
The Developed “Medical Commander Prognosis” Software Application

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ABSTRACT

The precise prediction in medicine (especially in oncology) plays a critical role in prevention, treatment, assessment of the effectiveness of methods of treatment and treatment outcomes for cancer patients. The most precise prognostication method in computational mathematics today is the interpolating method. In connection with this the fundamentally new “Medical Commander Prognosis” software application was developed. The software application “Medical Commander Prognosis” intended for optimal interpolation prediction of the studied symptoms in medicine (especially in oncology) permits in real-time prediction of the studied symptoms in medicine based on two principles of interpolation prognostication: of minimization of the difference (error) between the known and calculated by different methods of polynomial interpolation of the numerical values of the studied symptom ; of selection as the values of the studied symptom of the maximum number of statistical frequencies of the observed patients in the specified intervals of the study. The use of developed software application “Medical Commander Prognosis” in clinical conditions permitted to identify a splash (“hump”) of patients with metastases after surgery and to determine the effect of using various methods of preventive treatment after surgery on the increase of the time before the appearance of metastases among the patients, i.e. to determine the effectiveness of the applied treatments.

Keywords: *Computational Mathematics; interpolation; optimal interpolating prognostication; the software application; programming.*

INTRODUCTION

The precise prediction in medicine (especially in oncology) plays a critical role in prevention, treatment, assessment of the effectiveness of methods of treatment and treatment outcomes for cancer patients. The most precise prognostication method in computational mathematics today is the interpolating method. The interpolation in computational mathematics is a method of finding intermediate values of nodal points on an existing discrete set of known values. Under conducting scientific and engineering calculations, it is often necessary to operate with sets of values obtained experimentally or by random selection.

As a rule, on the basis of these sets, it is necessary to construct a function that can determine unknown values included inside of this set with high accuracy. This task is called approximation. The interpolation is a type of approximation in which the curve of an experimentally constructed function passes exactly through existing data points (anchor points).

In addition, interpolation permits to predict (extrapolate) the points of the experimentally constructed function out of limit of the interval in which the constructed function is specified.

The mathematical essence of interpolation consists in the following.

Frequently is required to restore the function $f(x)$ for all values of x on the interval, $a \leq x \leq b$, if its values are known in a certain finite number of points of this interval.

These values can be found as result of observations (measurements) in some full-scale experiment, or as result of the calculations. Furthermore, the function $f(x)$ is calculated by formula and the calculations of its values in this formula are very labor-consuming; therefore it is desirable to have for the function the simpler (less labor-consuming for the calculations) formula, which would permit to find the approximate value of the considered function with the required precision at any point of interval. As a result the following mathematical task appears.

Assume that the interval is assigned by the grid $\omega = \{x_0 = a < x_1 < \dots < x_n = b\}$ and its nodal points are assigned by the values of function $y(x)$, equally $y(x_0) = y_0, \dots, y(x_i) = y_i, \dots, y(x_n) = y_n$.

Necessary to construct interpolant - function $f(x)$, which coincides with the function $y(x)$ in the grid points:

$$f(x_i) = y_i, \quad i = 0, 1, \dots, n \quad (1)$$

The basic purpose of the interpolation - to obtain the fast (economical) algorithm of the calculation of values $f(x)$ for the values x , which are not contained in the table of data.

The selection of the interpolant $f(x)$ and estimation of error $y(x) - f(x)$ is carried out as follows.

The interpolating functions $f(x)$, as a rule, are built in the form of the linear combinations of some elementary functions:

$$f(x) = \sum_{k=0}^n c_k F_k(x) \quad (2)$$

where $F_k(x)$ - the fixed linearly independent functions, $c_0, c_1, \dots, c_n$ - not determined yet coefficients.

Thus, can obtain the system of $n+1$ of equations relative to the coefficients $\{c_k\}$:

$$\sum_{k=0}^n c_k F_k(x(i)) = y(i) \quad (3)$$

Assume that system of functions $F_k(x)$ is such that with any selection of nodal points $a = x_0 < x_1 < \dots < x_n = b$ the determinant of the system is different from zero:

$$\begin{array}{ccccccc} F_0(x_0) & F_1(x_0) & F_2(x_0) & \dots & F_n(x_0) \\ F_0(x_1) & F_1(x_1) & F_2(x_1) & \dots & F_n(x_1) \\ \dots & \dots & \dots & \dots & \dots \\ F_0(x_n) & F_1(x_n) & F_2(x_n) & \dots & F_n(x_n) \end{array} \quad (4)$$

Then on assigned $y(i)$ ($i = 0, 1, \dots, n$) the coefficients c_k ($k = 0, 1, \dots, n$) are uniquely determined from the following system:

$$\begin{array}{l} c_0 F_0(x_0) + c_1 F_1(x_0) + c_2 F_2(x_0) + \dots + c_n F_n(x_0) = y(0) \\ c_0 F_0(x_1) + c_1 F_1(x_1) + c_2 F_2(x_1) + \dots + c_n F_n(x_1) = y(1) \\ \dots \\ c_0 F_0(x_n) + c_1 F_1(x_n) + c_2 F_2(x_n) + \dots + c_n F_n(x_n) = y(n) \end{array} \quad (5)$$

The selection of the form of $F(x)$ defines the type of interpolation and on the obtained coefficients c_k and its values at the points can determine $f(x)$ interpolation points.

The most commonly used in practice is the polynomial interpolation. This interpolation includes the following well-known methods described in [1]:

- 1) Newton's interpolating formula[2-4];
- 2) Lagrange polynomial[5];
- 3) Spline function and cubic spline[6, 7].

The paper presents a new developed "Medical Commander Prognosis" software application.

The software application "Medical Commander Prognosis" intended for optimal interpolation prediction of the studied symptoms in medicine (especially in oncology) permits in real-time the prediction of the studied symptoms in medicine based on two principles interpolation prognostication: of minimization of the difference (error) between the known and calculated by different methods of polynomial interpolation of the numerical values of the studied symptom; of selection as the values of the studied symptom of the maximum number of statistical frequencies of the observed patients in the specified intervals of the study.

The use of developed software application "Medical Commander Prognosis" in clinical conditions permitted to identify a splash ("hump") of patients with metastases after surgery and to determine the effect of using various methods of preventive treatment after surgery on the increase of the time before the appearance of metastases among the patients, i.e. to determine the effectiveness of the applied treatments.

MATERIALS

The use of developed software application "Medical Commander Prognosis" in clinical conditions, which uses two principles of optimal interpolation prognosis, was carried out on the example of studying of the symptom of the appearance of metastases among patients after surgery.

The use of developed software application "Medical Commander Prognosis" in clinical conditions for prognosis of the progression of tumor process among oncological patients was accomplished on the base of All-Union Scientific Oncological Centre of AMS of the USSR (Moscow, Russia) and Republic Clinical Oncological Dispensary (RCOD, Tajikistan).

METHOD AND RESULTS

The author [1] developed two principles of interpolatingprognostication in oncology: the minimizing of the difference (error) between the known and calculated by different polynomial interpolating methodsnumerical valuesof the investigated symptom; the selection as the values of the investigatedsymptom the maximum number of statistical frequencies of the observed patients in the given intervals of conducting study.

These principles led to the development of algorithm of developed "Medical Commander Prognosis"software applicationintendedfor optimal interpolatingprognostication of the investigated symptoms in oncology.

The modeling of the optimal calculation of the interpolating points of medical data was conducted via the comparison of all used by the algorithm interpolating methods on the error $y(x) - f(x)$ and the automatic selection of interpolation with the smallest value of error.

The following methods of polynomial interpolation were used: Newton interpolation (Newton's interpolating formula), Lagrange interpolation (Lagrange interpolating polynomial), and spline interpolation, when between any adjacent grid points the function is interpolated by linear (linear spline interpolating function) or by the polynomial of the third power (cubic spline interpolating function).

Figure 1 presents the block-schema of algorithm of developed "Medical Commander Prognosis" software application intended for optimal interpolating prognostication of the investigated symptom in oncology:

- 1) The frequencies of oncological patients, i.e., a percent quantity of patients in the assigned interval of the predictable symptom on relation to all patients on all intervals of the predictable symptom are entered using a previously developed "Medical Commander" computer medical process manager [8], figure 2.

If the predictable symptom is the period of time of the appearance of metastases among oncological patients after the carried out treatment, then in percentage expression, the number of patients, distributed by the program of the construction of histograms, on the time intervals of the periods of the appearance of metastases after the carried out treatment, is entered.

- 2) Entered data become the nodal points for conducting of the optimal interpolating prognostication.

The developed "Medical Commander Prognosis" software application consecutively produce the interpolating of points and error $y(x) - f(x)$ by the Newton interpolation (Newton's interpolating formula), by the Lagrange interpolation (Lagrange interpolating polynomial), by spline interpolation, when between any adjacent grid points the function is interpolated by linear (linear spline interpolating function) or by the polynomial of the third power (cubic spline interpolating function) until the optimal interpolating method with the minimum error will be determined.

- 3) The developed "Medical Commander Prognosis" software application builds and prints the graphs of main and interpolating functions of investigated symptoms according to obtained data of optimal interpolating prognosis and the numerical values of these functions of investigated symptoms (figure 3).

The developed "Medical Commander Prognosis" software application was realized on the computer language C. The time of the calculations of program on the personal computer composes several seconds.

RESULTS

Until now, oncologists [9] have an opinion that the dependence of the period of the appearance of tumor metastases has an exponential form, i.e., the number of patients with metastases that have appeared among patients after surgery decrease exponentially during time. However, still in 1991, the author developed a method for computer optimal interpolating prognostication of the investigated symptom in oncology [10] and set the task of using this method to determine the periods of the appearance of metastases among cancer patients after surgery. The results of the application of the developed method of computer optimal interpolating prognostication of the investigated symptom in oncology in the clinical

practice presented in [10], and later in [11, 12], showed that the number of patients with metastases that have appeared after surgery does not decrease exponentially during time, but there is a "hump" of number of patients with metastases after surgery and permitted to determine the effect of using various methods of preventive treatment after surgery on an increase of the time of the appearance of metastases among patients, i.e., to determine the effectiveness of the applied methods of treatment.

The use of the developed "Medical Commander Prognosis" software application intended for prognostication of the investigated symptom in clinical practice was carried out on the basis of the Republican Clinical.

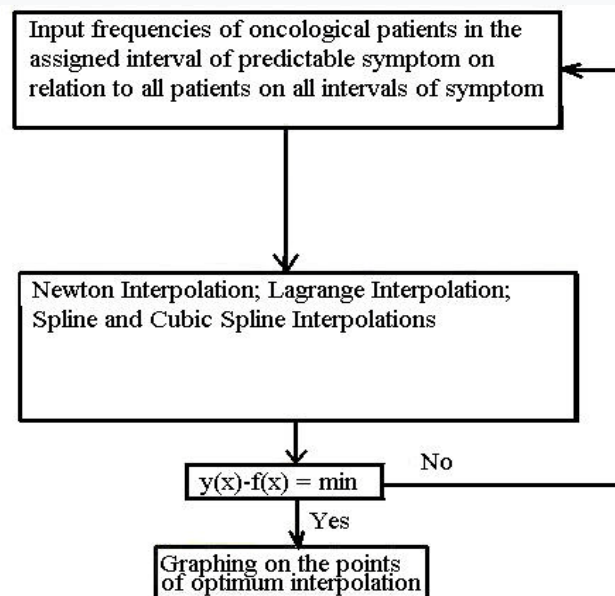


Fig. 1: Block-scheme of algorithm of developed software application "Medical Commander Prognosis".

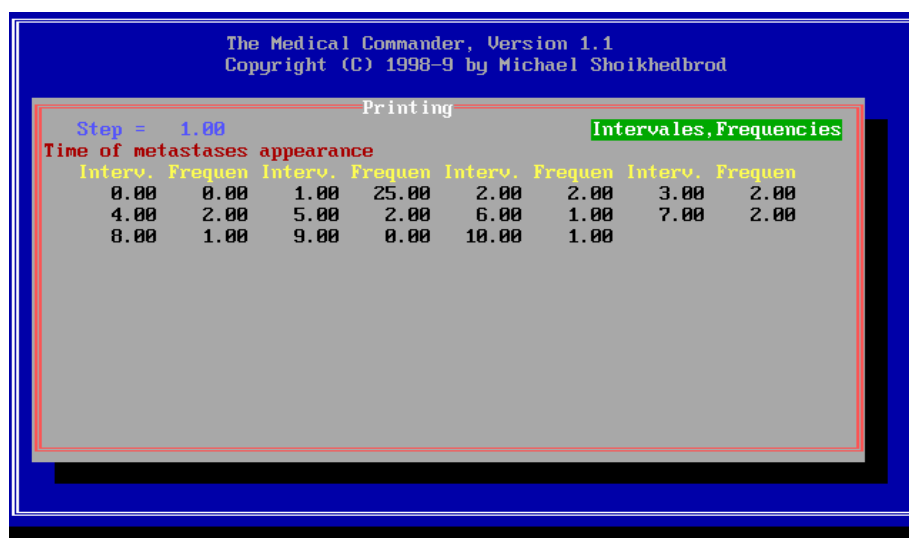


Fig. 2: The frequencies of oncological patients, i.e., a percent quantity of patients in the assigned interval of the predictable symptom on relation to all patients on all intervals of the Predictable symptom are entered using a previously developed computer medical process Manager "Medical Commander".

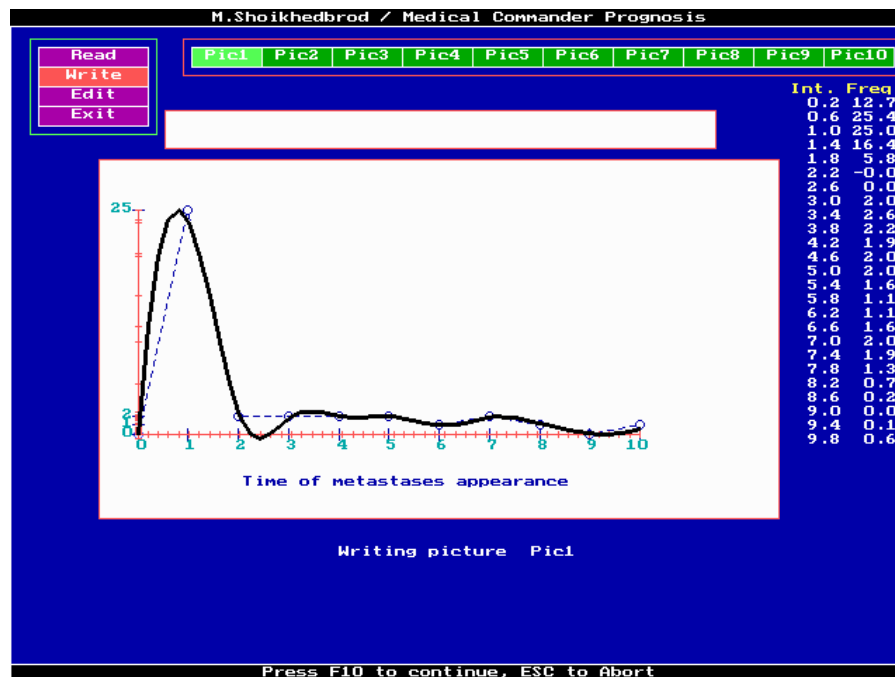


Fig. 3: The developed software application "Medical Commander Prognosis" builds and prints the graphs of main and interpolating functions of investigated symptoms according to obtained data of optimal interpolating prognosis and the numerical values of these functions of investigated symptoms.

Oncological Dispensary (RKOD, Tajikistan) to determination of the periods of metastases appearance among patients with lung cancer, breast cancer among women and men, and malignant egg tumors after surgery [13].

The determination of the individual prognosis of the outcome of treatment of patients with lung cancer became possible due to the application of the methodbased of two principles of interpolation prediction using developed "Medical Commander Prognosis"software application intended for the computer optimal interpolating prognostication of the investigated symptom: the period of the appearance of metastases among patient after the surgery. Depending on the selected control observation period, the prognosis of treatment outcomes was divided into favorable and unfavorable.

The following periods were selected as the control periods: 5 years, 18 and 36 months from the date of surgery. In clinical oncology, a period of 5 years has been established as a criterion for a long-term recovery. The choice of 18 and 36 month periods is associated with analysis using computer optimal interpolating prognostication of the investigated symptom of dependence of disease progression on different period after surgery (figure 4).

The peak of this "hump" occurs at 21 months, ranging from 12 to 30 months after surgery. Thus, the appearance of metastases among cancer patients with lung cancer should be most likely during this period. The remaining weak peaks onfigure 4 can be classified as small statistical fluctuations of the exponential decreaseof the number of patients with lung cancer having metastases. The obtained results permitted to develop new approaches to the postoperative management of patients after surgery and to the choice of periods of test examinations after the surgery. Patients with a predicted favorable outcome do not need frequent examinations during the first 3 years after surgery. During this period, the

examination is possible once / every six months. The frequency of inspections should be increased in proportion to the coming five-year period. The frequency of examinations of patients with a predicted adverse outcome should be increased to monthly follow-up examinations with the achievement of prognosis periods for metastases in the period from **12** months to **30** months, with particular attention to **21** months. The use of the developed "Medical Commander Prognosis" software application intended for optimal interpolating prognostication of the investigated symptom: the dynamics of the appearance of the first symptoms of disease progression in the group of operated women with breast cancer was studied. The research results are shown in figure 5.

Figure 5 shows that the surge of the "hump" among patients with the first metastases after surgery appears in the period from **6.5** to **24** months, and the peak falls on the **18th** month. The remaining weak peaks on figure 5 can be qualified as small statistical fluctuations of the subsequent exponential decrease of the number of women with breast cancer having metastases. On the basis of the data research of the Kiev Research Institute of Oncology and Radiology, the dynamics of generalization of breast cancer among men after treatment was studied using the computer optimal interpolating prognostication method. The results of the studies showed that, just as in the case of breast cancer among women, men with the first metastases after the treatment have formed a splash ("hump"). The period of this spike is removed to the right compared with the case of breast cancer among women and has period from **12** months to **27** months, and the peak of the spike occurs on the **22nd** month.

The obtained results permitted to develop some approaches to their implementation in practice. The period of the appearance of the "hump" of generalization of breast cancer among women and men should become a criterion for choosing regimes of test examinations of patients for their preventive treatment. The existing procedure for test examinations in the period after the surgery is completely contrary to the obtained data. This procedure does not lead to the identification of symptoms of disease progression during the spread of the "hump" of metastases and practically deprives the patient of chances, since during this period patients are rarely examined even with annual intervals. The developed approach is based on the principle of maximizing of the number of test examinations before the period of "hump" of generalization of the tumor neoplasm.

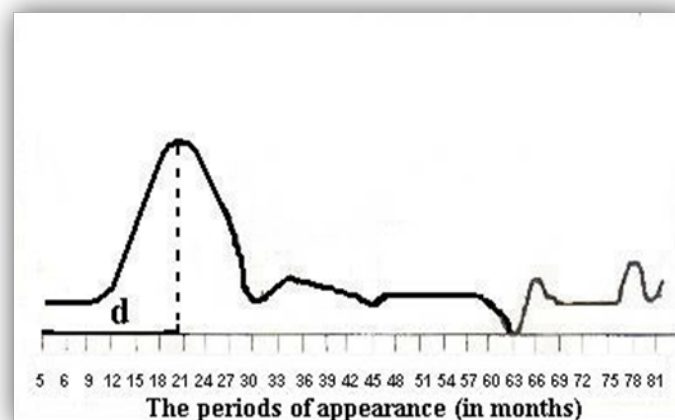


Fig. 4: The dynamics of the generalization of lung cancer in the group of patients after the surgery. (d - time of the splash of the maximum number of patients with the first metastases after the surgical operation).

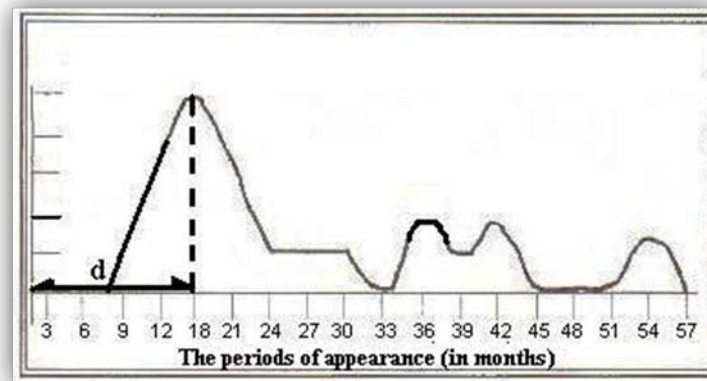


Fig. 5: Dynamics of the generalization of breast cancer in the group of woman with breast cancer after surgery. (d - time of the splash of the maximum number of woman with the first metastases after surgery)

The obtained data of the period of the appearance of the “hump” of generalization can serve as a criterion for the choice of chemotherapy regimens carried out before the “hump” of generalization. There is all reason to expect that this approach will significantly improve the results of breast cancer treatment among women and men. For prediction of the dynamics of the progression of malignant neoplasms of the eggs and for establishment of the real timing of special antitumor therapy after surgical removal of the egg, method of computer optimal interpolating prognostication was used. The **104** patients with reliably established timing of the appearance of metastases after treatment were processed. None of these patients had metastases at the time of initiation of treatment.

In this case the splash of patients (“hump”) with the appeared metastases that were subjected only of surgical treatment was determined in the group of seminoma tumors of the egg. The period of appearance of the “hump” was **3-6** months after surgery for the primary tumor (orchiecnikulektomy), and the peak of the “hump” came at the **5th** month.

For teratomatous tumors of the egg, the dynamics of the development of primary metastases in the group of only operated patients was as follows: in the period from **3** to **5** months, there was a splash of the “hump” of patients from the moment of surgery with a peak at the point of the **4th** month.

The splash of “hump” of the patients, relative to patients, who received preventive medicinal treatment during the postoperative period, was noted and the period of the appearance of metastases was fallen at the point of the period from **8** to **10** months with the peak at the point of **9th** month. This result testifies the effectiveness of use of the postoperative period of preventive chemotherapy and proves the ability of developed computer optimal interpolating prognostication method for evaluation of the effectiveness of the conducted preventive treatment.

CONCLUSION

Thus, the use of the developed “Medical Commander Prognosis” software application based on two principles of interpolation prediction in oncology: the minimizing of the difference (error) between the known and calculated using various methods of polynomial interpolation numerical values of the studied symptom and selection as the values of the

investigated symptom the maximum number of statistical frequencies of the observed patients in the specified intervals permitted to precisely predict the studied symptoms in oncology. The use of developed "Medical Commander Prognosis" software application in clinical oncological practice permitted to identify a splash ("hump") of patients with lung cancer, breast cancer among women and men, and malignant egg tumors with metastases after surgery and precisely to determine time of appearance of metastases among these patients.

Based on this result, a technique was developed that allows planning the optimal tactics of postoperative management of the patient, selection of the periods of test examinations and regimens for prophylactic treatment of cancer patients, which plays a huge role in improving long-term results of treatment and of the success of this treatment.

The use of developed "Medical Commander Prognosis" software application for investigated symptom: time of appearance of metastases among oncological patients can serve as a test-scheme that precisely determines the dependence of the time of the appearance of metastases among patients after surgery on the postoperative treatment, on the type and properties of a malignant tumor, on geographical and many other factors.

The use of developed "Medical Commander Prognosis" software application permitted to reduce frequency, but also to considerably move aside the periods of the appearance of metastases thereby proving the ability of its use for determination of the effectiveness of the used methods of preventive treatment of the oncological patients. The use of developed "Medical Commander Prognosis" software application can be applied to predict any investigated symptom in order to identify hidden patterns not only in oncology, but also in other areas of medicine.

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