

Differential diagnostic of the COVID-19 long-term effects using the method of Mueller-Matrix Map reproduction of optical activity in kidney parenchyma samples

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ABSTRACT

Results of the experimental testing of the azimuthally-invariant Mueller-matrix microscopy method for native histological sections of kidneys from deceased individuals, with algorithmic reproduction of coordinate distributions of circular birefringence (optical activity) in the parenchyma architecture.

As part of the comprehensive algorithmic analysis, a set of diagnostic markers was identified (asymmetry and excess of circular birefringence distribution, and the amplitudes of their wavelet transformation, the scale self-similarity type of OA maps) that are sensitive to changes in the polycrystalline structure of the kidney parenchyma of deceased individuals with varying times since death from COVID-19. The diagnostic efficacy of the azimuthally-invariant Mueller-matrix microscopy method with algorithmic reproduction of circular birefringence maps for kidney parenchyma in deceased individuals was established for determining long-term effects of COVID-19 with an excellent level of accuracy (up to 97%), with the ability to differentiate the time since death with very good precision (93%-95%).

Keywords: polarization, Mueller matrix, circular birefringence, correlation, wavelet analysis, kidney parenchyma, COVID-19

1. INTRODUCTION

Modern not invasive and not destructive methods of optical diagnostics of biological tissue and liquid samples, saw wide and effective use in various areas of medicine in recent years¹⁻¹⁶. Based on this research:

1.The kidney native histological section is a two-component structure, that consists of amorphous (optically isotropic) and optically anisotropic polycrystalline components¹⁷⁻²⁴.

2.Light absorption of amorphous component of a kidney sample is coordinate dependent, as the result coordinate distribution of laser light intensity can be formed, or a classic microscopic image, which is an object of traditional histological researches.

3.The polycrystalline architectonic structure is comprised of adrenal cortex outer layer and adrenal medulla inner layer. Adrenal medulla consists of conical shaped structures that are forming a transverse pillars, and generally exhibit circular birefringence. Adrenal cortex houses nephrons that are structurally anisotropic units with linear birefringence.

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The goal of our work is an experimental approbation and definition of the set of markers for comprehensive statistical¹⁷, wavelet²⁴, correlational^{18,22,24} and fractal²⁴ differential diagnostics for deceased individuals with varying times since death from COVID-19, using Mueller-matrix²⁵ cartography method with algorithmic recreation of circular birefringence in parenchyma of kidney samples.

2. METHODOLOGY

Azimuth invariant method of experimental measurement of coordinate distributions of Mueller matrix elements of kidney native histological section of deceased is performed in following steps: kidney biological sample is placed at the working area of laser Mueller matrix multichannel polarimeter (detailed structure and a description of device's optical and optoelectronic parameters was given in^{20,25}); for each channel of polarized ($0^0; 90^0; 45^0; \otimes$) light in parallel laser beam four Stokes parameters ($St_{i=1;2;3;4}$) are being computed.

$$St = \begin{pmatrix} St_1^{0^0;90^0;45^0;\otimes} = R_0^{0^0;90^0;45^0;\otimes} + R_{90}^{0^0;90^0;45^0;\otimes} \\ St_2^{0^0;90^0;45^0;\otimes} = R_0^{0^0;90^0;45^0;\otimes} - R_{90}^{0^0;90^0;45^0;\otimes} \\ St_3^{0^0;90^0;45^0;\otimes} = R_{45}^{0^0;90^0;45^0;\otimes} - R_{135}^{0^0;90^0;45^0;\otimes} \\ St_4^{0^0;90^0;45^0;\otimes} = R_{\otimes}^{0^0;90^0;45^0;\otimes} - R_{\oplus}^{0^0;90^0;45^0;\otimes} \end{pmatrix} \quad (1)$$

Coordinate distributions of values of partial matrix elements, computed for all pixels of light sensitive area of CCD camera are forming Mueller matrix images of optically anisotropic polycrystalline architectonic of kidney parenchyma of deceased individuals with varying times since death from COVID-19.

$$\begin{aligned} m_{22} &= 0.5(St_2^0 - St_2^{90}); m_{23} = St_2^{45} - m_{21}; m_{24} = St_2^{\otimes} - m_{21}; m_{31} = 0.5(St_3^0 + St_3^{90}); \\ m_{32} &= 0.5(St_3^0 - St_3^{90}); m_{33} = St_3^{45} - m_{31}; m_{34} = St_3^{\otimes} - m_{31}; m_{41} = 0.5(St_4^0 + St_4^{90}); \\ m_{42} &= 0.5(St_4^0 - St_4^{90}); m_{43} = St_4^{45} - m_{41}; m_{44} = St_4^{\otimes} - m_{41}. \end{aligned} \quad (2)$$

MMI OA and MMI LB are a base for algorithmic reconstruction of circular birefringence (CB) maps of polycrystalline architectonic of blood films.

$$CB = 0.5 \arcsin \left(\frac{(m_{23} - m_{32})}{(m_{22} + m_{33})} \right) \quad (3)$$

Obtained distributions of CB value are algorithmically processed by the sequence of analytical methods.

Autocorrelation approach provides a description of correlational homogeneousness of coordinate distributions of random CB values. The main analytical instrument is computation of one- and two-dimensional autocorrelation functions of CB in MATLAB. Wavelet approach is an analog of mathematical microscope for various complex distributions – in our case CB of kidney parenchyma of deceased.

3. DATA AND RESULTS

Four groups of samples of kidney native histological section of deceased were used. Control group 1 (25 samples) – death caused by myocardial infarction; experimental group 2 (50 samples) – time since death from COVID-19 – 1 year; experimental group 3 (50 samples) – time since death from COVID-19 – 2 years; experimental group 4 (50 samples) – time since death from COVID-19 – 3 years.

On Figures 1 (control group 1), 2 (experimental group 2), 3 (experimental group 3) and 4 (experimental group 4) displayed the results of wavelet (coordinate (fragments (1), linear dependence of amplitude of wavelet coefficients (fragments (3)), and fractal (power spectrum density PSD (fragments (2), logarithmic relation of PSD (fragments (4)) algorithmic transformation of optical activity maps of kidney parenchyma native histological section of deceased individuals with various times since death of COVID-19.

Discovered a possibility of differential diagnostics using wavelet transform of CB maps by using correlational and wavelet markers (Table 1).

Table 1. Circular birefringence map markers of kidney parenchyma native histological section of deceased.

Sample	Kidney native histological section		
Groups	Group 1	Group 2	Group 3
Parameters	Wavelet		
Asymmetry, W_3	0.14 ± 0.006	0.26 ± 0.012	0.37 ± 0.018
p_{ik}	$p_1 < 0.001; p_{2,3} < 0.001; p_{2,4} < 0.001; p_{3,4} < 0.001$		
Excess, W_4	1.65 ± 0.084	2.72 ± 0.13	4.73 ± 0.21
p_{ik}	$p_1 < 0.001; p_{2,3} < 0.001; p_{2,4} < 0.001; p_{3,4} < 0.001$		
Parameters	Autocorrelation		
Excess, K_4	1.64 ± 0.077	1.36 ± 0.068	0.98 ± 0.048
p_{ik}	$p_1 < 0.001; p_{2,3} < 0.001; p_{2,4} < 0.001; p_{3,4} < 0.001$		
Area, SK	0.189 ± 0.089	0.231 ± 0.011	0.254 ± 0.012
p_{ik}	$p_1 < 0.001; p_{2,3} < 0.001; p_{2,4} < 0.001; p_{3,4} < 0.001$		

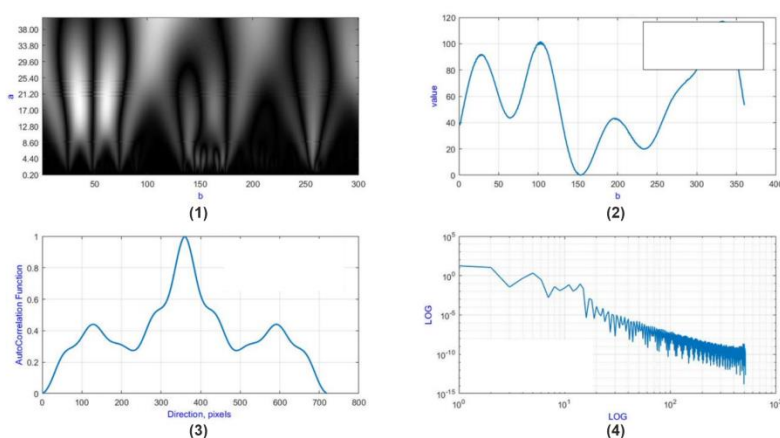


Figure 1. Coordinate (fragment (1)), linear (fragment (2)), autocorrelation (fragment (3)) and fractal (fragment (4)) characteristics of circular birefringence map wavelet transform of kidney native histological section of deceased from control group 1.

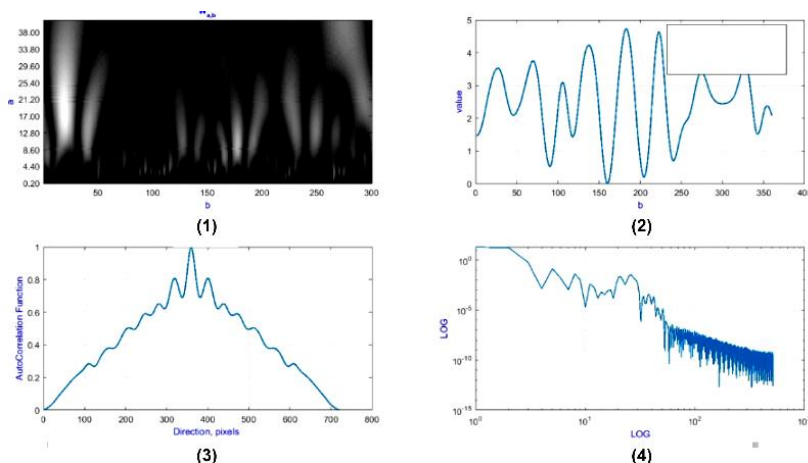


Figure 2. Coordinate (fragment (1)), linear (fragment (2)), autocorrelation (fragment (3)) and fractal (fragment (4)) characteristics of circular birefringence map wavelet transform of kidney native histological section of deceased from experimental group 2 (time since the death from COVID-19 – 1 year).

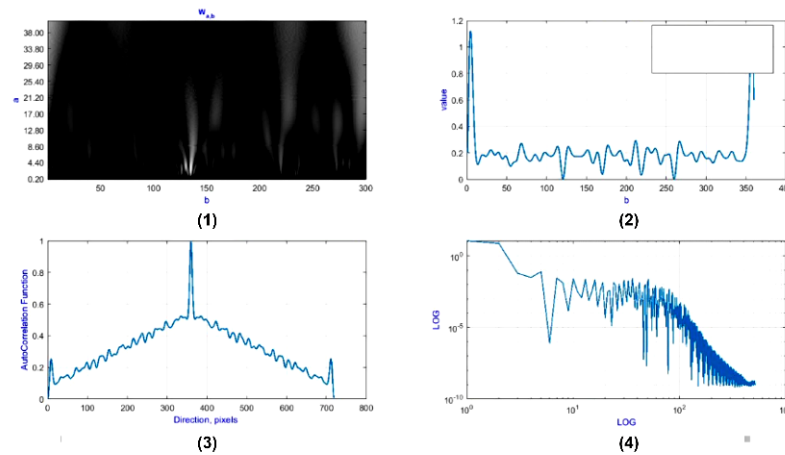


Figure 3. Coordinate (fragment (1)), linear (fragment (2)), autocorrelation (fragment (3)) and fractal (fragment (4)) characteristics of circular birefringence map wavelet transform of kidney native histological section of deceased from experimental group 3 (time since the death from COVID-19 – 2 years).

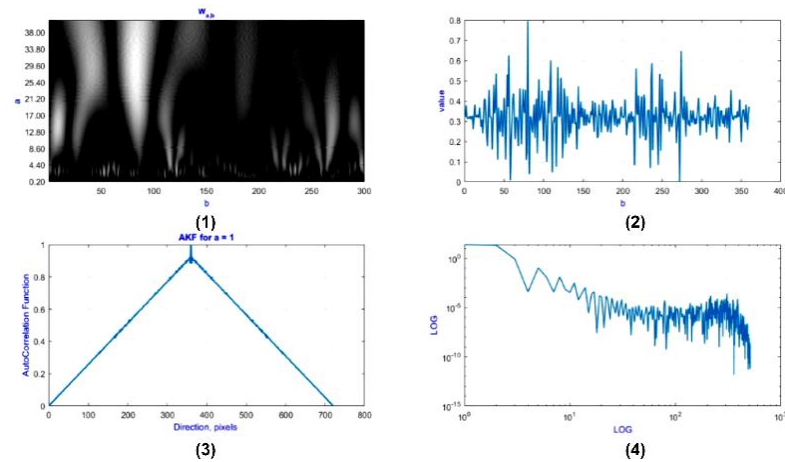


Figure 4. Coordinate (fragment (1)), linear (fragment (2)), autocorrelation (fragment (3)) and fractal (fragment (4)) characteristics of circular birefringence map wavelet transform of kidney native histological section of deceased from experimental group 4 (time since the death from COVID-19 – 3 years).

It was established that:

- The excess K_4 of the autocorrelation functions of the amplitude distribution wavelet coefficients of the circular birefringence (CB) maps of the kidney parenchyma in the experimental samples of native histological kidney sections from deceased individuals had a statistically significant change (< 0.001) – a decrease from 1.64 to 0.93.
- The correlation area SK of the autocorrelation function of the linear distribution of the amplitude wavelet coefficients of the scale-selective transformation of the CB map had a statistically significant change (< 0.001) – an increase from 0.189 to 0.277.
- The central statistical moment of the 3rd order W_3 , whose magnitude characterizes the asymmetry of the linear distributions of amplitude wavelet coefficients of the algorithmic transformation of the CB maps, had a statistically significant change (< 0.001) – an increase from 0.14 to 0.54.
- The 4th-order statistical moment - excess W_4 , whose magnitude characterizes the sharpness of the peak in the linear distributions of the amplitude wavelet coefficients of the CB maps, had a statistically significant change (< 0.001) – an increase from 1.65 to 6.12.

The diagnostic effectiveness of the multiparameter method of azimuthally-invariant Mueller-matrix mapping with polarization reproduction of CB distributions is characterized by operational characteristics, systematically presented in Table 2.

Table 2. balanced accuracy of correlation and wavelet markers of differential diagnostics of long lasting effects of COVID-19

Sample Groups	Kidney native histological section		
	“1 – 2+4”		
$Q_{i=1;2;3;4}$	$Se, \%$	$Sp, \%$	$Ac, \%$
Asymmetry, W_3	$a = 24; b = 1;$	$c = 48; d = 2;$	96
Excess, W_4	$a = 25; b = 0;$	$c = 48; d = 2;$	97
Excess, K_4	$a = 24; b = 1;$	$c = 48; d = 2;$	96
ACF area, SK	$a = 23; b = 2;$	$c = 47; d = 3;$	94
Groups	“2 – 3”		
$Q_{i=1;2;3;4}$	$Se, \%$	$Sp, \%$	$Ac, \%$
Asymmetry, W_3	$a = 49; b = 1;$	$c = 46; d = 4;$	95
Excess, W_4	$a = 48; b = 2;$	$c = 47; d = 3;$	95
Excess, K_4	$a = 48; b = 2;$	$c = 46; d = 4;$	94
ACF area, SK	$a = 47; b = 3;$	$c = 46; d = 4;$	93
Groups	“2 – 4”		
$Q_{i=1;2;3;4}$	$Se, \%$	$Sp, \%$	$Ac, \%$
Asymmetry, W_3	$a = 47; b = 3;$	$c = 45; d = 5;$	92
Excess, W_4	$a = 48; b = 2;$	$c = 45; d = 5;$	93
Excess, K_4	$a = 47; b = 3;$	$c = 45; d = 5;$	92
ACF area, SK	$a = 47; b = 3;$	$c = 44; d = 6;$	91
Groups	“2 – 4”		
$Q_{i=1;2;3;4}$	$Se, \%$	$Sp, \%$	$Ac, \%$
Asymmetry, W_3	$a = 46; b = 4;$	$c = 44; d = 6;$	90
Excess, W_4	$a = 47; b = 3;$	$c = 45; d = 5;$	92
Excess, K_4	$a = 47; b = 3;$	$c = 44; d = 6;$	91
ACF area, SK	$a = 46; b = 4;$	$c = 44; d = 6;$	90

Here b – the number of false positives; d – the number of false negatives.

The following levels of diagnostic effectiveness for differentiating necrotic changes in optical activity of kidney samples from deceased individuals with long-term effects of COVID-19 using:

- Correlation markers K_4 ; SK in the wavelet transformation of polarization-reconstructed circular birefringence maps:
 - Diagnosis (“Control group 1 – Experimental groups 2, 3, 4”) – very good (SK) $Ac = 94\%$ and excellent (K_4) $Ac = 96\%$ level of balanced accuracy.
 - Differentiation (one year – two years) – very good $Ac = 93\% – 94\%$ level of balanced accuracy.
 - Differentiation (one year – three years) – good $Ac = 91\% – 92\%$ level of accuracy.
 - Differentiation (two years – three years) – good $Ac = 90\% – 91\%$ level of balanced accuracy.
- Statistical markers of the wavelet amplitude coefficient distribution W_3, W_4 :
 - Diagnosis (“Control group 2.1 – Experimental groups 2.2, 2.3, 2.4”) – excellent $Ac = 96\% – 97\%$ level of balanced accuracy.
 - Differentiation (one year – two years) – very good level of balanced accuracy $Ac = 95\%$.
 - Differentiation (one year – three years) – very good $Ac = 92\% – 93\%$ level of balanced accuracy.
 - Differentiation (two years – three years) – good (W_4) $Ac = 90\% – 92\%$ level of balanced accuracy.

4. CONCLUSIONS

The method of azimuthally-invariant Mueller-matrix microscopy with algorithmic reproduction of the optical activity maps of the polycrystalline architectonics of the parenchyma in experimental samples of kidney native histological sections from deceased individuals with varying times since death from COVID-19 has been experimentally tested.

As part of the comprehensive statistical analysis of correlation and wavelet transformations of coordinate distributions of random values of circular birefringence, a set of digital markers (central statistical moments of the 3rd and 4th orders of anisotropy parameter distributions and wavelet transformation coefficient amplitudes, as well as excess and correlation areas of the autocorrelation functions of such distributions) for differential diagnostics of necrotic changes in the optical activity of kidney native histological sections from deceased individuals was determined. The balanced accuracy values for the differential diagnosis of long-term effects of COVID-19 were also established.

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