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DETERMAINATION OF STANDARD VALUES ON INDIRECT INDEX OF ERYTHROCYTES FORM REPRESENTATION

Determination of pathology presence in human organism by the level of deviation of mean statistic form of erythrocyte of the sick person relatively analogous level of healthy person is considered. Statistic calculations of convectional division of confidence intervals of erythrocytes of sick and healthy persons and diagnosis performing on their basis is proved.

Key words: *blood test, scanning, means statistic form of erythrocyte, laser beam.*

Introduction

Nowadays investigations of form elements of blood [4] allow to speak about new trends and directions in medicine, namely about the possibilities of diagnosis of certain diseases by the level of deviation of mean statistic form of sick person erythrocyte relatively analogous of healthy person erythrocyte.

Problem set-up

As a result of research, performed by the American scientists in 90's of the XX^{th} century, it was established that, applying statistic methods some diseases can be revealed by the form of erythrocytes, namely: tropical malaria, leukemia, anemia. In forensic medicine form of erythrocytes enables to determine rare kinds of poisons, that cannot be detected by convectional analysis.

Scientist of USA and Israel at the international symposium held in 2008 at Columbia University put forward the idea of creation of certified list of most promising modern technologies of diagnosis among these technologies the technique of express-diagnostics by patient blood test was considered.

For instance, nowadays optical monitoring of neural activity based on values of optical properties of blood, applied in investigations of somatosensory and acoustic structures (Godde, Hess) as well for the analysis of anabolic corticonuclear structures (Pabva, Weliky).

Nowadays the creation of express-system of blood analysis is very actual problem. Commonly this type of analysis is closely connected with application of probabilistic approach, which in its turn, enables to obtain only qualitative judgment regarding the presence of a disease. It is, for instance, systems of analysis, based on the study of the image of laser beam dissipation from the blood sample. We can avoid probabilistic approach only I case of the analysis of each separate particle in the group, since before that we have analyzed the whole group (for instance, dissipation of the laser beam by a group of erythrocytes). That is why, in our opinion, the express-system of blood analysis must be based on study of each information element (erythrocyte). This is possible due to application of the principle of blood sample scanning by the laser beam, the dissipation from each form element can influence the change of intensity level of reflected radiation. Having analyzed the dependence of intensity change in time, in the process of scanning, we may speak with sufficient degree of accuracy about mean statistical form of erythrocyte in investigated blood sample. The characteristic feature of the given system is the classification of experimentally obtained signal (time dependence of reflected laser beam intensity on the sample of blood solution while scanning) according to corresponding training samples.

Aim of research

The aim of the given research is to make applicable for practical usage in medical laboratories for diagnosis of anemia, leukemia and tropical malaria the suggested system of express-analysis of

form elements of blood by the method of suspension scanning with certain concentration of erythrocytes.

In this case it is necessary that the value of intensity level change of laser beam reflected the sample (ΔI_{max}) allows to characterize mean statistical parameters of erythrocyte with high accuracy (error must not exceed 20%), determine the influence on the accuracy of diagnosis by the given method of erythrocytes concentration in blood solution.

The aim of research is to verify the concentration of erythrocytes in blood solution applying Goriayev grating or calculation chambers as the basis for experimental stand. By means of computation of erythrocytes in cell we must obtain initial value of their concentration in blood solution and make sure that blood solution is prepared correctly before the experiment.

Material and methods of research

The property to generate and registrate biological objects along with its demasking signal, that is result of internal distribution of probing signal energy is the ability to reveal by radioelectronic means the components of biological objects. The measure characterizing the ability to reveal the erythrocytes of corresponding concentration in blood solution by means of laser beam scanning is maximum variation of beam intensity ΔI_{max}, reflected from investigated sample, that changes within the range 0,5 – 14 mV. For convenience sake, the variation of intensity level we will consider taking into account variation of proportional voltage level, measured at the output of optical converters. The higher is the value of ΔI_{max} the better is the ability to registrate the form of investigated biological objects. Indirect index of erythrocytes form representation is average time $\Delta\tau_a$ that equals the duration of intensity "drop" of laser beam reflected from investigation sample.

As the investigated parameter we will consider average duration of the pulse in experimentally obtained graphs, that present distribution of erythrocytes of corresponding concentration in blood solution by means of variation of intensity level of reflected laser beam while scanning of the blood samples of healthy persons. Tables 1 and 2 contain the results of investigations of eight blood investigation samples taken from each of five participants of the experiment, who belong to the group of sick persons. Each blood sample from certain person was taken with the interval of one week, after that averaging of the values of ten recurrent blood samples was performed. Thus, we can sate the statistic significance with confidence coefficient of 95% of research data. It was established experimentally, that limiting value I_{lim}=15 мV corresponds to intensity drop level.

Table 1

Results of investigation of blood samples of healthy persons

Number of experiment		1	2	3	4	5	6	7	8
Average duration of intensity level "drop" of reflected laser beam for the group persons, μ sec	y_1	2,81	3,49	3,51	3,2	3,46	3,33	3,67	3,88
	y_2	3,72	3,45	3,47	3,43	3,21	3,18	3,3	3,13
	y_3	2,92	3,52	3,56	3,62	3,11	3,27	3,16	3,47
	y_4	3,53	3,38	3,32	3,41	3,08	3,69	3,49	3,77
	y_5	3,28	3,44	3,39	3,15	3,28	3,35	3,71	2,98

Table 2

Results of investigation of blood samples of sick persons

Number of experiment		1	2	3	4	5	6	7	8
Average duration of intensity level "drop" of reflected laser beam for group of sick persons, μ sec	y_1	4,21	4,35	4,59	4,83	5,07	4,85	5,08	4,37
	y_2	4,32	4,61	5,39	4,43	4,87	4,63	5,43	5,12
	y_3	4,63	4,45	5,14	4,89	5,51	5,58	4,91	4,51
	y_4	4,69	5,53	5,17	4,9	4,56	4,71	4,93	5,63
	y_5	5,24	4,75	4,96	5,28	4,8	4,99	5,33	4,99

Verification of the hypothesis relatively the type of distribution function was the type of

distribution function was carried out in accordance with matching criteria − Pirson, Kolmogoroff. Verification of the hypothesis relatively type of distribution function, is recommended to perform, due to small volume of sample, by the approximate methods − graphic method or by asymmetry and excess.

Graphic method provides arrangement of experimentally measured values (x_1, x_2, ..., x_n) of certain physical magnitudes in ascending order, after that, each magnitude is matched with average value of "drop" duration of intensity level of reflected laser beam of corresponding probability P_k, calculated by the formula:

$$P_k = \frac{k - 3/8}{n + 1/4}, \tag{1}$$

where k is ordinal number of experimental measurement of physical value x, $k=1, 2, ..., n$.

By the results of experimental study of blood samples of healthy persons and calculations of corresponding elements of the sample of pro probability P_k values, calculated by the formula (1); cumulative function of distribution of average duration "drop" of intensity level of reflected laser beam for the group of healthy persons, presented in Fig 1

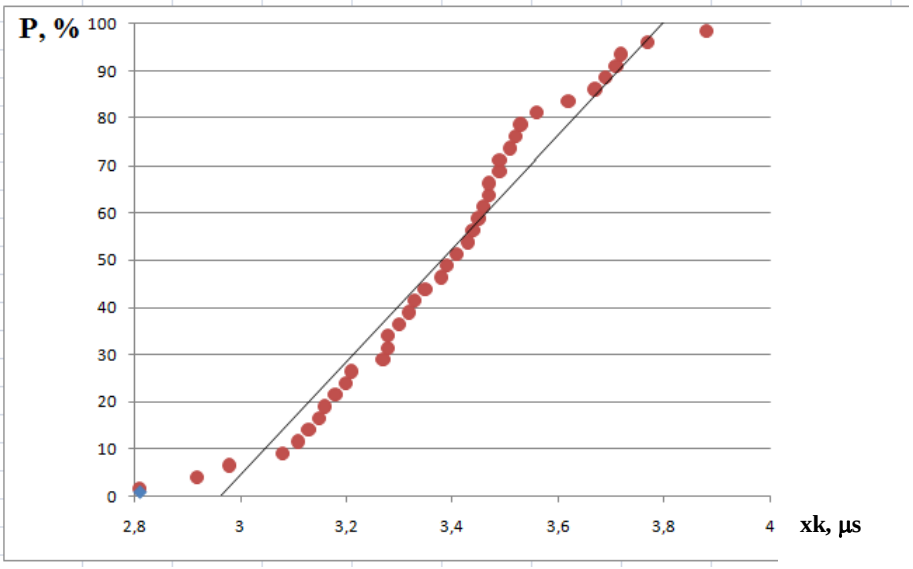

Fig. 1. Cumulative function P of distribution of average duration "drop" of intensity level of reflected laser beam for the group of healthy persons

We will present the cummulative function of distribution of average "drop" duration of intensity level of reflected laser beam for the group of sick persons (Fig 2).

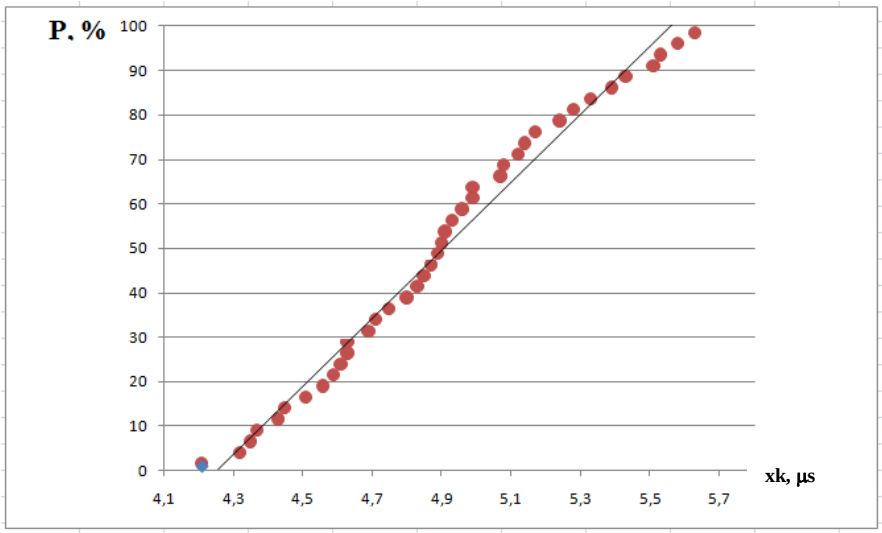

Fig. 2. Cumulative function *P* of distribution of average "drop" duration of intensity level of reflected laser beam for the group of sick persons

Visual analysis of the given cummulative function for these two samples enables to make a conclusion that distribution law is normal with high degree of validity.

While verification of the hypothesis regarding normal distribution, indices of asymmetry and excess also were used. Asymmetry is the index that shows the degree of dissymmetry of differential function curve of experimental distribution as compared with the function of normal distribution.

Excess is the index, that shows the evolution of differential function curve of experimental distribution as compared with differential function of normal distribution [1].

$$A \approx \frac{1}{ns^3}\sum_{i=1}^{n}(x_i - \bar{x})^3 ,$$

$$E \approx \frac{1}{ns^4}\sum_{i=1}^{n}(x_i - \bar{x})^4 - 3 ,$$

where $\bar{x}$ – is arithmetical average of the sample; s – is standard deviation of the sample; x_i – is i-th value of measured physical value in the sample.

Verification of the hypothesis relatively normal distribution by the indices of asymmetry and excess was performed in MS Excel 2007environment for distribution function of average "drop" duration of intensity level of reflected laser beam for, the group of healthy persons and for the group of sick persons, correspondingly. Verification performed with confidence coefficient of 95% proved that distribution law is normal.

In accordance with the International standard ISO 5479-97 "Statistic presentation of data. Verification of probabilities distribution deviation from normal distribution" in case, if three is no priori information regarding the type of deviation from normal distribution, it is recommended to use multilateral criterion Spario-Wilky, that is applied for samples from $8 \le n \le 5\,0$. Small samples ($n < 8$) while revealing deviations from normal distribution do not confirm reliably obtained results.

The criterion is based on regression analysis or ordinal statistic by their expected values and in analysis of variance for complete sample. Statistics of the given criterion is relation of sum square of liner difference of optionally arranged statistics to convectional evaluation of dispersion.

Since the criterion is based on arranged observations, then the first of independent observations are placed in acceding order and are designated by symbols $x_1, x_2, \ldots, x_n$, after that computation of so-called intermediate sum S is performed by the formula:

$$s = \sum_k a_k \left[x_{(n+1-k)} - x_k \right],$$

where k − is the index, having the value from 1 to $n/2$ or from 1 to $(n-1)/2$, if n is even and odd, correspondingly; відповідно; a_k − is the coefficient, having special values for the volume of sample n. In this case the statistics of criterion W will have the form:

$$W = S^2 / (nm_2),$$

where $nm_2 = \sum (x_i - \overline{x})^2$; n − is volume of the sample; m_2 is elective central moment of the second order.

If the value of certain observations are the same, the arranged series is humbered with interation of equal observations as they appear in initial series.

If $\alpha=p$, then critical region of the criteria is formed by the values less than , p-quantile for $\alpha=p$. ISO 5479-97 contains tables of p-quantilers of criterion W statistics for $\alpha=p=0{,}01$ and $\alpha=p=0{,}05$.

Using the data of arranged series with $n=40$ independent values of average duration of intensity level "drop" of reflected laser beam for the group of healthy persons, we will calculated: $\overline{x}$ =3,378, nm_2=1,155, and determine the value of intermediate sum S: S=1,47. We obtain experimental value W_{e1} = 1,87. In accordance with ISO 5479-97, the value of p-quantile of W_{gr} criterion statistics for $n=40$ and $\alpha=p=0{,}05$ equal 0,940. Since this value is less than experimental value W_{e1}, then zero hypothesis testifies that distribution in the sample is normal with coefficient 99,95%.

Thus, for "drop" average duration of intensity level of reflected laser beam for the group of healthy persons, that presents the form of "healthy" erythrocytes we obtain:

− arithmetical average of corresponding sample $\overline{x}$ =3,378 μsec;

− the nearest value from a series of nominal values, that corresponds to the accuracy of measurement of "drop" average duration of maximum intensity level of reflected laser beam, that presents the form of "healthy" erythrocyte is 3,4 μsec;

− average square deviation in the sample: σ=0,237 μsec;

− half interval of normative values: $3\sigma \approx 0{,}7$ μsec.

Thus, normative interval of values per average duration of intensity level "drop" of reflected laser beam for the group of healthy persons, that presents the form of "healthy" erythrocyte is that presents 3,4±0,7 μsec.

For average duration "drop" of intensity level of reflected laser beam for the group of sick persons, that presents the form of "sick" erythrocytes, we obtain:

− arithmetical average of corresponding sample: $\overline{x}$ =4,906 μsec;

−nearest value from the series of nominal values, that corresponds to the accuracy of measurement of average duration "drop" of maximum intensity level of reflected laser beam, that presents the form of "sick" erythrocytes is 5 μsec;

− average square deviation in the sample : σ=0,376 μsec;

−half interval of normative values: $3\sigma \approx 1$, μsec.

Normative interval of values per average duration of intensity level "drop" of laser beam for the group of sick persons, that presents the form of "sick" erythrocytes 5±1,3 μsec.

Conclusions

In the considered system of express – analysis of blood form elements indirect index of erythrocytes form presentation is average time $\Delta\tau_{ep}$ of intensity level "drop" duration of the laser beam, reflected from investigated sample. Measurement and statistic calculations of indirect index show that normative interval of values for the group of sick people is 5±1,3 μsec, and for the group of healthy people – 3,4±0,7 μsec.

Possibility of conventional division of confidence interval allows to define with certain probability by corresponding analysis of blood test of certain person the diagnosis of diseases,

diagnosis of which requires numerous investigations, expensive reagents and considerable time.

Possibility of convectional division of confidence intervals allows to establish with certain probability by corresponding analysis of human blood test the diagnosis of the diseases, diagnosis of which required numerous procedures, expensive reagents and considerable time.

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