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APPLYING NEURON NETWORKS TO DEFINE THE MOST APPROPRIATE WAY OF TREATMENT IN PATIENTS WITH CERVICAL CANCER IIB STAGE

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ABSTRACT
The tactics of treatment patients with cervical cancer (CC) II B stage has not been chosen entirely, and in the standards of diagnostics and treatment there are different variants of treatment of the given pathology, and choosing the most appropriate one as a rule depends on the subjective opinion of a doctor. Applying neuron networks in prognosticating the results of treatment will allow excluding the subjective point of view in choosing the method of treatment.
Keywords: cervical cancer, neuron networks, IIB stage, chemotherapy, radiation therapy.

INTRODUCTION

Cervical cancer (CC) takes one of the most fundamental places in the sphere of malignant tumors in women in Ukraine. Thus, according to the national cancer database of Ukraine (2011 year), it is discovered 5344 primary patients on CC, CC morbidity in Ukraine made up — 8, 9 out of 100 000 of female population. It was inferred, that the most part of patients is women with the 1st stage (35, 9 %) and 2nd stage (40, 3 %), 16, 9 % of the sick with the 3rd stage and only 5 % of the sick with the 4th stage of the process[1]. The indexes of the 5th year survival among the sick in CC IIB stage, that took radiation therapy (RTH), as an independent method of treatment makes up from 42 to 64, 2 %, and during complex treatment from 55, 2 to 76, 9 %[2]. The choice of a method of CC treatment in patients is a subject of a long term discussions among oncologists-gynecologists, radio-therapists and surgeons. The disadvantages of it are RTH at the 1st stage resulting in fibrous changes, vessel sclerosis and correspondingly the medicines can hardly flux into the zone of radiation. In spite of the fact that radiation equipment is advanced, with dosimetric appliances, different doze variations are set, radio modificators are in use though at present there is no appropriate cure. A sufficient frequency of appearing recurrence in parametric and regional lymph is a result of relative radio resistance of metastatic cancer cells which are located in regional lymph and possess less mycotic activity at a smaller quantity of DNA. The renovation of the initial tumor growth is provided by intensification of mycotic cell activity in clonogenic cell population that have remained, and they are developing under conditions of immune disability of the regional lymph and the organism in particular[2]. Searching and improving well-known methods of CC treatment led a lot of scholars to the conclusion to apply chemotherapy broader in treatment of this pathology. This type of treatment is not enough of itself, however could be supplementary to surgery or/and radiation. Unsatisfactory results of treating locally-spread forms of CC, caused by inability of surgery, stimulate working out new and updated methods of neoadjuvant therapy[3]. Due to neoadjuvant chemotherapy the possibility of resectable tumor and reducing the risks of intra operational dissemination of neoplastic cells increases. Neoadjuvant chemotherapy for locally spread CC IIB stage will allow increasing the chance of successful surgery for this category of patients up to 85 % and, moreover, to remove potentially resistent metastatic focuses; to reduce recurrence frequency by 18 % and the frequency of finding out in regional lymph nodes by 17 %. All the above mentioned considerably increases non recurrence surviving[4]. So, the tactics of treatment patients with CC II B stage has not been chosen entirely, and in the standards of diagnostics and treatment there are different variants of treatment of the given pathology, and choosing the most appropriate one as a rule depends on the subjective opinion of a doctor. Applying neuron networks in prognosticating the results of treatment will allow excluding the subjective point of view in choosing the method of treatment.

MATERIALS AND METHODS

There were analyzed the results of treatment of 227 patients with CC IIB stage, that had taken radical treatment in Ivano-Frankivsk oncological dispensary from 1998 to 2012. The selective criterion of patients was squamous cell cervical carcinoma of IIB stage that had been verified in every patient while examining morphologically the cervical tumor. CC was being diagnosed, considering the clinical findings, gynecological examining (the sizes of the initial tumor, the stage of vaults and parameters), cytology and histology of target of the tumors and the results of additional methods of examination (cystoscopy, rectoromanoscopy, roentgenogram, USD and MRI of abdominal cavity and small pelvis). The division of patients according to treatment schemes: 85 patients – neoadjuvant systematical polichemotherapy according to FP (cysplastyn 75 mg/m^2, 5-phtoruracyl 1000 mg/m^2 from day 1 to day 4) 2-3 courses every three weeks, surgical intervention in amplitude of pangisterectomy of type III, and post surgical course of polichemotherapy; 68 patients took pre surgical course of distant polichemotherapy 2 g added to the total doze of 30 g with potentiality of cysplastyn 40 mg/m^2 every week, surgical intervention in aptitude of

pangisterectomy of type III, post surgical course of polichemotherapy in necessary; 74 patients – complete course of combined radiation therapy to the total focus doze 80-100 g with potentiality of cysplastyn 40 mg/m^2 every week (6 weeks). This research aims to work out the system of defining the most appropriate way of treatment of diagnosed disease considering simultaneously the following indexes: age, type and location of a tumor (exophytic, endophytic and combined), presence or absence of contaminant diseases, hemoglobin index, weight and height.

RESULTS AND DISCUSSION

Even at wide distribution of different methodical approaches and row of protocols which regulate the order of works in this sphere it cannot be decided the noted problem of authentication of the most acceptable method of treatment on the basis of prognoses of probability of survival (deaths) effectively without application of modern and at the same time, accessible and clear technologies and instruments of account of separate informing parameters for nonlinear classification (recognition of patterns). In this case, as a rule, parameters which can be certain apriori serve as informing parameters, and typical having a special purpose offenses is the most acceptable method of treatment. Tasks of choice of signs (informing parameters) are in general case multi extreme. The most known algorithms of decision of these tasks do not allow to attain a global extremum – most optimum complex of informing parameters which would allow to determine a having a special purpose parameter (probability of survival) with satisfactory exactness. In addition, as it was already marked higher, this task cannot be at most cases decided analytically. Therefore for finding of its extremum different procedures of surplus of tops are used with the current evaluation of their value. The criterion of search is determined coming from a priori information and previous analysis of aggregate of informing parameters. Before Karpash O.M.[5] suggested using the newest genetic methods for the decision of the problem marked higher in industry of technical diagnostics – algorithms of artificial neuron networks. On the basis of the executed analysis of experience and possibilities of algorithms of artificial neuron networks methodology of selection of optimum complex of informing parameters was developed, that would enable to develop new methodology of choice of the most acceptable method of treatment after the values of probability of survival in the case of application of that or other method. We will consider an order and features of realization of the higher described steps in our case. Step 1: Selection of plural of informing parameters, following having a special purpose parameters. Basic influence on the selection of plural of informing parameters of control has an experience of researcher, understanding and aim of problems, influential factors, methods and sources of receipt of results of supervisions, t was in this case select by having a special purpose values: +1 – in the case of survival of patient after treatment and in default of relapses, 0 – in the case of death of patient. Step 2: Correlation regressive analysis. Correlation regressive analysis is the method of processing of statistical data, with the help of which measured connection between two or anymore by variables. Correlation analysis is used for determination of necessity of including of those or other factors to equalizations of regression, and also estimates they got equalization of regression on accordance found out copulas. Thus, as a rule, build expect the table of coefficients of correlation, and after them determine a presence and degree of connection between the elements of the selected plural of informing parameters and having a special purpose parameter. The positive values of coefficients of correlation specify on direct proportion connection, while subzero – on reverse. It should be noted that in most cases in practice the coefficients of correlation do not arrive at values near to 1. As a rule, values, which are scope from 0, 4 to 0, 8 specify not on an in communication between the probed descriptions, but on his nonlinear character. It is recommended in such cases or to divide or narrow the range of values of informing parameters, or execute a grafoanalitichniy analysis. Step 3: Forming and preparation of sets of complexes of informing parameters. On this stage it follows to turn the special attention on forming of sets given of most dimensions, providing the observance of the followings limitations:

- must be the dimension of groups of informing and having a special purpose parameters even;
- statistical variation of values of all parameters must be maximal;
- Distributing of values of parameters, especially having a special purpose, must be maximally close to homogeneous.

Every separate aggregate of values of complex of informing parameters and proper them having a special purpose parameter named an educational pair. With the purpose of facilitation of implementation of next step it is expedient to bring a value over of informing and having special purpose parameters to the values scope from 0 to 1. It is for this purpose better in all to take advantage of functions of normalization in obedience to the following formula (1):

$$aa = (AA - \min AA) \max AA \quad (1)$$

where: AA is an actual value of parameter; aa is the value parameters resulted to the range [0; 1]; min AA is a «minimum» value which it follows to elect as the least value from a set of values of parameter minus 5-7 % this value; max AA is a «maximal» value which it follows to elect as a most value from a set of values of parameter plus 5-7 % this value

Addition is equal 5-7 % concrete value entered, coming from the followings reasonings[6]:

- Error of most values of parameters, certain experimentally or mathematically does not exceed 5 %. It is in addition, impossible to eliminate situations, when the values of informing parameters, measured in the process of researches in the future, will go beyond the chosen limits;
- It is not recommended to «lead» neuron networks in the process of training in extreme values 0 or 1;
- Areas of multidimensional space of values of parameters out of certain limits, is legalistically unknown for neuron networks, that is why probability of reliable prognostication of values of having a special purpose parameters it is not possible to estimate in these areas.

For select parameters values are followings:

minP1 = 20	maxP1 = 50
minP2 = 0	maxP2 = 10
minP3 =	maxP3 =
minP4 =	maxP4 =
minP5 =	maxP5 =
minP6 =	maxP6 =
minP7 =	maxP7 =
minP8 = 40	maxP8 = 120
minP9 = 40	maxP9 = 110

On this step and in all followings for their most high-quality implementation it is recommended to use the package of application software for the calculations of Matlab R2011 and higher. The characteristic positive feature of this software is a matrix form of implementation of calculations. Farther the sets of data geared-up it follows to divide into 2 parts:

- A training set is sets of informing and having a special purpose parameters which will be used for training of neuron networks;
- Test set – will be used for verification of rightness of training of neuron networks. The dimension of this set must make from 10 to 30 % dimension of initial set. In addition, with the purpose of providing of authenticity of testing results, it follows to turn the special attention on that educational pair which are included in a test set no wise not used for training.

For all databases in to the test sets were selected for 7 pair – 4 patients which have treated (survived) successfully, and 3 – dyings.

Step 4: A design by artificial neuron networks.

On the base of experience of row researchers[7] are set that most acceptable to swinging majority of tasks of selection of complexes of parameters for non-destructive control and estimation of the technical state there are multi-layered neuron networks which practice after the algorithm of reverse distribution of error of Levenberga-Markvardta. The basic paradigm of studies in this case is studies with a teacher. Conceptually participation of teacher can be examined as a presence of knowledge about an environment, presented as pair entrance-output. Thus, an environment is unknown taught neuron network. We will assume now, that an educational vector is given a teacher and taught network from an environment. On the basis of built-in knowledge a teacher can form and pass to the taught neuron network the desired review, proper this entrance vector. This desired result is optimum actions which a neuron network must execute. The parameters of network are corrected taking into account an educational vector and signal of error. A signal of error is a difference between the desired signal and current review of neuron network. The correction of parameters is executed step by step with the purpose of imitation of neuron a network conduct of teacher. This emulation in some statistical sense must be optimum. Thus, in the process of studies of knowledge teachers are passed in a network in a maximally complete volume. Upon termination of studies of teacher it is possible to disconnect and allow a neuron network to work with an environment independently. The described form of studies with a teacher is nothing other, as by studies on the basis of correction error – reverse distribution of error. It is the closed system of reverse connection, which does not include for itself an environment. The productivity of such system can be estimated in terms of middle squarable error or sum of squares of errors on an educational selection, presented as a function from the free parameters of the system. For such function it is possible to build the multidimensional surface of error in the co-ordinates of free parameters. Thus the real surface of error re equal in relation to all possible examples, presented as pair "entrance-output"; any concrete action of the system with a teacher appears one point on-the-spot errors. For the increase of the productivity of the system in time, the value of error must be displaced in the side of minimum on-the-spot errors. This minimum can be both local and global. It can be done, if the system has useful information about the gradient of surface of errors, to proper current conduct of the system. A gradient of surface of errors in any point is a vector which determines direction of the most rapid lowering on this surface. In the case of studies with a teacher on examples the instantaneous estimation of vector of gradient, in which an entrance vector is considered the function of time is calculated. For drawing on the results of such estimation of moving of point for the surfaces of errors usually has the appearance of "casual wander". However, for the use of the proper algorithm of minimization of function of cost, adequate set of educational examples in form "entrance-output" and to sufficient time for the studies of the system studies with a teacher, capable to decide such tasks, as classifications of appearances approximation of functions. For realization of the described sequence of operation from training of artificial neuron networks it is recommended to use the specialized programmatic addition of Neural Network Toolbox in the environment of Matlab R14. Training error during establishment of tuning in addition of Neural Network Toolbox it follows to choose 5 %. It is explained that as a rule, total level of errors of measuring of having a special purpose and informing parameters, and also does not exceed stochastic constituents 5 %. It is recommended for every case of select complexes of informative parameters to execute training 5-7 networks of identical architecture. Such amount of networks is arbitrary, however it allows avoiding the cases of ascent of algorithm of training in a local minimum and effect of «restuding», which will be accompanied memorizing of having a special purpose values which answer informing, but not to establishment of dependence between them[8]. As a rule, for most cases most acceptable is classic architecture of multi-layered neuron network[9]. By a select neuron network which was accepted for base in our researches there is a multi-layered network with three hidden layers on the chart of 8 x 40 x 20 x 1.

Step 5: Determination of complex of parameters which are optimum from point of exactness of determination of them and having a special purpose parameters and possibility of their measuring. After completion of process of training of all neuron networks for all possible combinations it follows to conduct testing by the preliminary neat test sets of information which was not used during training. Go for it follows to compare the results of calculation of values of having a special purpose parameters to standard (from a test set) by the calculation of absolute and at a necessity a relative error and calculation of them mean value. Among the got results of outputs of neuron networks it follows to choose the least. Extraordinarily low (near to the zero) values of errors for all values it follows to cast aside as such which testify to the phenomenon of «restuding». Farther it follows to execute the same choice for every set of complex of informing parameters. As criteria of optimum, in this case, the followings are select:

- Minimum possible complex of informing parameters;
- The greatest exactness of determination of having a special purpose parameter (in absolute or percent expression).

It follows to consider the complex of informing parameters chosen after the criteria indicated higher optimum and acceptable; appeared other substantial purpose of this stage of researches choice adequate complication of task of training algorithm which on the essence is the algorithm of decision

of task of optimization of weighed coefficients and delays of neurons. It was succeeded to set as a result of factor analysis, that most suitable is an algorithm of reverse distribution.

CONCLUSION

So, the received results showed the possibility of applying neuron networks to define the most appropriate method of treatment of diagnosed CC with the help of simultaneous calculation of several patients' indexes. The application of neuron networks is the most effective method of defining the most appropriate way of treatment of the CC patients on the IIB stage.

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