Neural Network Based Model for Radioiodine (I-131) Dose Decision in Patients with Well Differentiated Thyroid Cancer

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Abstract. A classifier system based on Artificial Neural Network is developed to suggest I-131 iodine dose in radioactive iodine therapy. The inputs to the system consist of patient's diagnosis based on histopathologic findings, patient's age, and TNM classification. The output of the neural network is proposed I-131 iodine dose that should be given to the patient. The training group was composed of 72 patients with well differentiated thyroid cancer. The test group consisted of 20 patients. An artificial neural network was trained using Levenberg-Marquardt back-propagation algorithm. By comparing the results obtained through the model with those resulting from the physician's decision, it has been found that the developed model is highly compatible with reality. The accuracy of the developed neural network has been exceptional. The developed classifier system could be used in educational purposes.

Keywords: Neural networks, radioactive iodine therapy, thyroid cancer.

1 Introduction

Although thyroid cancers represent less than 1% of all malignances, they are most common endocrine carcinomas, and ones of the ten most common cancers in women [6]. Between these, more than 95% are well differentiated thyroid cancers (WDTC) of follicular cell origin, papillary and follicular carcinomas. After the Chernobyl nuclear disaster the incidence of WDTC has increased in many European countries. Age, female sex, radiation exposure of neck region (particularly in children), and the positive familiar anamnesis of other malignances are the most important risk factors that increase the probability of WDTC.

Although WDTC have a very good prognosis in the vast majority of patients, there are still patients with high risk factors, who need, after total or near total thyroidectomy, the

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radioactive iodine therapy [7, 11]. Ability of the thyroid follicular cells to take up iodine via sodium iodide symporter at the basolateral cell membrane, enable the use of radioiodine for the therapy of WDTC.

Experienced physician relatively easily determines the dose of I-131 iodine in WDTC treatment. On the other hand, this task is very complex for beginners and/or computers. Choice of dose proposed by a physician cannot be easily described by precise rules and/or mathematical algorithms. Artificial Neural Networks (ANN) that are information-processing systems are able to learn from experience, and to apply to new cases generalizations derived from previous instances [3, 12]. They are also capable to abstract essential characteristics of input data that often contain irrelevant information. ANN have been applied to various biomedical problems during last few decades [4, 5, 8, 9, 10]. The most important ANN applications in medicine are in the areas of image analysis, diagnostic systems, and drug development.

In this paper, we developed simple neural network for prescription of the I-131 iodine dose in WDTC treatment. We used a great number of medical records. All medical records that we used contain information on patient's diagnosis, age, TNM classification (T - Tumor size, N - metastases in lymph nodes, M - distant metastases), as well as I-131 dose proposed by a physician. We trained artificial neural network by presenting to the network set of patient's characteristics (histopathologic diagnosis, age, TNM classification of tumor), and applied therapy (doses). In other words, we created many (patient, therapy) pairs and presented them to the network. Trained network has been capable to propose the best therapy for every new case.

The main objective of this paper is to research the possibility of developing a classifier system that could improve the quality of decisions of young physicians that treat WDTC. In other words, our intention is to use the classifier system mainly in educational purposes. Since neural networks are well known for being a black box, the medicine student won't learn how to reach an appropriate decision. On the other hand, our main attention is to help students in testing of their acquired knowledge.

To the best of our knowledge, this research represents first attempt to apply neural network concepts in WDTC therapy. The paper is organized as follows. Neural networks fundamentals are given in Section 2. Section 3 describes proposed neural network for prescription of the I-131 iodine dose in WDTC therapy. Results and discussion are given in Section 4. Section 5 contains conclusion.

2 Neural Networks Fundamentals

The Artificial Neural Network (ANN) is a mathematical model that is based on a simplified model of the brain, the processing task being distributed over numerous neurons (nodes, units, or processing elements). The power of a neural network is obtained as the result of the connectivity and collective behavior of these simple nodes. Artificial neural networks demonstrate a notable number of the brain's properties. For example, they are able to learn from experience, to apply to new cases generalizations derived from previous instances, and to abstract essential characteristics of input data that often contain irrelevant information.

Neural networks have been applied in medicine during the last few decades. There are a lot of various clinical and laboratory data related to every patient. The basic idea of using ANN in medicine is to have better diagnoses, predictions, decision making, and medical image analysis based on clinical and laboratory data. The pioneers of using ANN in medicine were Anderson [1], and Specht [9]. Donald Specht [9] used neural network to detect heart abnormalities. The inputs were EKG data. The possible outputs were "normal", or "abnormal" [2, 9]. Anderson [1] developed "Instant Physician". The main idea was to develop neural network capable to make diagnosis and recommend patient's treatment based on a set of symptoms. The network developed performed well and was capable to give the same diagnosis and treatment as proposed by physician. We follow this idea in our paper.

3 Neural Network for Prescription of the I-131 Iodine Dose in WDTC Treatment

The problem considered in this paper belongs to the pattern classification problems. In pattern classification problems, every input vector belongs to a specific category. In our case, input vectors (patterns) are patient's characteristics (age, histopathologic diagnosis, TNM classification of tumor). Various doses of I-131 iodine given by a physician represent categories. In the numerical example that we consider we have three categories (doses of 1.85 GBq, 3.7 GBq, 5.5 GBq respectively).

We set a two-layered neural network (Figure 1). Between input and hidden layers there is a full connectivity. We use the proposed network to determine the dose of I-131 iodine. The dose is determined according to patient's histopathologic diagnosis, age, as well as TNM classification. The input layer has 5 nodes, as well as hidden layer. The output layer contains one node. The following are inputs to the network:

PD - patient's diagnosis
PA - patient's age
T - tumor size
N - metastases in lymph nodes
M - distant metastases

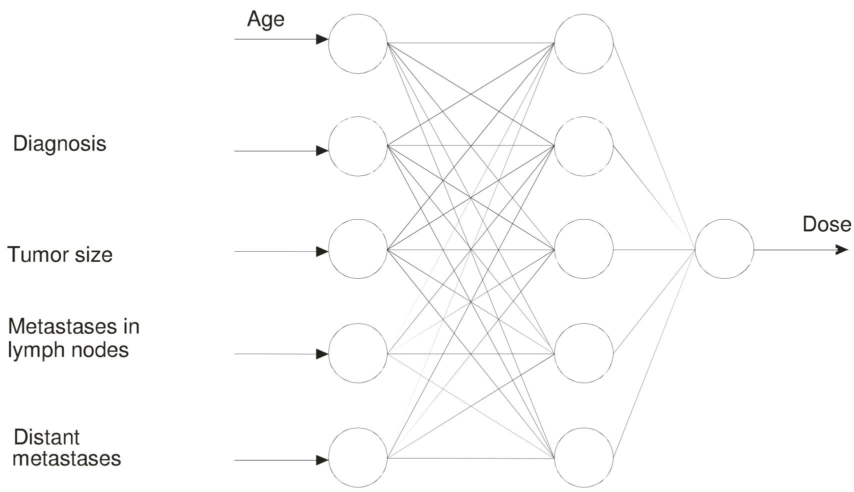

Fig. 1. Neural network for choice of the I-131 iodine dose.

The output of the network *D* represents the dose received by a patient. We described patients' diagnosis by the following integer numbers:

1 – Microcarcinoma papillare glandulae thyreoideae,
2 - Ca papillare glandulae thyreoideae multifocale,
3 - Ca papillare glandulae thyreoideae,
4 - Hurtle cell carcinoma glandulae thyreoideae,
5 - Ca folliculare gl. thyreoideae (multifocale),
6 - Ca folliculare gl. thyreoideae,
7 - Ca folliculare gl. thyreoideae (atypicum),
8 - Microcarcinoma papillare multicentricum.

The proposed neural network for choice of the I-131 iodine dose is shown in Fig. 1.

4 Results and Discussion

The proposed neural network is trained on 72 examples of physician's decisions, and after that tested on 20 examples. Patients used in this research were patients from the University Clinical Center in Kragujevac, Serbia. They had undergone I-131 iodine therapy between 2005 and 2011. The physician whose decisions were used to train the neural network has 23 years of experience in nuclear medicine.

During network preparation there were three kinds of sets. All of these sets were generated by random splitting. First set was presented to the network during training, and network was adjusted according to its error. In our code, training set was 70% from whole set of patients characteristic (50 patents from 72). Second set was used for validation. These patients were used to measure network generalization, and to halt training when generalization stops improving. Finally, third set was used for testing. These patients' characteristics have no effects on training and so provide an independent measure of network performance during and after training. In our code these two sets included 15 % of whole data set (in total 11 patients).

The characteristics of the patients from the training and testing groups are given in the Table 1.

Table 1. Training and testing groups: Patients' age, diagnosis, tumor size, metastases in lymph nodes and distant metastases.

Patient Ordinary Number	Age	Diagnosis	T	N	M	Dose
1	33	1	2	0	0	2
2	21	1	2	0	0	1
3	65	2	2	0	0	2
4	77	4	4	1	0	2
5	81	5	4	0	1	2
….						…
91	63	5	3	0	0	2
92	56	3	1	1	0	3

Patient's age (*PA*) is expressed in integer numbers. Tumor size (*T*) is expressed in [cm]. The variable (*N*) that describes existence of the metastases in the lymph nodes has the following possible values: 0 (in the case when there are no metastases in the lymph nodes (*N0*)); 1 (in the case when there are metastases to level VI: pretracheal, paratracheal, and prelaryngeal (*N1a*)); 2 (in the case when there are metastases from to unilateral, bilateral, contralateral cervical or superior mediastinal node (*N1b*)). The variable *M* that describes existence of the distant metastases has the following possible values: 0 (in the case when there are no distant metastases); 1 (in the case when there are distant metastases).

The trained neural network made the same decision as a physician in 66 cases (91%) in the case of training group. In the case of test group network made the same decisions as a physician in all 20 cases (100%). The regression plot is shown in Fig. 2. On the abscissa are target values (doses given by physician), while on the ordinate output values (dosed recommended by trained neural network) are given. As it can be seen from this plot, in all cases target value of proposed dose was equal to output value.

5 Conclusion

The physician needs to be very knowledgeable, experienced and trained properly to adequately perform the studied task. In order to imitate physician's decisions we developed a simple neural network that has the ability to adapt and learn. Training of the proposed neural network involves use of a data base of collected physician's decisions that are values for the input and the output of the neural network. The neural network learns by adjusting the connection strengths to minimize the error of the outputs.

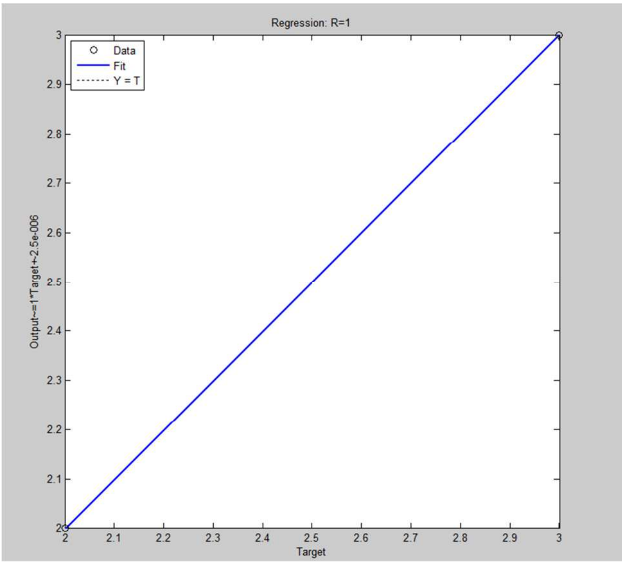

Fig. 2. Regression plot.

The experience gained during this research indicated the importance of getting enough representative training and testing data. However, due to the nature of the information and all the difficulties of obtaining them, the number of available data was limited.

The purpose of the study in this phase of work was to develop a simple judgment system. Our aim was to create artificial neural network that would assist medical students to test their knowledge. We proposed neural network, which in the simplest form, is able to describe the actual judgment process. In other words, we showed that the proposed feedforward neural network has capability to imitate the actual decisions of the experienced physician. The developed classifier system could be used in educational purposes. It could assist and guide young physicians. The system developed can make the appropriate decision without knowing the functional relationships between individual variables.

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