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Applying of neuron networks to define the most appropriate way of treatment of the patients with cervical cancer IIB stage

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Cervical cancer (CC) takes one of the most fundamental places in the sphere of malignant tumors in women in Ukraine. We have analyzed the results of treatment of 227 patients with CC IIB stage, which had taken radical treatment in Ivano-Frankivsk oncological dispensary from 1998 to 2012. Our 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.

Keyword: Cervical cancer, Treatment, Neuron networks.

1. 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), 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 % ^[8].

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, radiomodifiers 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 ^[8]. 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 [7]. 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 to increase the chance of successful surgery for this category of patients up to 85% and, moreover, to remove potentially resistant 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 [9].

Within last ten years there have appeared a lot of works on the successful applying neuron networks in biomedical researches. Ochi T., Murase K. and others (2002) assessed the possibility of applying neuron networks in prognosticating patients with CC survival that had been treated with the help of RTH. The treatment data of 134 patients with CC were included in the research, which had received combined-radiation therapy between 1978 and 1993. Neuron network was taught on 67 randomly chosen patients with CC. Having applied trained neuron networking, the authors predicted 5 year old survival in the latter 67 patients and compared it to the well-known one already. The major factors such as age, general status, hemoglobin, protein, disease stage, histological type of tumor were used as inlet point into neuron network. Radiation patomorphosis data were used as an extra factor. To define it a biopsy was held periodically, as well as the data of cytological analysis of radiation modifications were taken to define the latter, cytological smear tests were taken, these factors did not differ considerably from those cases, where only the main factors had been applied. The conclusions of this research are that neuron network will allow to estimate the importance of prognosticated factors, as well as will allow to

predict every patient's survival. Neuron network applying, where to the main factors extra data of radiation pathamorphosis are added according to the results of regular biopsies, is the most effective way to prognosticate survival of CC patients.

The researches on neuron network applying in survival prediction in patients after operation were published in April 2013 on STMOPEN.net. The clinical finding was based on the results of treatment of 125 patients with CC; sick women were divided randomly in ratio 4:1 in training groups and test-groups respectively. Through logistic regression prognosticating factors were analyzed to build up the model of this regression, and a possible neuron network for these factors was created. With the help of training group neuron network was taught and the test group was defined by this neuron network. The accuracy, sensitivity and specifics of neuron network model made up 92%, 75% and 95, 23% respectively. The accuracy, sensitivity and specifics of logistic regression made up 84%, 50% and 82, 61% respectively. Thus, neuron networks were more flexible while analyzing survival. Nonlinear effects might be located in the model and random data characteristics such as divisions without assumption and those which can correspond to neuron network assumption. Neuron networks have sufficient prospective of usage.

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 to exclude the subjective point of view in choosing the method of treatment.

2. 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/m², 5-phtoruracyl 1000 mg/m² 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 gr added to the total doze of 30 gr with potentiality of cysplastyn 40 mg/m² 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 gr with potentiality of cysplastyn 40 mg/m² 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), histology, presence or absence of contaminant diseases, hemoglobin index, weight and height, pain syndrome, pregnancies.

3. Results and Discussion

After finishing up the process of training of all neuron networks for all possible combinations, the testing was performed with the help of previously selected testing sets of data that had not been used during training session.

Received calculation results of indexes of targeted parameters were compared to models

(from the testing set) by calculating absolute value and with consideration of absolute deviation and calculation of its mean.

Among the results of neuron networks output we chose the smallest. Very low (about zero) deviations for all the indexes should be excluded as such that evidence the effect of “overdoing”.

Further the same choice was made for each set-complex of informative parameters.

The most optimal criteria in this case are:

1. minimally possible complex of informative parameters;
2. The highest accuracy of defining the target parameter (either absolutely or in percentages).

The chosen complex was selected according to the above mentioned criteria – that is the informative complex should be considered as the most optimal and acceptable.

In our case the research was being held with reference to the selection of parameters according to the following logical chain:

1. All 10 parameters
2. 9 parameters – exclude “pain” – too subjective, and besides this parameter could be connected with contaminant diseases, so it does not show the spread of cancer process accurately.
3. 8 parameters – exclude “histological form of tumor”, as in each patient scuamous cell carcinoma had been verified.
4. 7 parameters – exclude “pregnancies”, the given parameter belongs to the risk factor of appearing CC, but does not matter to a patient already sick in CC.

Further reducing in parameters number does not seem to be back grounded, because all the parameters (age, growing and location of tumor, hemoglobin before treatment begins, contaminant diseases, weight, height) are the factors of CC prognosticating, thus, each separately taken element influences disease flux and prognosis as well as the choice of the most effective method of treatment.

At each stated stage one neuron network was being trained for each base (method of treatment) with further testing. Average mean deviation of patient’s survival/death was evaluated.

Another fundamental aim of this stage of research is the choice of adequacy in task complication of algorithm of training, which is the algorithm of solving the task of optimization of weight modules and neuron retardation. As a result of

factor analysis we have managed to define the most appropriate one – failure resistant algorithm of reverse spread.

According to the results of the research – we managed to choose the optimal number and the combination of informative parameters unequivocally.

Chart 1: The Trained Neuron Network

Number of parameters	Mean absolute deviation		
	Group 1	Group 2	Group 3
10	0,4214	0,3657	0,4514
9	0,4587	0,4561	0,4963
8	0,4028	0,4200	0,4400
7	0,4338	0,4228	0,5542

So, according to the minimum deviation criterion of defining the probability of survival in each group of patients the optimal number of parameters was estimated as eight, that is: age,

form of growth and location of a tumor, hemoglobin before the treatment begins contaminant diseases, weight and height.

Chart 2: Network 4 – Trained for Group 1

Group 1 Test	0,98	0,99	0,96	0,99	0,91	0,85	0,99	0,403
Group 2 Test	0,71	0,99	0,84	0,80	0,89	0,79	0,96	0,47
Group 3 Test	0,99	0,81	0,96	0,88	0,95	0,90	0,94	0,45
Target indexes	1	1	1	1	0	0	0	Deviation

The final stage of research was the testing of the trained neuron networks both at corresponding test groups enrolment and cross examining (Chart 2-4). It is important to mention that the information about the patients at enrolment testing was not used with training purposes and is completely unknown for neuron networks – thus, the prognosticating process of survival is being modeled.

In general, we can see, that for its own group testing results for each network are the best – it

proves that the training is correct – on the basis of the analysis of the array of the entry data neuron networks can differentiate the method of treatment, and it is critical for its further usage. In prospect on condition the statistical base of the research increases, there exists the possibility of creating automatic (programming) system of prognosticating survival probability by means of comparing such indexes for each of treatment methods.

Chart 3: Network 5 – Trained for Group 2

Group 1 Test	0,28	0,67	0,92	0,70	0,92	0,69	0,92	0,57
Group 2 Test	0,73	0,91	0,96	0,93	0,84	0,77	0,86	0,42
Group 3 Test	0,56	0,77	0,92	0,53	0,93	0,44	0,67	0,46
Target indexes	1	1	1	1	0	0	0	Deviation

Chart 4: Network 6 – Trained for Group 3

Group 1 Test	0,20	0,32	0,79	0,32	0,64	0,57	0,33	0,56
Group 2 Test	0,58	0,37	0,71	0,14	0,59	0,68	0,61	0,58
Group 3 Test	0,50	0,39	0,34	0,72	0,74	0,04	0,34	0,45
Target indexes	1	1	1	1	0	0	0	Deviation

Now we will research results separately for each group of patients. For this it would be appropriate to analyze the results for several test cases:

1) the worst variant of prognosticating for Group 1 for the network, trained for Group 1 – “0,96” instead of “1”. For this very case the probability at the other two networks is “0, 84” and “0,71”. It means that in case of choosing the first and the third methods of treatment for this patient the probability of a successful treatment is lower than in the second variant;

2) the best option of prognosticating in Group 2 for the network, trained for Group 2 – “0,99” instead of “0”. For this very case the probability at the other two networks is “0, 92” and “0, 33”. So, in case of choosing the third method of treatment for this patient the most evident will be lethal outcome, and in case of applying other ways patient’s chances on successful treatment are substantially higher;

3) testing results for the network trained with the help of the third method of treatment are generally lower – it can be easily explained from the medical point of view, as these patients were not operated. The evidence of it is all the variants, but the worst variant of prognosis for Group 3 is significant in the network, trained for Group 3 – “0,34” instead of “1”. For this very case the probability at two other networks is “0, 92” and “0, 96”. Correspondingly for this patient any other method of treatment is to be the most

effective, than in the case of applying the third method of treatment.

4. 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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