrams-Griffiths number (AG-number); the input parameters were all the available non-invasive test results plus the patient age. Prostate volume, Qmax, voided volume and post void residual urine showed

substantial predictive value concerning the outcome, while patient age, PSA-level, IPSS and quality of life did not add much to that prediction. Using a cut-off value of 40 cm  $H_2O$ , the neural network approach yielded a sensitivity and specificity of 71% and 69%, respectively. The linear regression model produced quasi-identical results. The authors have concluded that the models cannot replace pressure-flow studies if exact urodynamic information is needed.<sup>27</sup>

Pantazopoulos et al. have trained different MLP and LVQ networks to differentiate between benign and malignant cells arising from lower urinary system lesions. The input variables were morphometric data, obtained using an image analysis system. Both ANN types were highly accurate, reaching a 91% agreement with an experienced cytologist.<sup>28</sup>

Qureshi et al. tried to evaluate retrospectively in 1999 the ability of an ANN (based on self organizing maps and the radial basis function algorithm) to predict bladder cancer recurrence within 6 months of diagnosis and stage progression in 195 patients with  $T_a/T_1$  bladder cancer, and 12-month cancer-specific survival in patients with  $T_2$ - $T_4$  bladder cancer, using distinct patient groups for each prediction; ANN predictions were compared with those of four consultant urologists. The accuracy of the neural network in predicting stage progression and recurrence within 6 months for  $T_a/T_1$  tumors and 12-month cancer-specific survival for  $T_2$ - $T_4$  cancers was 80%, 75% and 82% respectively, with corresponding figures for clinicians being 74%, 79% and 65%. Restricting the validation subset to patients with  $T_1G_3$  tumors in relation to stage progression, the sensitivity of the ANN analysis increased to 100%, with a specificity of 78% and an overall accuracy of 82%, outperforming the clinicians' predictions.<sup>29</sup>

Kellner et al. have realized a MLP model, trying to diagnose erectile dysfunction using EMG digital signals derived from corpus cavernosum of 100 men. The MLP produced an accuracy of 78% in the test set, compared with the opinions of a renowned medical expert.<sup>30</sup>

Cummings et al. have used an ANN to evaluate data in patients with ureteral calculi, to predict whether a stone would pass spontaneously or require intervention. Patient input from 181 patients presenting with renal colic included age, sex, race, marital status, insurance, stone side, level and size, hydronephrosis and obstruction grades, duration of symptoms before presentation, serum creatinine, history of stone passage or intervention and nausea, vomiting or fever. The investigators have used a feed forward, back propagation, error adjustment ANN.

The network correctly predicted outcome in 76% of the patients; in the patients in whom the stones passed spontaneously the sensitivity was 100%. Duration of symptoms before presentation was the most influential factor in network's ability to accurately predict the stone passage, followed by the grade of hydronephrosis.<sup>31</sup>

Poulakis et al. have performed a comprehensive evaluation of variables (patient characteristics, laboratory values, stone characteristics and the spatial anatomy of the lower renal pole) reported to affect lower pole stone clearance after shock wave lithotripsy, on a study group of 680 patients. The ANN analysis had 92% accuracy for correctly predicting stone clearance. The pattern of dynamic urinary transport represented the most influential predictor of stone clearance, followed by a measure of the infundibulo-uretero-pelvic angle, body mass index, caliceal pelvic height and stone size.<sup>32</sup>

## CONCLUSIONS

In the last few years the possible applications of ANNs in everyday urological practice have multiplied, with a large number of studies focusing on prostate cancer diagnosis and staging. However, in order to have a generally accepted model for a specific prediction, the ANN should utilize a small number of input parameters (which must be accepted and reproducible anywhere) and should give a significantly higher accuracy than the conventional statistical methods.

Another important thing to keep in mind is the fact that ANNs should be utilized only on prospective studies, where the obtained input information is very well defined, in order to decrease any possible error. When ANNs are used on retrospective studies, the bias caused by the poor selection of cases or parameters could lead to significant errors when the prediction is performed for new patients.

## REFERENCES

1. Anagnostou A, Remzi M, Lykourinas M, et al. Artificial Neural Networks for Decision-Making in Urologic Oncology *Eur Urol* 2003;43:596-603.
2. S. Haykin, *Neural Networks: A Comprehensive Foundation*, Macmillan College Publishing Company, 1994.
3. Finne P, Finne R, Stenman UH. Neural network analysis of clinicopathological factors in urological disease: a critical evaluation of available techniques. *Br J Urol* 2001;88:825-31.
4. Dayhoff JE, DeLeo JM. Artificial Neural Networks – Opening the black box. *Cancer* 2001;91:1615-35.
5. Wei JT, Zhang Z, Barnhill SD, et al. Understanding artificial neural networks and exploring their potential application for the practicing urologist. *Urology* 1998;52:161-72.
6. Foresee FD, Hagan MT. Gauss-Newton approximation to Bayesian Regularization. *Proceedings 1997 Int Joint Conf Neural Networks* 1997;3:1930-5
7. Gomari M, Finne P, Jaarvi T, et al. Learning vector quantization, multilayer perceptron, neurofuzzy network and logistic regression in the diagnosis of prostate cancer. *Proceedings of the 1998 International Conference on Parallel and Distributed Processing Techniques and Applications* 1998:516-25.
8. Finne P, Finne R, Auvinen A et al. Predicting the outcome of prostate biopsy in screen-positive men by a multilayer perceptron network. *Urology* 2000;56:418-22.
9. Loch T, Leuschner I, Genberg C et al. Artificial neural network analysis (ANNA) of prostatic transrectal ultrasound. *Prostate* 1999;39:198-204.
10. Ronco AL, Fernandez R. Improving ultrasonographic diagnosis of prostate cancer with neural networks. *Ultrasound Med Biol* 1999;25:729-33.
11. Mattfeldt T, Gottfried H, Schmidt V, et al. Classification of spatial textures in benign and cancerous glandular tissues by stereology and stochastic geometry using artificial neural networks. *J Microsc* 2000;198:143-58.
12. Babaian JR, Fritsche H, Ayala A, et al. Performance of a neural network in detecting prostate cancer in the prostate-specific antigen reflex range of 2.5-4 ng/ml. *Urology* 2000;56:1000-6.
13. Tewari A, Narayan P. Novel staging tool for localized prostate cancer: a pilot study using genetic adaptive neural networks. *J Urol* 1998;160:430-6.
14. Murphy GP, Snow PB, Brandt J, et al. Evaluation of prostate cancer patients receiving multiple staging tests, including ProstaScint scintiscans. *Prostate* 2000;42:145-9.
15. Batuello JT, Gamito EJ, Crawford ED et al. Artificial neural network model for the assessment of lymph node spread in patients with clinically localized prostate cancer. *Urology* 2001;57:481-5.
16. Han M, Snow PB, Brandt JM, et al. Evaluation of artificial neural networks for the prediction of pathologic stage in prostate carcinoma. *Cancer* 2001;91:1661-6.
17. Borque A, Sanz G, Allepuz C et al. The use of neural networks and logistic regression analysis for predicting pathological stage in men undergoing radical prostatectomy: a population based study. *J Urol* 2001;166:1672-8.
18. Zlotta AR, Remzi M, Snow PB et al. An artificial neural network for prostate cancer staging when serum prostate specific antigen is 10 ng/ml or less. *J Urol* 2003;169:1724-8
19. Snow PB, Smith DS, Catalona WJ. Artificial neural networks in the diagnosis and prognosis of prostate cancer: a pilot study. *J Urol* 1994;152:1923-6.
20. Ragde H, Elgamal AA, Snow PB et al. Ten-year disease free survival after transperineal sonography-guided iodine-125 brachytherapy with or without 45-gray external beam irradiation in the treatment of patients with clinically localized, low to high Gleason grade prostate carcinoma. *Cancer* 1998;83:989-1001
21. Mattfeldt T, Kestler HA, Hautmann R, et al. Prediction of prostatic cancer progression after radical prostatectomy using artificial neural networks: a feasibility study. *BJU Int* 1999;84:316-23
22. Han M, Snow PB, Epstein JI et al. A neural network predicts progression for men with Gleason score 3+4 versus 4+3 tumors after radical prostatectomy. *Urology* 2000;56:994-9
23. Zupan B, Demsar J, Kattan MW, et al. Machine learning for survival analysis: a case study on recurrence of prostate cancer. *Artif Intell Med* 2000;20:59-75.
24. Potter SR, Miller CM, Mangold LA, et al. Genetically engineered neural networks for predicting cancer progression after radical prostatectomy. *Urology* 1999;54:791-5.
25. Naguib RN, Robinson MC, Neal D et al. Neural network analysis of combined conventional and experimental prognostic markers in prostate cancer: a pilot study. *Br J Cancer* 1998;78:246-50.
26. Baegli DJ, Agarwal SK, Venkateswaran S et al. Artificial neural networks in pediatric urology. Prediction of sonographic outcome following pyeloplasty. *J Urol* 1998;160:980-3.
27. Sonke GS, Heskes T, Verbeek AL, et al. Prediction of bladder outlet obstruction in men with lower urinary tract symptoms

- using artificial neural networks. *J Urol* 2000;163:300-5.
28. Pantazopoulos D, Karakitsos P, Iokim-Liossi A, et al. Back propagation neural network in the discrimination of benign from malignant lower urinary tract lesions. *J Urol* 1998;159:1619-23.
29. Qureshi KN, Naguib RN, Hamdy FC, et al. Neural network analysis of clinicopathological and molecular markers in bladder cancer. *J Urol* 2000;163:630-3
30. Kellner B, Stief CG, Hinrichs H, et al. Computerized classification of corpus cavernosum electromyogram signals by the use of discriminant analysis and artificial neural networks to support diagnosis of erectile dysfunction. *Urol Res* 2000;28:6-13.
31. Cummings JM, Boullier JA, Izenberg SD, et al. Prediction of spontaneous ureteral calculous passage by an artificial neural network. *J Urol* 2000;164:326-8.
32. Poulakis V, Dahm P, Witzsch U. Prediction of lower pole stone clearance after shock wave lithotripsy using an artificial neural network. *J Urol* 2003;169:1250-6