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ABSTRACT

The method of mapping the ellipticity of the polarization image of blood plasma films and the analysis of the statistical moments of the obtained distributions underlies the evaluation of the mammary gland condition is considered in the article. Indicators of sensitivity and specificity of this method were evaluated and graphs of ROC curves for control group, malignant group and benign group were constructed.

Keywords: blood plasma films, polarization ellipticity images mapping, breast, informativeness, receiver operating characteristic curve, diagnosis

1. INTRODUCTION

The successful history of the achievements of polarization diagnostics of biological structures can be demonstrated from the study of transparent tissues, in particular, the determination of glucose concentration in diabetes mellitus [1,2], determination of the polarization characteristics of bacterial [3,4] and red blood cells [5], by continuing examples of differentiation of normal and oncological layers of superficial tissue [6,7,8] polarization approaches for monitoring the status of the myocardium in the treatment of the heart [9] and use in other biomedical programs.

Methods for multivariable laser polarimetry of blood plasma films, combined with modern computer analysis of the measured distributions of their polarization parameters, have the potential to become the basis of a new technology for the assessment of pathological changes in breast detected in the early stages [10,11,12]. Changes in the tertiary and quaternary structures of blood plasma proteins with unchanged biochemical structure are characteristic of pathological changes in biological tissues that occur in the early stages of the disease[13,14,15]. They are detected by changes in the birefringence of blood plasma in the system of multiparameter laser polarimetry of biological layers [16,17].

In papers [11,14], the relationship between the birefringence (different velocity of orthogonally polarized waves) of a protein crystal biological substance and the elliptical polarization transformed by it of a laser wave was analyzed.

Statistical estimates of the distributions of the ellipticity of the polarization images of blood plasma films, identified as central moments of the 3rd and 4th order, proved to be the most informative for the further classification of the states of "norm", "malignant formation", "mastopathy" of mammary glands.

In paper [18], the operational characteristics of the force of the mapping method of the polarization ellipticity distributions of blood plasma film images were analyzed based on the determining the sensitivity, specificity, accuracy, predictability of the positive and the prognosticity of the negative result.

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Thus, the accuracy of the mentioned above method is 80%-83% [18], the values of the predictive parameters are positive $+VP = 82\% - 87\%$ and negative $-VP = 78\% - 79\%$ level [18]. High specificity of multidimensional mapping of polarization ellipticity distributions of microscopic images of blood plasma films was revealed.

In the article we will analyze the classifications of polarization ellipticity distributions of microscopic laser images of albumins and globules of blood plasma films in the diagnosis of physiological states of the breast using ROC (receiver operating characteristic) curves (ROC analysis). The principle of such analysis is to compare the sensitivity and specificity of classification by the level of true positive decisions under the conditions of the so-called randomized ("blind") research method.

The method of ROC analysis determines the informativeness of the method of multiparameter laser microscopy of the ellipticity of polarization of images of polycrystalline networks of blood plasma films in the diagnosis and differentiation of benign and malignant changes of the breast.

2. METHOD OF POLARIZATION MAPPING AND ANALYSIS OF ELLIPTICITY OF POLARIZATION IMAGES OF BLOOD PLASMA FILMS IN THE EVALUATION OF THE STATE OF THE BREAST

The method of mapping the polarization ellipticity distributions of laser images differs significantly from the investigated the many parametric microscopy of the polarization azimuths of the polycrystalline networks of albumins and globulins of optically thin layers of blood plasma described in papers [19]. First of all, this refers to the mechanisms of formation of polarization state distributions in the corresponding laser images. The fact is that the main agents of this process are birefringent large-scale needle crystals of albumin.

Based on the following relation determine the values of ellipticity β_{ik}, polarization at the point with coordinates (i,k) of laser image of a layer of human blood plasma at the appropriate intensities $I_{ik}(45^\circ - \otimes), I(45^\circ - \oplus), I(45^\circ - 0^\circ), I(45^\circ - 90^\circ)$ of polarized filtered microscopic images measured in the system of laser polarimetry of biological layers [20,21].

$$\beta_{jk} = 0,5 \arcsin\left[\frac{I_{jk}(45^0 - \otimes) - I_{jk}(45^0 - \oplus)}{I_{jk}(45^0 - 0^0) + I_{jk}(45^0 - 90^0)}\right].$$

A series of blood plasma smear samples from three patient groups were used as objects of investigation:

- healthy people(donors) – group 1 (30 samples);
- patients with benign breast changes – group 2 (30 samples);
- patients with malignant breast changes – group 3 (30 samples).

Table 1 summarizes the average values and ranges of their changes within the statistical moments M_k^β of the polarization ellipticity distributions of laser microscopic images of blood plasma films from all patient groups.

Table 1. Mean M_1^β, dispersion M_2^β, asymmetry M_3^β and excess M_4^β of polarization ellipticity distributions $\beta(m \times n)$ of laser microscopic images of blood plasma films of patients of all groups

M_k^β	Group 1 (35 samples)	Group 2 (35 samples)	Group 3 (35 samples)
M_1^β	$0,17 \pm 0,029$	$0,23 \pm 0,035$	$0,29 \pm 0,055$
M_2^β	$0,19 \pm 0,027$	$0,23 \pm 0,036$	$0,25 \pm 0,047$
M_3^β	$1,48 \pm 0,21$	$1,07 \pm 0,19$	$0,89 \pm 0,17$
M_4^β	$1,83 \pm 0,38$	$1,59 \pm 0,25$	$1,18 \pm 0,21$

3. METHOD OF ROC ANALYSIS OF POLARIZATION MAPPING OF THE ELLIPTICITY OF POLARIZATION OF DIGITAL LASER MICROSCOPIC IMAGES OF BLOOD PLASMA FILMS IN THE DIAGNOSIS AND DIFFERENTIATION OF BREAST PATHOLOGY

For the implementation of this randomized method of diagnosis, samples of blood plasma films taken from patients of group 1 and group 2 were "mixed". Next, a series of so-called blind measurements of the polarization maps of elliptical states of microscopic laser images of blood plasma film samples within the two patient groups was conducted. The statistical, correlation and spectral moments of the 1st - 4th orders, which characterize the coordinate distributions of the ellipticity of polarization, were calculated. Then, based on the known methodology, the coordinates of the points of operational ROC curves for group 1 and group 2 were determined.

Similar actions were done for blood plasma samples taken from group 1 and group 3 patients.

3.1 ROC ANALYSIS OF THE EFFECTIVENESS OF POLARIZATION DIAGNOSTICS OF BENIGN BREAST CONDITIONS

There were presented the results of the ROC analysis of so-called blind method of polarization mapping of the polarization ellipticity distributions of digital laser microscopic images of polycrystalline "mixed" blood plasma film samples taken from healthy women (group 1) and patients with benign changes (group 2).

According to the histogram of the distribution of values of each of the statistical moments of the 1st - 4th orders, which characterize the coordinate distributions of the ellipticity of polarization within the set of pixels of the plane of laser microscopic images of blood plasma films, the results of determining the scale of decisions by the known method were obtained. Thus, each determined interval is conditionally divided into four equal segments $\left(X_1; X_2 = X_1 + \frac{\Delta X_0}{4}; X_3 = X_1 + \frac{\Delta X_0}{2}; X_4 = X_1 + \frac{3\Delta X_0}{4}; X_5 = X_1 + \Delta X_0 \right)$. Based on that the number of values of the parameter under investigation is determined $N_1(X_1)$; $N_2(X_2)$; $N_3(X_3)$; $N_4(X_4)$; $N_5(X_5)$; and the decision category levels were determined by the patient group under consideration

$$\Delta X_0^{\beta}\left(M_{k=1;2;3;4}^{\beta}\right) = \left[X - X_1\right] = \left[\left(X_1 + \Delta X_0\right) - X_1\right].$$

The data obtained are shown in Table 1.

Table 1. The scale of decisions by statistical moments characterizing the polarization ellipticity distributions of microscopic images of plasma films of patients in group 1 and group 2.

M	Group	1	2	3	4	5
M_1	Group 2	6	7	7	7	8
	Group 1	13	9	6	5	2
M_2	Group 2	6	6	7	8	8
	Group 1	11	8	7	6	3
M_3	Group 2	4	5	5	6	15
	Group 1	19	5	5	5	2
M_4	Group 2	4	4	5	5	17
	Group 1	20	5	5	3	2

The tabular representation (Table 2) and construct the ROC curve (Fig. 1) of informativeness of the diagnostic method for the ellipticity parameter of images of multivariable laser microscopy of biological preparations were determined.

As can be seen from Figure 1, the analysis of higher order statistical moments M_3^{β} and M_4^{β} and the map ellipticity of a series of digital microscopic images is the most informative in the case of a randomized trial. The least informative is the analysis of the informativeness of the method of randomized mapping of polarization ellipticity, based on the use of statistical moments of the 1st M_1^{β} and 2nd M_2^{β} order.

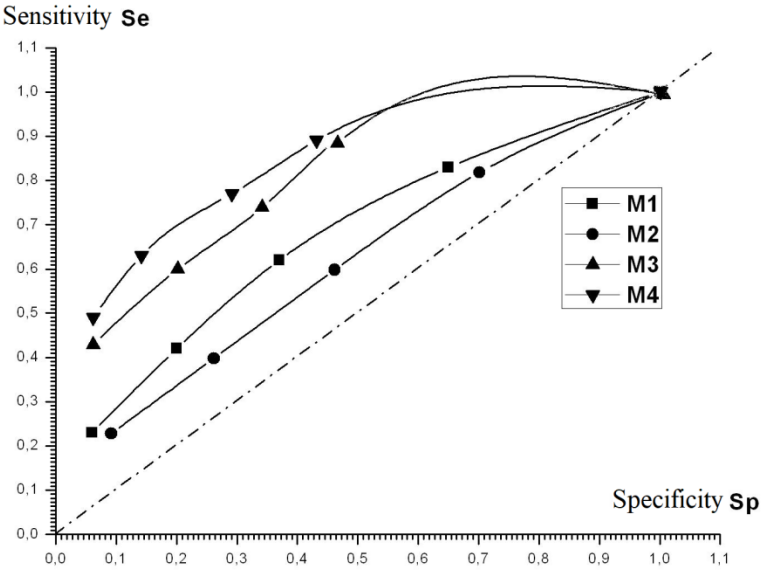

Fig. 1. ROC curves of the mapping the elliptical polarization method of laser microscopic images of blood plasma films taken from patients of group 1 and group 2.

Thus, it is possible to ascertain the high level of informativeness and specificity of the method of laser microscopic mapping of the ellipticity of polarization of images of blood plasma films under the conditions of blind diagnosis of benign changes of the breast.

Table 2. Parameters of ROC curves for - group 2 (mastopathy) - 1 (norm).

M	Parameter	1	2	3	4	5
M_1	Sensitivity Se (Y)	0,23	0,42	0,62	0,83	1,0
	Specificity Sp (X)	0,06	0,2	0,37	0,65	1,0
M_2	Sensitivity Se (Y)	0,23	0,4	0,6	0,82	1,0
	Specificity Sp (X)	0,09	0,26	0,46	0,7	1,0
M_3	Sensitivity Se (Y)	0,43	0,6	0,74	0,89	1,0
	Specificity Sp (X)	0,06	0,2	0,34	0,46	1,0
M_4	Sensitivity Se (Y)	0,49	0,63	0,77	0,89	1,0
	Specificity Sp (X)	0,06	0,14	0,29	0,43	1,0

3.2 ROC ANALYSIS OF THE EFFECTIVENESS OF POLARIZATION DIAGNOSTICS OF MALIGNANT BREAST CONDITIONS

The results of the ROC analysis of a blind polarization mapping method for the polarization ellipticity distributions of laser images of "mixed" blood plasma film samples taken from healthy women (group 1) and patients with malignant breast changes (group 3) are presented below.

The scale of decisions on the statistical moments of the 1st - 4th orders, which characterize the distributions of the ellipticity of polarization of microscopic images of blood plasma of patients of the first group and the third group are presented in table 3.

Table 4 and Fig. Fig. 2 illustrates the parameters and dependencies determined on the basis of the decision scale (Table 3), the ROC curves of the blind mapping method of polarization ellipticity by the pixel set of digital images of blood plasma film samples within the combined donors of group 1 and patients of group 3.

Table 3. The scale of decisions by statistical moments characterizing the polarization ellipticity distributions of microscopic images of blood plasma films

M	Group	1	2	3	4	5
M_1	Group 3	5	6	7	8	9
	Group 1	14	9	6	3	3
M_2	Group 3	5	6	7	8	9
	Group 1	12	9	7	4	3
M_3	Group 3	3	3	5	5	19
	Group 1	20	5	5	4	2
M_4	Group 3	3	3	4	5	20
	Group 1	21	5	5	3	2

Table 4. Parameters of ROC curves for group 3 (cancer) and 1 (norm)

M	Parameters	1	2	3	4	5
M_1	Sensitivity Se (Y)	0,26	0,49	0,69	0,86	1,0
	Specificity Sp (X)	0,09	0,17	0,43	0,6	1,0
M_2	Sensitivity Se (Y)	0,26	0,49	0,69	0,86	1,0
	Specificity Sp (X)	0,09	0,2	0,46	0,66	1,0
M_3	Sensitivity Se (Y)	0,54	0,69	0,83	0,91	1,0
	Specificity Sp (X)	0,06	0,17	0,31	0,43	1,0
M_4	Sensitivity Se (Y)	0,57	0,71	0,83	0,91	1,0
	Specificity Sp (X)	0,06	0,14	0,29	0,4	1,0

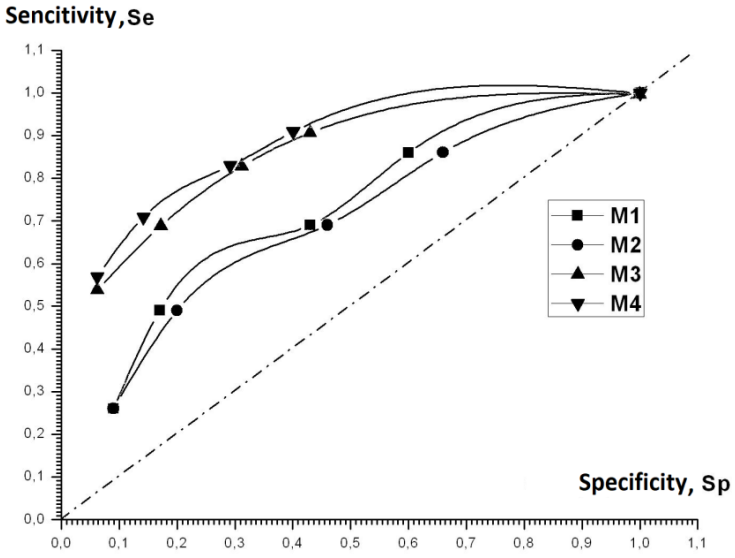

Fig. 2. ROC curves of informative mapping of elliptical polarization of laser microscopic images of blood plasma films taken from patients of group 1 and group 3

According to the results of ROC analysis, a high level of informativeness analysis was obtained based on the determination of higher order statistical moments $M^{\beta}_{k=3;4}$, which characterize the maps of elliptical polarization of digital images of blood plasma films taken from patients of group 1 and group 2 (Fig. 2).

Less informative was the analysis of a blind method for mapping the ellipticity of polarization formed by birefringence of albumin-globulin polycrystalline networks, based on the use of the statistical moments of the 1st M^{β}_{1} and the 2nd M^{β}_{2} order coordinate distributions of the ellipticity of polarization. The corresponding ROC curves are closer to the diagonal of the chosen coordinate system $X(Sp)-Y(Se)$ compared to the similar dependences obtained for higher order statistical moments.

Therefore, multiparameter laser microscopy of the polycrystalline structure of a series of experimental samples of blood plasma films with the analysis of polarization maps of ellipticity states was informative and specific in the case of blind diagnosis of malignant changes in the mammary gland.

3.3 ROC ANALYSIS OF THE EFFICIENCY OF POLARIZATION DIFFERENTIATION OF BENIGN AND MALIGNANT BREAST CONDITIONS

The results of the investigation of informativeness of the test based on mapping of polarization ellipticity distributions of polarization of microscopic images of blood plasma films, taken from patients with benign and malignant breast changes, using the blind method of ROC analysis for differentiation of such states are presented.

Table 5. Decision scale by statistical moments characterizing the polarization distributions of the polarization images of the plasma films of patients of group 2 and group 3

M	Group	1	2	3	4	5
M_1	Group 3	6	7	7	7	8
	Group 2	13	9	6	5	2
M_2	Group 3	6	6	7	8	8
	Group 2	11	8	7	6	3
M_3	Group 3	4	4	5	8	14
	Group 2	13	9	6	4	3
M_4	Group 3	4	5	5	8	13
	Group 2	14	9	5	4	3

Table 6 presents the parameters based on the data in table 5 ROC analysis of the method of blind polarization mapping.

Table 6. ROC curve parameters for group 3 (cancer) - 2 (mastopathy)

M	Parameters	1	2	3	4	5
M_1	Sensitivity Se (Y)	0,23	0,42	0,62	0,83	1,0
	Specificity Sp (X)	0,06	0,2	0,37	0,65	1,0
M_2	Sensitivity Se (Y)	0,23	0,4	0,6	0,82	1,0
	Specificity Sp (X)	0,09	0,26	0,46	0,7	1,0
M_3	Sensitivity Se (Y)	0,4	0,63	0,77	0,89	1,0
	Specificity Sp (X)	0,09	0,2	0,37	0,63	1,0
M_4	Sensitivity Se (Y)	0,4	0,63	0,74	0,89	1,0
	Specificity Sp (X)	0,09	0,21	0,38	0,65	1,0

Table 5 presents the results of the patient state decisions within the combined groups 2 and 3 according to the calculated statistical moments of the 1st - 4th order, which characterize the maps of elliptical polarization of microscopic digital images of a series of experimental samples of blood plasma films.

Fig. 3 illustrates a series of ROC curves calculated for a set of statistical moments from the 1st M_1^β to the 4th M_4^β order that characterize the distribution histograms of random polarization ellipticity values formed by the birefringence of albumin and globulin films.

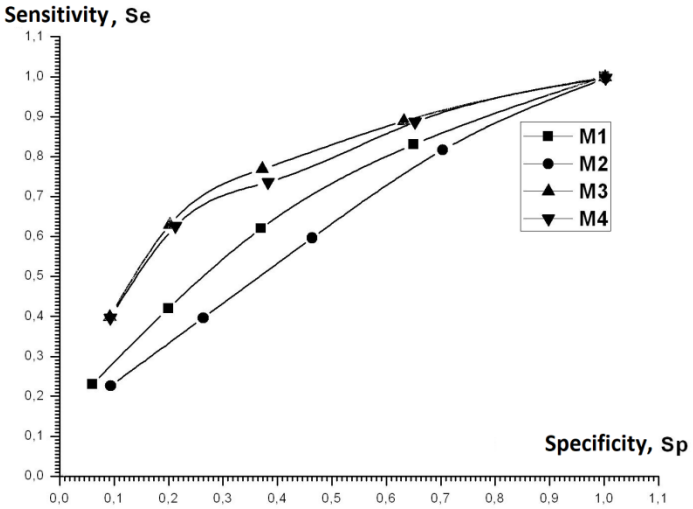

Fig. 3. ROC curves of informativeness mapping of the elliptical polarization of laser microscopic images of blood plasma films taken from patients of group 3 and group 2

From the results of ROC analysis, a high level of informativeness of the method of laser polarimetric mapping of ellipticals of images of blood plasma films and analysis of statistical moments of higher orders of these distributions become evident not only in the diagnosis but also in the differentiation of benign and malignant conditions of the breast from patients of group 2 and group 3 (Fig. 3).

Therefore, multiparameter laser microscopy of elliptical polarization maps of laser images of blood plasma films proved to be informative and specific and in the case of blind differentiation of benign and malignant changes of the breast.

CONCLUSIONS

Testing based on a highly specific discriminant test based on statistical estimates of polarization elliptical mapping is appropriate and effective in the second stage of diagnosis, when the suspected disease circle is narrowed, and the disease must be proven with greater certainty.

However, the increase in specificity is inevitably accompanied by a decrease in sensitivity and vice versa. Therefore, in order to create an optimal diagnostic multi-parameter system for laser polarimetry of blood plasma films in assessing the physiological states of the breast, a trade-off between sensitivity and specificity indices should be found, which will optimally reflect the balance between the risks of false alarms and disease omissions.

REFERENCES

[1] March, W.F., Rabinovitch B. and Adams, R.L., "Noninvasive glucose monitoring of the aqueous humor of the eye. Part II. Animal studies and the scleral lens," Diabet Care Journal. 5, 259–265 (1982).

[2] Cote, G.L., Fox, M.D. and Northrup, R.B., "Noninvasive optical polarimetric glucose sensing using a true phase measurement technique," IEEE Transaction in Biomedical Engineering 39, 752–756 (1992).

[3] Van de Merwe, W.P., Huffman, D.R. and Bronk, B.V., "Reproducibility and sensitivity of polarized light scattering for identifying bacterial suspension," Applied Optics 28(23) 5052–5057 (1989).

[4] Van de Merwe, W.P., Li, Z.Z., Bronk, B.V. and Czégé, J., "Polarized light scattering for rapid observation of bacterial size changes," Biophysical Journal 73(1), 500–506 (1997).
[5] Gross, C.T., Salamon, H. and Hunt, A.J., *et al*., "Hemoglobin polymerization in sickle cells studied by circular polarized light scattering," Biochimica et Biophysica Acta 1079(2), 152–160 (1991).
[6] Ushenko, A.G. and Pishak P., [Biomedical Diagnostics, environmental and material Science], Kluwer Academic Publishers, 93–136 (2004).
[7] Peresunko, A.P., Ushenko A.G. and Plavyuk L.A., "Polarization-correlation study of biotissues such as myoma and uterine cervix," Proc. SPIE 5067, 56–63 (2003).
[8] Ushenko, Yu.A., Peresunko, A.P. and Baku, A.B., "A new method of Mueller-matrix diagnostics and differentiation of early oncological changes of the skin derma," Advances in optical technologies 2010, 952423 (2010).
[9] Ghosh, N. and Vitkin, I.A., "Tissue polarimetry: concepts, challenges, applications, and outlook," Journal of Biomedical Optics 16(11), 110801 (2011).
[10] Mintser, O.P. and Oliinychenko, B.P., "Method for breast cancer diagnosis by phase specrtrophotometry of human blood plasma", Proc. of SPIE 8336, 83381Y (2011).
[11] Mintser, O.P., Oliinychenko, B.P. "Diagnosis of breast cancer by polarization cartography of human blood plasma", Proc. of SPIE 8338, 83381W (2011).
[12] Ushenko, Y.O., Tomka, Y.Ya, Dubolazov, O.V., Balanetska, V.O., Karachevtsev, A.O. and Angelsky A.P., "Wavelet-analysis for laser images of blood plasma," Advances in Electrical and Computer Engineering 11(2), 55–62 (2011).
[13] Ushenko, Yu.A., Dubolazov, A.V., Balanetskaya, V.O. and Zabolotna, N.I., "Mueller-matrix diagnostics of optical properties of polycrystalline networks of blood plasma," Optics and Spectroscopy 112(6), 884– 892 (2012).
[14] Mintser, O.P., Zabolotna, N.I., Oliinychenko, B.P. and Komada, P., "Differential phase analysis of laser images of a polycrystalline component of blood plasma in diagnostics of pathological changes in mammary gland," Proc. SPIE 8698, 86980D (2012)
[15] Zabolotna, N.I., Oliinychenko, B.P., Radchenko, K.O., Krasnoshchoka, A.K. and Shcherba, O.K., "System of polarization phasometry of polycrystalline blood plasma networks in mammary gland pathology diagnostics," Proc. of SPIE 9613, 961311 (2015).
[16] Zabolotna, N. I., Radchenko, K. O., Tarnovskiy, M. H., "System of Mueller-Jones matrix polarizing mapping of blood plasma films in breast pathology," Proc. SPIE 10407, 1040714 (2017).
[17] Zabolotna N.I. Analiz rozpodiliv azymutiv ta eliptychnostei poliaryzatsii lazernykh zobrazhen plazmy krovi dlia diahnostyky patolohichnykh zmin molochnykh zaloz / O.P. Mintser, S.V. Pavlov, N.I. Zabolotna, B.P. Oliinychenko // Fotobiolohiia ta fotomedytsyna. - 2011. - №1. - 118-123.
[18] Zabolotna, N.I., Pavlov, S.V. and Oliinychenko, B.P., "Informatyvnist metodiv kartohrafuvannia eliptychnostei poliaryzatsii lazernykh mikroskopichnykh zobrazhen plivok plazmy krovi u diahnostytsi onkolohichnykh zmin molochnykh zaloz," Zastosuvannia lazeriv u medytsyni ta biolohii: XXXXII Mizhnar. nauk. – prakt. konf., 151 – 154 (2014).
[19] Zabolotna, N.I., Sholota, V.V. and Oliinychenko, B.P., "ROC – analiz poliaryzatsiinoho kartohrafuvannia azymutiv zobrazhen plivok plazmy krovi u diahnostuvanni patolohii molochnykh zaloz," Optyko-elektronni informatsii-no-enerhetychni tekhnolohii 2(34), 52–59 (2017).
[20] Zabolotna, N.I., Sholota, V.V. and Okarskyi H.H., "Methods and systems of polarization reproduction and analysis of the biological layers structure in the diagnosis of pathologies," Proc. SPIE 11369, 1133691S (2020).
[21] Zabolotna, N.I. and Radchenko K.O., "A multifunctional automated system of 2D laser polarimetry of biological tissues," Proc. SPIE 9205, 92050V (2014).