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DIFFERENTIAL MUELLER-MATRIX MAPPING OF THE POLYCRYSTALLINE COMPONENT OF BIOLOGICAL TISSUES OF HUMAN ORGANS

Andrei Padure[1], Oksana Bakun[2], Ivan Mikirin[3], Alexander Dubolazov[3], Iryna Soltys[3], Oleksandr Olar[3], Yuriy Ushenko[3], Oleksandr Ushenko[3], Irina Palii[4], Saule Kumargazhanova[5]

[1]Nicolae Testemitanu State University of Medicine and Pharmacy, Kishinev, Moldova, [2]Higher State Educational Institution of Ukraine, Bukovynian State Medical University, Chernivtsi, Ukraine, [3]Yuriy Fedkovych Chernivtsi National University, Chernivtsi, Ukraine, [4]National Pirogov Memorial Medical University, Vinnytsia, Ukraine, [5]D. Serikbayev East Kazakhstan Technical University, Ust-Kamenogorsk, Kazakhstan

Abstract. *The article presents the materials of diagnostic application of the method of differential Mueller-matrix mapping of optically anisotropic architectonics of the layers of soft matter of the female reproductive sphere – histological sections of uterine biopsy. The efficiency and accuracy of differential diagnostics of benign and precancerous conditions of endometrial tissue are considered using statistical analysis of algorithmically reproduced maps of average values of linear and circular birefringence and dichroism parameters of optically anisotropic architectonics of representative samples of native histological sections of the uterine wall. The values of the balanced accuracy of differential diagnostics are presented by using the technique of statistical analysis of coordinate distributions of the mean values of the optical anisotropy parameters.*

Keywords: polarization, correlation, Mueller matrix, statistical analysis, biological tissues

RÓŻNICOWE MAPOWANIE MATRYCY MUELLERA POLIKRYSTALICZNEGO SKŁADNIKA TKANEK BIOLOGICZNYCH NARZĄDÓW LUDZKICH

Streszczenie. *W artykule przedstawiono materiały dotyczące zastosowania diagnostycznego metody mapowania różnicowego macierzy Muellera optycznie anizotropowej architektury warstw materii miękkiej żeńskiej sfery rozrodczej – wycinków histologicznych z biopsji macicy. Skuteczność i dokładność diagnostyki różnicowej łagodnych i przedrakowych stanów tkanki endometrium są rozpatrywane przy użyciu analizy statystycznej algorytmicznie odtworzonych map średnich wartości liniowej i kołowej dwójłomności oraz parametrów dichroizmu optycznie anizotropowej architektury reprezentatywnych próbek natywnych przekrojów histologicznych ściany macicy. Wartości zrównoważonej dokładności diagnostyki różnicowej przedstawiono za pomocą techniki analizy statystycznej rozkładów współrzędnych średnich wartości parametrów anizotropii optycznej.*

Słowa kluczowe: polaryzacja, korelacja, macierz Muellera, analiza statystyczna, tkanki biologiczne

Introduction

Methods of Mueller-matrix polarimetry of biological tissues and liquids have become widespread in the diagnosis of optically anisotropic structure of the morphological structure [1–3]. Currently, a wide class of optical-electronic devices has been created for the instrumental implementation of such Mueller-matrix polarimetric techniques [4–12]. As a result, the possibility of successful diagnosis of pathological (cancer) conditions of biological tissues was demonstrated. [13]. At the same time, such methods do not provide direct information about the parameters of optical anisotropy of the polycrystalline architectonics of biological objects. There is a small number of publications devoted to the Mueller-matrix reproduction of optical anisotropy maps [14]. However, such information can be decisive in improving the sensitivity of laser polarimetry methods in diagnosing pathological conditions.

Our work is devoted to the study of linear and circular birefringence of histological sections of uterine biopsy in order to determine the most sensitive diagnostic markers by statistical analysis of the coordinate distributions of elements of the 1st order differential matrix [14].

1. Methodology and short theory of Mueller-matrix mapping

The optical scheme of laser Mueller-matrix polarimetry [13] of biological layers, is shown in Fig. 1.

In order to improve the perception of further experimental material, we have given a brief theoretical description of the method for differential description of the optical anisotropy of the polycrystalline component of biological tissues [15].

The following expressions can be written for Mueller's partial matrices, which characterize the structural and chiral anisotropy of the architectonics of the optically thin biological layer of soft matter.

Structural anisotropy includes the mechanisms of linear birefringence LB and dichroism LD.

Chiral anisotropy includes the mechanisms of circular birefringence CB and dichroism CD.

Polarization manifestations of structural optical anisotropy of the architectonics of polycrystalline supramolecular networks of the layer of soft matter are characterized by the following set of partial Mueller matrix operators.

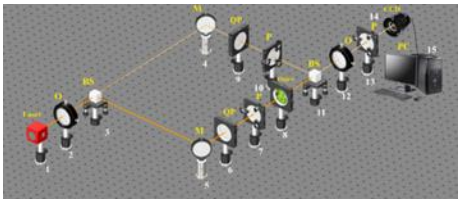

Fig. 1. Optical scheme of polarization interference mapping of the Mueller matrix: 1 – He-Ne laser; 2 – collimator – "O"; 3, 11 – light splitters – "BS"; 4, 5 – mirrors – "M"; 7, 10, 13 – polarizer "P"; 6, 9 – quarter-wave plates – "QP"; 8 – object; 12 – polarizing lens – "O"; 14 – digital camera – "CCD"; 15 – personal computer – "PC"

Linear birefringence LB

The polarization manifestations of linear birefringence are characterized by the partial Mueller matrix$\{\nabla\}$

$$\{\nabla\} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & \nabla_{22} & \nabla_{23} & \nabla_{24} \\ 0 & \nabla_{32} & \nabla_{33} & \nabla_{34} \\ 0 & \nabla_{42} & \nabla_{43} & \nabla_{44} \end{bmatrix} \tag{1}$$

where

$$\begin{pmatrix} \nabla_{22} \\ \nabla_{23} = \nabla_{32} \\ \nabla_{33} \\ \nabla_{42} = -\nabla_{24} \\ \nabla_{34} = -\nabla_{43} \\ \nabla_{44} \end{pmatrix} = \begin{pmatrix} cos^2 2\gamma + sin^2 2\gamma \cos\delta \\ \cos 2\gamma \sin 2\gamma (1 - \cos\delta) \\ sin^2 2\gamma + cos^2 2\gamma \cos\delta \\ \sin 2\gamma \sin\delta \\ \cos 2\gamma \sin\delta \\ \cos\delta \end{pmatrix} \tag{2}$$

here γ – optical axis direction; $\delta = \frac{2\pi}{\lambda}\Delta n l$ – phase shift; λ – wavelength; Δn – birefringence value; l – geometrical thickness.

Linear dichroism *LD*

The partial Mueller matrix operator, which describes the mechanism of optically anisotropic absorption of the linear components of the laser radiation amplitude, has the following analytical form

$$\{\Delta\} = \begin{bmatrix} 1 & \Delta_{12} & \Delta_{13} & 0 \\ \Delta_{21} & \Delta_{22} & \Delta_{23} & 0 \\ \Delta_{31} & \Delta_{32} & \Delta_{33} & 0 \\ 0 & 0 & 0 & \Delta_{44} \end{bmatrix} \quad (3)$$

where

$$\begin{pmatrix} \Delta_{12} = \Delta_{21} \\ \Delta_{13} = \Delta_{31} \\ \Delta_{22} \\ \Delta_{23} = \Delta_{32} \\ \Delta_{33} \\ \Delta_{44} \end{pmatrix} = \begin{pmatrix} (1-\Delta\tau)\cos 2\gamma, \\ (1-\Delta\tau)\sin 2\gamma, \\ (1+\Delta\tau)\cos^2 2\gamma + 2\sqrt{\Delta\tau}\sin^2 2\gamma, \\ (1-\Delta\tau)\sin 2\gamma, \\ (1+\Delta\tau)\sin^2 2\gamma + 2\sqrt{\Delta\tau}\cos^2 2\gamma, \\ 2\sqrt{\Delta\tau}. \end{pmatrix} \quad (4)$$

here $\Delta\tau = \frac{\tau_x}{\tau_y}$, $\begin{cases} \tau_x = \tau\cos\gamma \\ \tau_y = \tau\sin\gamma \end{cases}$, τ_x, τ_y – absorption coefficients.

Polarization manifestations of chiral optical anisotropy of the architectonics of polycrystalline supramolecular networks of the layer of soft matter are characterized by the following set of partial Mueller matrix operators.

Circular birefringence *CB*

The matrix operator $\{\Theta\}$, which describes the circular birefringence caused by the optical activity of molecules of the medium, has the following form

$$\{\Theta\} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos 2\vartheta & \sin 2\vartheta & 0 \\ 0 & \sin 2\vartheta & \cos 2\vartheta & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \quad (5)$$

here ϑ – rotation angle.

Circular dichroism CD

Polarization manifestations of the physical mechanism of such anisotropic absorption of the circular components of the laser radiation amplitude are described by the following partial Mueller matrix operator

$$\{\Psi\} = \begin{bmatrix} 1 & 0 & 0 & \psi_{14} \\ 0 & \psi_{22} & 0 & 0 \\ 0 & 0 & \psi_{33} & 0 \\ \psi_{41} & 0 & 0 & 1 \end{bmatrix} \quad (6)$$

where

$$\psi_{ik} = \begin{pmatrix} \psi_{22} = \psi_{33} \\ \psi_{14} = \psi_{41} \end{pmatrix} = \begin{pmatrix} \frac{1-\Delta\chi^2}{1+\Delta\chi^2} \\ \pm\frac{2\Delta\chi}{1+\Delta\chi^2} \end{pmatrix} \quad (7)$$

here $\Delta\chi = \frac{\chi_\otimes - \chi_\oplus}{\chi_\otimes + \chi_\oplus}$, $\chi_\otimes$, $\chi_\oplus$ – absorption coefficients dor left ($\otimes$) and wright ($\oplus$) circular polarized components of laser amplitude.

A generalization of this Mueller matrix approach can be the Stokes parametric formalism, which was developed for layer-by-layer description of polarization properties of diffuse object fields of layers of soft matter

$$dVS/_{dh} = \{diff(M)\}VS \quad (8)$$

here $\{diff(M)\}$ – differential Mueller matrix; VS – Stokes vector of optical field; h – geometrical pass in optically anisotropy biological tissue.

The differential matrix $\{diff(M)\}$ is interconnected with the generalized Mueller matrix $\{M\}$ (relation (8)) of the optically anisotropic layer of soft matter by the Barakat relation using Kronecker's analytic matrices *K*

$$\{diff(M)\} = \mathrm{K}^T(N \otimes I + I \otimes N^*)\mathrm{K} \quad (9)$$

where

$$\mathrm{K} = \frac{1}{\sqrt{2}}\begin{pmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & -i \\ 0 & 0 & 1 & i \\ 1 & -1 & 0 & 0 \end{pmatrix} \quad (10)$$

here i is an imaginary unit.

Analytically, such a matrix dependence is illustrated by an equation of the following form

$$d\{M(h)\}/_{dh} = \{M(h)\}\{diff(M(h))\} \quad (11)$$

where $\{M(h)\}$ – Mueller matrix of object in the plane h.

For optically thin non-depolarizing layers, the differential matrix $\{diff(M(h))\} \Longrightarrow \{\mathrm{A}\}$ consists of six elementary polarization properties that fully characterize the optical anisotropy of the architectonics of supramolecular networks of biological crystals of a soft matter sample.

$$\{\mathrm{A}\} = \begin{bmatrix} 0 & a_{12} & a_{13} & a_{14} \\ a_{21} & 0 & a_{23} & -a_{24} \\ a_{31} & -a_{32} & 0 & a_{42} \\ a_{41} & a_{42} & -a_{43} & 0 \end{bmatrix} =$$

$$= \begin{bmatrix} 0 & LD_{0-90} & LD_{45-135} & CD \\ LD_{0-90} & 0 & CB & -LB_{45-135} \\ LD_{45-135} & -CB & 0 & LB_{0-90} \\ CD & LB_{45-135} & -LB_{0-90} & 0 \end{bmatrix} \quad (12)$$

here LD_{0-90} and LB_{0-90} are the values of random variables of structural anisotropy – linear dichroism and birefringence for orientations $\gamma = 0^0 - 90^0$ and LB_{45-135} for orientations $\gamma = 45^0 - 135^0$; CD and CB – the value of random variables of chiral anisotropy – circular dichroism and birefringence.

In our work we used the radiation of a "red" (wavelength λ = 0.6328 μm) He-Ne laser. In this spectral region the absorption of protein structures is minimal. Therefore, we limited ourselves to considering the linear LB and circular CB birefringence, which are determined by the following relations

$$LB_{0-90} = \frac{2\pi}{\lambda}\Delta n_{LB} h \quad (13)$$

$$LB_{45-135} = \frac{2\pi}{\lambda}\Delta n^*_{LB} h \quad (14)$$

$$LB = \sqrt{(LB_{0-90})^2 + (LB_{45-135})^2} \quad (15)$$

$$CB = \frac{2\pi}{\lambda}\Delta n_{CB} h \quad (16)$$

here Δn_{LB};Δn^*_{LB} and Δn_{CB} – linear and circular birefringence indices; h – geometrical thickness.

2. Experimental results and their discussion

To conduct the research, two representative samples of native (obtained on a microtome with rapid freezing) histological sections of endometrial biopsy with different pathological conditions, which were previously confirmed by histological studies, were formed:

- polyp (benign neoplasms) – control group 1 (37 samples);
- atypical simple hyperplasia (precancerous condition) – experimental group 2 (37 samples).

To determine the statistical significance of a samples number representative sampling by the cross-validation method [16]. The standard deviation σ^2 for each statistical moment $Z_{i=1;2;3;4}(n)$ was calculated. The specified number (37 for each group) of samples provided the level $\sigma^2 \le 0.025$. This standard deviation corresponds to a confidence interval $p < 0.05$, which demonstrates the statistical reliability of the Mueller-matrix mapping method.

Within the set of samples of control group 1, "threshold" average values were determined using algorithm (12)–(16) ($max\langle LB\rangle \sim 0.6 \times 10^{-3}$; $max\langle CB\rangle \sim 0.4 \times 10^{-3}$) and the ranges of change($\Delta\langle LB\rangle \sim 0.3 \times 10^{-3}$; $\Delta\langle CB\rangle \sim 0.2 \times 10^{-3}$) of the phase anisotropy parameters of native histological sections of the endometrium.

In a series of fragments of Fig. 2 and Fig. 3 shows maps $LB(x \times y \equiv 1000pix \times 1000pix)$; $CB(1000pix \times 1000pix)$ (fragments (1), (2)) and histograms $H(LB \times 10^{-3})$; $G(CB \times 10^{-3})$ (fragments (2), (4)) of the distributions of anisotropy parameters of the architectonics of samples of native histological sections of the endometrium with benign (fragments (1),(3)) and precancerous (fragments (2),(4)) changes.

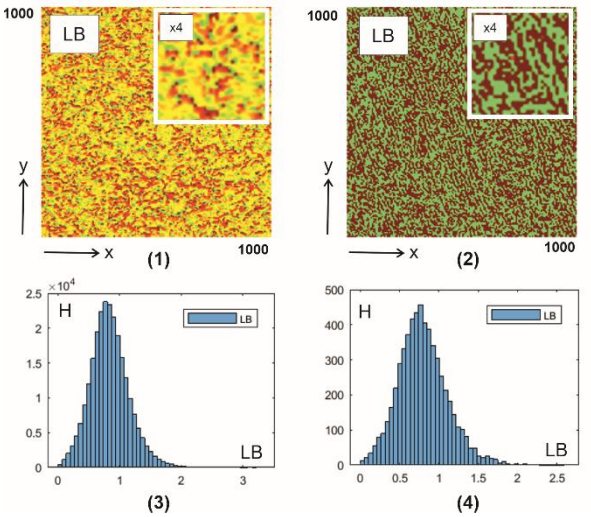

Fig. 2. Linear birefringence maps $LB(m \times n)$ (top line) and histograms $H(LB)$ (bottom line) of distributions of linear birefringence of histological sections of the endometrium from group 1 (left column) and group 2 (right column)

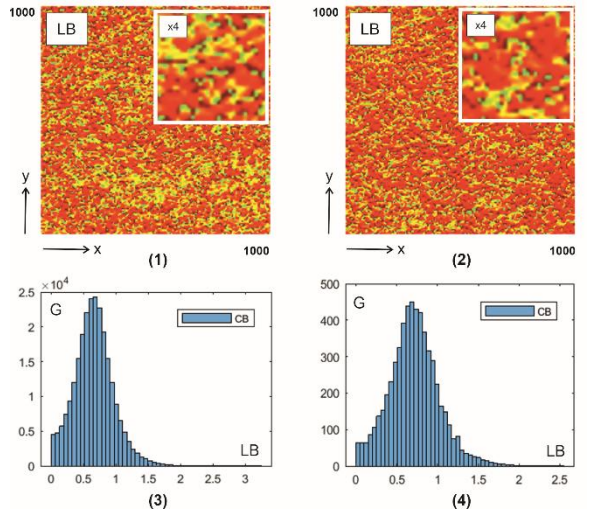

Fig. 3. Circular birefringence maps $CB(m \times n)$ (top line) and histograms $G(CB)$ (bottom line) of distributions of circular birefringence of histological sections of the endometrium from group 1 (left column) and group 2 (right column)

Analysis of the results of the experimental method of differential Mueller-matrix algorithmic reproduction of maps of average values of the totality of mechanisms of phase anisotropy of polycrystalline architectonics of samples of native histological sections of the endometrium with benign (group 1) and precancerous (group 2) changes showed:

- different values of the main extrema $max\langle OA\rangle$ and scatter ranges $\Delta\langle OA\rangle$ of random values of the optical anisotropy parameters $\langle OA\rangle$ as for different birefringence mechanisms $\langle LB(m,n)\rangle, \langle CB(m,n)\rangle$, and for various pathological transformations of polycrystalline architectonics of samples of native histological sections of soft tissue of the endometrium of the uterine wall from group 1 and group 2, – Fig. 2, Fig. 3, fragments (3),(4);
- higher level of structural anisotropy $\langle LB(m,n)\rangle$, polycrystalline architectonics of samples of native histological sections of endometrial biopsy in a cancerous state from group 2, manifested in large values of the main extrema $max(\langle LB(m,n)\rangle) \sim 0.7 \times 10^{-3}$ and scatter range $\Delta(\langle LB(m,n)\rangle) \sim 0.36 \times 10^{-3}$ of the corresponding distributions of random values of linear birefringence parameters $\langle LB(m,n)\rangle$, – Fig. 2, Fig. 3, fragments (3), (4).

From a physical point of view, the identified results can be associated with the following considerations.

Firstly. The architecture of the polycrystalline component of the uterine wall and its surface layer of the endometrium represents a rather complex "morphological symbiosis" of different types of biological tissues – muscle tissue, connective tissue and epithelial tissue.

The main morphological components of the first two types of tissues are fibrillar protein networks $\langle LB(m,n)\rangle$ spatially structured and ordered in laying directions, which are formed by optically active $\langle CB(m,n)\rangle$ molecules of myosin, collagen and elastin.

Secondly. The initial ("pre-tumor") signs of malignant pathological changes in the morphological structure of the architectonics of biological tissues are the formation and growth of newly formed fibrillar networks of the connective tissue component. In our case, this is the proliferation of collagen fibrillar networks of the uterine wall or endometriosis. As a result, in the polarization properties of the layer of pathologically altered endometrium, the statistical weight of the set of physical mechanisms of structural optical anisotropy increases ↑ – linear birefringence and dichroism $\langle LB(m,n)\rangle \uparrow$ fibrillar component of polycrystalline architectonics of soft matter.

Quantitatively, within the framework of the statistical approach, physical scenarios of polarization manifestations of the pathological transformation of the optically anisotropic architectonics of soft matter of native histological sections of uterine tissue biopsies from both groups are identified, illustrating a set of central statistical moments of 1–4 orders.

The results of using information analysis of differential Mueller-matrix mapping data within the framework of evidence-based medicine are shown in Table 1 and Table 2.

Table 1. Statistical moments of the 1st – 4th orders of uterine tissue

OA	LB		CB	
$Z_{i=1,2,3,4}$	Group 1	Group 2	Group 1	Group 2
$Z_1 \times 10^{-3}$	0.61±0.035	0.78±0.042	0.41±0.024	0.44±0.025
$Z_2 \times 10^{-3}$	0.29±0.018	0.36±0.019	0.19±0.011	0.22±0.013
Z_3	0.48±0.026	0.31±0.017	0.37±0.021	0.32±0.018
Z_4	0.54±0.029	0.42±0.023	0.44±0.024	0.33±0.018

Table 2. Accuracy of differential diagnosis

$Ac, \%$				
$Z_{i=1,2,3,4}$	Z_1	Z_2	Z_3	Z_4
LB	78.9	84.2	95.7	95.7
CB	73.7	73.7	89.5	89.5

Analysis of the calculation of a set of central statistical moments of the 1st–4th orders $Z_{i=1;2;3;4}$ confirmed the correlation of the experimental data of the method of polarization-interference differential Muller-matrix mapping of samples of native histological sections of the endometrium of both types and physical substantiation of polarization manifestations of pathological conditions of optically anisotropic polycrystalline architectonics:

- central statistical moments of the 1st–2nd order $Z_{i=1;2}$, characterizing the average and dispersion of the coordinate distributions of the average values of the structural anisotropy parameters $\langle LB(m,n)\rangle$ of endometrial samples in a precancerous state increase in the range from 1.28 to 1.38 times;
- the opposite trend is observed for the central statistical moments of the 3rd and 4th orders $Z_{i=3;4}$, characterizing the asymmetry and kurtosis of the coordinate distributions

of the average values of the structural anisotropy parameters $\langle LB(m,n)\rangle$ of endometrial samples in a precancerous state – there is a decrease in average statistical values ranging from 1.47 to 1.55 times;

- the most sensitive to pathological precancerous changes in the optically anisotropic chiral component of the architectonics of native histological sections of the endometrium was the central statistical moment of the 4th order $Z_{i=4}$, which characterizes the sharpness of the peak of the set of coordinate distributions of the average values of the parameters of circular birefringence and dichroism $\langle LB(m,n)\rangle$ – the value of which increases to 1.34 times.

3. Conclusions

A brief theory of the method of differential Mueller-matrix mapping of biological tissue preparations with reconstruction of maps of optical anisotropy of polycrystalline architectonics is presented.

Within the framework of statistical analysis of distributions of linear and circular birefringence of native histological sections of the endometrium, the most sensitive markers (statistical moments of the 3rd and 4th orders) of clinical diagnostics of precancerous conditions of the endometrium (atypical simple hyperplasia) are determined.

As part of the information analysis of the diagnostic capabilities of differential Mueller matrix mapping, the following maximum levels of balanced accuracy for detecting precancerous conditions of the endometrium were established:

- excellent $Ac(\langle LB\rangle) = 95.7\%$ level,
- good $Ac(\langle CB\rangle) = 89.5\%$) level.

Acknowledgments

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D.M. Andrei Padure
e-mail: andrei.padure@usmf.md

Andrei Padure, 01.07.1975, associate professor, Ph.D., Dr. Med. Habil., Chairman of the Forensic Medicine Chair from Nicolae Testemitanu State University of Medicine and Pharmacy; Head of the Scientific Department of the Center of Forensic Medicine, the Republic of Moldova.

https://orcid.org/0000-0003-4249-9172

Prof. Alexander Dubolazov
e-mail:.a.dubolazov@chnu.edu.ua

Alexander Dubolazov is a Doctor of Physics and Mathematics, professor at the Department of Optics and Publishing and Printing at Y. Fedkovych Chernivtsi National University Chernivtsi, Ukraine.
His research interests include laser polarimetry and correlometry of optically aniso-tropic biological tissues and human organ fluids.

https://orcid.org/0000-0003-1051-2811

Ph.D. Oksana Bakun
e-mail: kupchanko06@gmail.com

Oksana Bakun is a Ph.D. in Physics and Mathematics, associate professor at the Department of Obstetrics and Gynecology at Bucovinian State Medical University, Chernivtsi, Ukraine.
Her research interests include in medical aspects of Obstetrics and Gynecology.

https://orcid.org/0000-0002-4742-2265

Ph.D. Iryna Soltys
e-mail: i.soltys@chnu.edu.ua

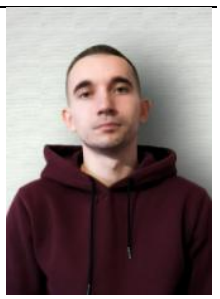
Iryna Soltys is a Ph.D. in Physics and Mathematics, associate professor at the Department of Optics and Publishing and Printing at Y. Fedkovych Chernivtsi National University, Chernivtsi, Ukraine.
Her research interests include digital holography and laser polarimetry of polycrystalline facets of optically anisotropic biological fluids of human organs.

https://orcid.org/0000-0003-2156-7404

M.Sc. Ivan Mikirin
e-mail: mikirin.ivan@chnu.edu.ua

Ivan Mikirin is a Ph.D. student at the Department of Optics and Publishing and Printing at Yuriy Fedkovych Chernivtsi National University.
His research interests include laser polarimetry of optically anisotropic biological tissues and fluids of human organs.

https://orcid.org/0000-0002-7319-6636



Ph.D. Oleksandr Olar
e-mail: cablaze9@gmail.com

Oleksandr Olar is a Ph.D. in Physics and Mathematics, associate professor at the Department of Optics and Publishing and Printing at Y. Fedkovych Chernivtsi National University.
His research interests include digital holography and Mueller matrix laser polarimetry of poly-crystalline facets of optically anisotropic biological fluids of human organs.

https://orcid.org/0000-0002-3625-8439

Prof. Yuriy Ushenko
e-mail: y.ushenko@chnu.edu.ua

Doctor of Physics and Mathematics, professor, Head of the Department of Computer Science, Y. Fedkovych Chernivtsi National University Chernivtsi, Ukraine.
His research interests include Muller matrix analysis and laser polarimetry of optically anisotropic biological tissues and human organ fluids.

https://orcid.org/0000-0003-1767-1882

Prof. Oleksandr Ushenko
e-mail: o.ushenko@chnu.edu.ua

Oleksandr Ushenko is a Doctor of Physics and Mathematics, Head of the Department of Optics and Publishing and Printing at Y. Fedkovych Chernivtsi National University, Chernivtsi, Ukraine.
His research interests are laser polarimetry and correlometry of optically anisotropic biological tissues and fluids of human organs, statistical, singular and fractal analysis of polarization maps and Mueller matrix images.

https://orcid.org/0009-0002-5088-592X

Ph.D. Irina Palii
e-mail: irina.med.1202@gmail.com

Ph.D. in medicine, associate professor, Department of Internal Medicine, Faculty of Medicine No. 2, National Pirogov Memorial Medical University, Vinnytsya, Ukraine. In 1995, she graduated from VNMU named after E. Pirogov with honors. In 2002, she defended her dissertation on the topic "Evaluation of recombinant alpha-2 interferon and its use in complex treatment of chronic viral hepatitis B", specialty – internal diseases. Author of 32 printed works, co-author of 2 patents for inventions.

https://orcid.org/0000-0002-8000-1702

Ph.D. Saule Kumargazhanova
e-mail: SKumargazhanova@gmail.com

She is currently the dean of the Department of Information Technologies and Intelligent Systems of D. Serikbayev East Kazakhstan Technical University. She is a co-author over 50 papers in journals and conference proceedings.
Her professional interests are software engineering, data processing and analysis.

https://orcid.org/0000-0002-6744-4023