



Components of Oranta-AO software expert system for innovative application of blood pressure monitors

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Received: 23 February 2022 / Accepted: 2 September 2022
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Abstract

The authors developed and substantiated the original methods of arterial oscillography, which were implemented in the developed Oranta-AO information system. The methods of application to the arterial oscillogram registered at measurement of arterial pressure gives the possibility to carry out the supplementary systematic assessment of health, functional state of cardiovascular system, its reserve possibilities etc. The authors also developed an Expert System (based on machine-learning methods) for the differential diagnosis of risks of heart, lung, mental illness and prognosis of some blood parameters. Oranta-AO software system was created based on research results due to methods and algorithms that were innovate. For the mathematical modeling of arterial oscillograms used cyclic random processes. Methods of arterial oscillograms processing based on its model in the form of a cyclic random process was developed. The method of evaluation of the rhythm function of arterial oscillograms and statistical methods for estimating the probabilistic characteristics of arterial oscillograms were developed. To solve the clustering problem, the Python k -means and k -means++ algorithm were used. Oranta-AO information system consists of three interrelated parts: mobile application, computing kernel and web system. Computing kernel and web system are deployed on AWS servers and have been tested already. The developed environment aims to be integrated into every new model of electronic meters in the world. Certification (EN 62304:2014, ISO 13485: 2018) in Ukraine is completed, PCT priority is completed. The next step will be to establish cooperation with manufacturers of electronic pressure monitors, patenting and certification in world.

Keywords Blood pressure monitor · Heart rate · Health level · Pulsation · Information system · Machine learning

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1 Introduction

The cardiovascular system (CVS) is an indicator of the body's adaptive capacity. Cardiovascular system disease is one of the most common human diseases (WHO). Their "rejuvenation" dictates the need to find new methods of the disease prevention, early diagnosis and treatment, as soon as improve the existing methods [1–4].

Blood pressure (BP) measurement is a mandatory procedure in doctor's work at all stages of medical care [5, 6]. To evaluate the waveforms in arteries of the upper extremities, the authors first proposed a new method—arterial oscil-

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lography (AOG), which allows significantly expanding the informativeness for blood pressure measuring [4, 7].

The rapid development of digital technologies penetrates all spheres of life, it's time to apply them to the pulsations that occur when measuring BP. The oscilloscope was designed for the first time by Uskov (1934) [6]. The essence of this method is to register with an oscilloscope the magnitude of the pulse oscillations of the arterial wall at different pressures in the cuff, and the resulting curve reflects the amplitude of stretching of the artery wall. As a rule, their analysis is aimed at determining the rapid increase and decrease of oscillations (the first—systolic, the second—diastolic pressure) and oscillometric index (OI)—the height of the maximum wave of the oscillogram in millimeters, which is its main indicator [4]. The equipment used to obtain oscillograms had high inertia and low sensitivity. The widespread implementation of oscillatory methods in clinical practice was hampered by the complexity of the traditional processing of oscillatory signals and the lack of accuracy and reliability of blood pressure measurement, hardware and metrological support. The analysis of arterial oscillograms is performed in each electronic blood pressure monitor, but the whole analysis comes down to the determination of systolic and diastolic pressure and heart rate, sometimes there is a violation of pulsation rhythm [4, 8–10].

The authors developed Oranta-AO based on the method (Arterial oscillography) to analyze pulsations occurring in the cuff in response to compression of the shoulder (other part of the body) under the influence of pulse vascular activity on compression or (and) decompression to assess the body's adaptive resources, the state of the autonomic nervous and cardiovascular systems, the state of blood vessels and the risks of various diseases [11–13].

The work goal is developing concepts, substantiation, methods, algorithms and tools of the new information technology for assessment and prediction of human health based on arterial oscillography data obtained from a blood pressure monitor. It includes:

1. to adapt methods of arterial oscillograms processing based on its model in the form of a cyclic random process: additional evaluation of adaptive components involved in the reaction to cuff compression (correlation analysis);
2. to apply total and instantaneous spectral power of the signal to estimate the total and instantaneous reaction of the body for the shoulder cuff compression;
3. to solve the clustering problem with k -means and k -means++ algorithm to extract the most informative indicators to use them then in machine-learning task;
4. to solve classification problem with decision tree induction method as part of expert system to detect probabilities of cardiovascular, lung, and mental diseases;

5. to add the developed methods to the architecture and software implementation of the Oranta-AO information system.

2 Literature review

For registration of arterial pulsations the electronic tonometer VAT41-(1,2) and meters of other manufacturers were used that are capable to register pressure values in a cuff during the period of compression increase (and/or decrease) to carry out calculations by arterial oscillography (AOG) methods and to export the obtained values for further analysis in the user's personal account in the web environment.

The validity of studies is confirmed by registered and analyzed 4000 AOGs in people of different ages and sexes, almost healthy and with abnormalities in health (14 nosological conditions), at rest and under the influence of various external factors. In addition, the correspondence of values of some studied indicators of AOG to the indicators of heart rate variability (HRV) of the electrocardiographic signal obtained from the literature was confirmed. There was also a coincidence of separate studied parameters obtained from simultaneously registered by the authors of electrocardiograms (ECG) and AOG (correlation 0.75–0.98) in 354 almost healthy and people with abnormalities in health. The same direction of dynamics of the studied parameters obtained by the authors before and after the procedure of segmental reflex massage in patients with dorsopathy of the cervical spine, registered by AOG (VAT41-1,2) and HRV (Omega-M), which was confirmed by the dynamics of biochemical parameters adrenaline, noradrenaline in the urine, acetylcholinesterase in the blood [14–18].

Significant advances in the analysis of electrocardiograms, rheograms and encephalograms and the scientific substantiation of the results made it possible to adapt this knowledge to the analysis of arterial oscillograms. Since the necessary terminology that would characterize the calculations characteristics and results to describe the pressure oscillogram was not found, the terms and methods used in related areas of cardiovascular research (rheography, electrocardiography) and nervous (encephalography) systems were used. In Electrocardiography, methods of temporal and spectral analysis (Fourier transform) are used, in rheography—methods of morphological analysis, and in encephalography—methods of spectral analysis of the signal (Fourier transform). Since during the pressure measurement the body builds an adaptive response to shoulder compression and there are different types of reactions, the Hilbert–Huang transformation was additionally introduced to assess the body instantaneous adaptive reactions [1–4, 11–14, 24–28].

In world practice, there are three types of pulsations that can be analyzed: compression, decompression and together.

More than 500 sequentially recorded oscillograms of each type were analyzed to understand better the characteristics of each type of pulsations.

Morphological analysis provides the following information: vascular tone and patency, functional capacity, cause of abnormalities (functional or organic), cardiac activity, blood pressure and neuro-reflex effects on their condition.

The objects of research in morphological analysis are the general shape of the oscillogram and the nature of individual pulsations in different phases of compression. In the general analysis of the oscillogram the following features are used: rhythmicity of oscillations, nature of amplitude growth, achievement of maximum and their decrease in the process of shoulder compression, number of maximum amplitude oscillations, shape and symmetry of envelope placement created at maximum and minimum extremes [4, 11–13].

The nature of individual oscillations in different phases of compression is evaluated by: duration of ascending and descending part in one pulsation, forms of peaks of maximum and minimum extremes, dynamics of change of ascending and descending oscillations areas, presence, localization, magnitude of dichroic and additional waves on separate oscillations. In AO, depending on the degree of compression, there are three (from the registered oscillations at the minimum pressure in the cuff to reaching diastolic pressure (APd), between APd and systolic pressure (APs), from APs to maximum compression) and five parts (from registered oscillations at the minimum pressure in the cuff to achieving APd, from the appearance of APd to 70% of the pulsation amplitude, from 70 to 100% of the amplitudes, from 100% to the appearance of APs, from the appearance of APs to maximum compression).

Variability of the oscillations duration (using methods and indicators of temporal analysis and variation pulsometry, adopted to assess electrocardiographic signals), correlation rhythm or scatterogram, chaosgram are analyzed and evaluated.

In addition, in spring 2020, a comprehensive clinical study was conducted, where 172 people were examined: 112 without health complaints, 60 with diseases of CVS (aged 18–65). The general biochemical analysis of blood, coagulogram, ELISA G, M (COVID-19), Endothelin were studied in each patient. Spirogram, ECG (12 leads) was recorded. In addition, a rheogram (8-channel rheo-complex REOCOM) was recorded in the following leads: central hemodynamics (by Kubicek), on both forearms, on the shoulder, cuff pressure channel and ECG channel. And also—a test with a 5-min contraction of the shoulder with a cuff (to assess the endothelium condition). Vascular stiffness (VAT-41-2) was determined. Martine–Kushelevsky test (according to the methods described above) and a test with Nitroglycerin were performed. Their results were compared and adapted to the assessment of vascular condition by AOG. Currently,

research and analysis are ongoing. The results of previous studies are confirmed. Thus, among 88 examined without health complaints according to the results of the Martine–Kushelevsky test, 70% of them registered transient types of reaction, which is a sign of premorbid conditions that require further in-depth examination. Some results were published.

Regarding the contingent of respondents, the method is new. The examination of healthy people made it possible to develop standards of AOG indicators, which highlight the participation of cardiovascular and hemodynamic factors and levels of regulation of their activity in the compression of the shoulder at rest and under the influence of various factors. The obtained results make it possible to use them for comparison with various diseases, which is the next stage of research. Currently, AOG and ECG are the most registered. Among them there are diseases of various stages and clinical manifestations: coronary heart disease (303 people), hypertension (160), psychoneurological diseases (294), patients diagnosed with tuberculosis (204), COVID-19 (74 people, 287 measurements) and others [19–21].

The analysis of the results obtained gave the authors an opportunity to develop and substantiate the methods of arterial oscillography for the first time. The obtained results are presented in the Thesis work of the doctor of biological sciences, monograph, methodical recommendations (approved by the Ministry of Health), 7 patents; 72 articles in journals [11–13, 19, 20, 24–27]. Certification (EN 62304:2014, ISO 13485: 2018) in Ukraine is completed, PCT priority is completed. The next step will be to establish cooperation with manufacturers of electronic pressure monitors, patenting and certification in world.

The use of morphological, temporal, spectral analysis of the arterial oscillogram registered at measurement of arterial pressure gives the chance to carry out in addition a complex assessment of health, a functional condition of cardiovascular system, its reserve possibilities; get information from 4 levels of regulation of CVS activity (peripheral—autonomous, autonomic, hypothalamic-pituitary, central nervous system); to study the condition of blood vessels: their tone, elasticity, quality of adaptation to different levels of compression when measuring blood pressure; identify the state of the disease, the effectiveness of therapeutic, preventive and rehabilitative measures. The authors also developed an Expert System (based on machine-learning methods) for the differential diagnosis of risks of heart, lung, mental diseases and prognosis of some blood parameters [11–14].

Based on the methods and algorithms developed as a result of research, Oranta-AO software package was designed and developed, which allows the user to take measurements with an electronic blood pressure monitor, load them into the system, get calculated indicators, view them in a convenient way and see analytical information on the basis of which you can

assess the state of the cardiovascular system and decide on further action [11–15, 21–24, 28].

Application of methods of Arterial oscillography (D. Vakulenko, L. Vakulenko) AO is possible in the electronic blood pressure monitors supporting work with Oranta-AO information system. The scope of the AO method is possible in all accepted areas of application of blood pressure monitors. The AO innovation provides extended and additional diagnostics, especially relevant for sports, space and military medicine, daily monitoring, fitness, preventive and functional examinations, as well as for household use. A patient, nurse, family doctor, cardiologist and others can be a user of the AO [25–27].

The work [30–32] shows that cyclic heart signals, can be adequately described on the basis of the mathematical apparatus of cyclic random functions, namely, using a cyclic random process and a vector of cyclic rhythmically related random processes, because these mathematical models and developed based on them, the methods of statistical processing of cardio signals take into account both the cyclicity and stochasticity of their morphological structure and the variability of the rhythmic structure of cardiac signals, and with proper modification, as discussed in [33], allow to take into account the stochasticity of their rhythm. A similar approach should be applied to the arterial oscillography signals.

To solve the classification problem the well-known methods were used: *k*-means algorithm [54] and its modification—the *k*-means++ algorithm [46].

To solve the classification problem, a forest of decision trees was built on the basis of machine-learning methods [14].

In previous research concepts, substantiation, methods, algorithms, and tools of the new blood pressure monitor application were developed:

- The methods for the analysis of pulsations that occur in a pressure monitor cuff in response to shoulder (or other part of the body) compression under the influence of blood vessels pulse activity on compression or (and) decompression [17, 19, 28].
- Selection and justification of the use of mathematical apparatus to solve problems for the methods implementation was made [17, 19, 24, 28].
- The software allowing the user to go through all the stages from direct measurement to full analysis of the results. In more details, it receives data from the pressure monitor, transfers data for calculations, makes calculations on the basis of the developed methods, saves the results and presents them to the user in the form convenient for the analysis [17, 19, 23, 28].
- Mathematical models and methods of ECG processing based on cyclic random functions [30–33].

The methods provided the analysis of:

- morphological component of the arterial oscillogram, individual pulsations and their components in different phases of compression [17, 19, 28];
- intervalogram at positive and negative intervals—for the use of methods of heart rate variability [17, 19, 20, 28];

3 Arterial oscillogram analysis methods

3.1 Algorithm for identifying pulse component of vessels from additive mixture obtained from pressure sensor using moving average

The task of identifying extremums is an important task because the final result objectivity depends on the algorithm quality. Extremum identification algorithms are used for various periodic signals of electrocardiography, pulsegraphy, phonocardiography, rheography. The task is complicated by the dynamic nature of the arterial oscillogram filled with various artifacts. Due to the participation in the pulse component of cardiac (maximum extremities of AO) and vascular (minimum extremes of AO) factors, it is necessary to identify the maximum and minimum extremes. To solve this problem, the moving average method was adapted [29].

Smoothing using two-sided moving averages was used for development of arterial oscillogram curves. It is common for a time series to consist of a smooth underlying trend observed with error:

$$y_t = f(t) + \varepsilon_t,$$

where $f(t)$ is a smooth and continuous function of t and ε_t is a zero-mean error series.

A moving average is a time series constructed by taking averages of several sequential values of another time series. It is a type of mathematical convolution. If we represent the original time series by y_1, \dots, y_n , then a two-sided moving average of the time series of $\{y_t\}$. Thus z_{k+1}, \dots, z_{n-k} forms a new time series which is based on averages of the original time series. The estimation of $f(t)$ is known as smoothing, and a two-sided moving average is one way of doing so:

$$z_t = \frac{1}{2k+1} \sum_{j=0}^k y_{t+j}, \quad t = k+1, k+2, \dots, n-k.$$

The idea behind using moving averages for smoothing is that observations which are nearby in time are also likely to be close in value. So taking an average of the points near an observation will provide a reasonable estimate of the trend at that observation. The average eliminates some of the randomness in the data, leaving a smooth trend component. Moving

averages do not allow estimates of $f(t)$ near the ends of the time series (in the first k and last k periods). This can cause difficulties when the trend estimate is used for forecasting or analyzing the most recent data. Each average consists of $2k + 1$ observations. Sometimes this is known as a $(2k + 1)$ MA smoother. The larger the value of k , the flatter and smoother the estimate of $f(t)$ will be. A smooth estimate is usually desirable, but a flat estimate is biased, especially near the peaks and troughs in $f(t)$. When $\{\epsilon t\}$ is a white noise series (i.e., independent and identically distributed with zero mean and variance 2), the bias is given by $E[f(x)] - f(x) \approx 16 f''(x)k(k + 1)$ and the variance by $V[f(x)] \approx 2/(2k + 1)$. So there is a trade-off between increasing bias (with large k) and increasing variance (with small k).

3.2 Modeling arterial oscillograms based on its model in the form of a cyclic random process

In this work, the mathematical model in the form of a cyclic random process is extended to arterial oscillograms. Thus, based on the above considerations, for the mathematical modeling of arterial oscillograms used cyclic random processes, which more fully (see Table 1) take into account the morphological and rhythmic structures of cyclic cardio signals in comparison with their well-known mathematical models.

The domain of the definition of the cyclic random process is ordered in a discrete manner

$$W = D = \left\{ t_{ml} \in R, m \in Z, l = 1, \dots, L, L \geq 2 \right\}$$

plural or plural $W = R$ real numbers. In the case of discrete domain definition $W = D$ for its elements there is the following type of linear ordering:

$$t_{m_1 l_1} < t_{m_2 l_2}, \text{ if } m_2 > m_1, \text{ or if } m_2 = m_1, \text{ and } l_2 > l_1, \text{ in others cases } t_{m_1 l_1} > t_{m_2 l_2} \\ \left(m_1, m_2 \in Z, l_1, l_2 \in 1, L, 0 < t_{m, l+1} - t_{m, l} < \infty \right).$$

According to works [29, 30] give definitions of cyclic random process of continuous argument and cyclic discrete random process.

Definition 1 Separable random process $\xi(\omega, t), \omega \in \Omega, t \in R$, is called cyclic random process of continuous argument, if such a function exists $T(t, n)$ which satisfies the conditions of the rhythm function that are finite-dimensional vectors $(\xi(\omega, t_1), \xi(\omega, t_2), \dots, \xi(\omega, t_k))$ and

$$(\xi(\omega, t_1 + T(t_1, n)), \xi(\omega, t_2 + T(t_2, n)), \dots, \xi(\omega, t_k + T(t_k, n))), n \in Z$$

where $\{t_1, t_2, \dots, t_k\}$ —the set of separability of the process $\xi(\omega, t), \omega \in \Omega, t \in R$, for all integers $k \in N$ are stochastically equivalent in a broad sense.

The rhythm function $T(t, n)$ satisfies such conditions:

- (a) $T(t, n) > 0$ if $n > 0$ ($T(t, 1) < \infty$)
- (b) $T(t, n) = 0$ if $n = 0$
- (c) $T(t, n) < 0$ if $n < 0$ ($t \in W$)

For any $t_1 \in W$ and $t_2 \in W$, for which $t_1 < t_2$, for functions $T(t, n)$ a strict inequality holds:

$$T(t_1, n) + t_1 < T(t_2, n) + t_2, \forall n \in Z \tag{2}$$

Functions $T(t, n)$ has a smallest in modulus $(|T(t, n)| \leq |T_\gamma(t, n)|)$ among all such features $\{T_\gamma(t, n), \gamma \in \Gamma\}$ which are satisfy (1), (2).

The cyclic random process of a continuous argument is characterized by the fact that the family of its consistent distribution functions satisfies the following equations:

$$F_{k\xi}(x_1, \dots, x_k, t_1, \dots, t_k) = F_{k\xi}(x_1, \dots, x_k, y(t_1, n), \dots, y(t_k, n)) = F_{k\xi}(x_1, \dots, x_k, t_1 + T(t_1, n), \dots, t_k + T(t_k, n)), x_1, \dots, x_k, t_1, \dots, t_k \in R, n \in Z, k \in N \tag{3}$$

If $T(t, n) = n \bullet T, T = const, T > 0$ then we will have a random cyclic process with a stable rhythm, which in the literature is known as a stochastically periodic process (cyclostationary random process, periodically distributed random process). If $(t, n) \neq n \bullet T$, then we will have a random cyclic process with a variable rhythm.

Similar to Definition 1, we define a cyclic random process with a discrete argument.

Definition 2 Discrete random process $\xi(\omega, t_{ml}), \omega \in \Omega, t_{ml} \in D$ is called cyclic discrete random process if such a discrete function exists $T(t_{ml}, n)$, which satisfies the conditions of the rhythm function that are finite-dimensional vectors $\xi(\omega, t_{m_1 l_1}), \xi(\omega, t_{m_2 l_2}), \dots, \xi(\omega, t_{m_k l_k}), \xi(\omega, t_{m_1 l_1} + T(t_{m_1 l_1}, n)),$

$$\xi(\omega, t_{m_2 l_2} + T(t_{m_2 l_2}, n)), \dots, \xi(\omega, t_{m_k l_k} + T(t_{m_k l_k}, n)), n \in Z,$$

for all integers $k \geq 1$ are stochastically equivalent in a broad sense.

For a discrete cyclic random process, the family of its distribution functions satisfies the following equations:

$$F_{k\xi}(x_1, \dots, x_k, t_{m_1 l_1}, \dots, t_{m_k l_k}) = F_{k\xi}(x_1, \dots, x_k, t_{m_1 l_1}$$

Table 1 Comparative characteristics of known and new mathematical models of cardio signals

	Known mathematical models of cardio signals (CS)							New model
	Deterministic			Stochastic				
	Deterministic function that describes the shape of one cardiac cycle	Periodic and almost periodic functions	Vector of random variables as a model of cardiocycle reference points	Additive, multiplicative, additive-multiplicative models	Periodically correlated random process	Periodically distributed random process	Linear periodic random process	
Takes into account the cyclicity of the CS	-	+	-	+	+	+	+	+
Takes into account the random nature of the CS	-	-	+	+	+	+	+	+
Takes into account the stochastic relationship between cardiocycles	-	-	-	-	+	+	+	+
Describes the CS in terms of distribution functions	-	-	+	+	-	+	+	+
Takes into account the variability of the rhythm of the CS	-	-	-	-	-	-	-	+
Takes into account the change in the rhythm of the CS by arbitrary law	-	-	-	-	-	-	-	+
Takes into account the common rhythm of synchronously registered CS	-	-	-	-	-	-	-	-

“+” —takes into account (displays)
 “-” —does not take into account (does not display)

$$\begin{aligned}
 &+T(t_{m_1l_1}, n), \dots, t_{m_kl_k} + T(t_{m_kl_k}, n)) \\
 = &F_{k\xi}(x_1, \dots, x_k, y(t_{m_1l_1}, n), \dots, y(t_{m_kl_k}, n)), \\
 &x_1, \dots, x_k \in R, t_{m_1l_1}, \dots, t_{m_kl_k} \in D, n \in Z, k \in N \quad (4)
 \end{aligned}$$

3.3 Evaluation of the rhythm function of arterial oscillograms

Consider the simplest type of interpolation—piecewise-linear interpolation. In this case, the interpolation function $\widehat{T}(t, 1)$ will look like:

$$\widehat{T}(t, 1) = \sum_{m \in Z} \sum_{i=1}^N \widehat{T}_{mi}(t), t \in R \quad (5)$$

where $\{\widehat{T}_{mi}(t)\}$ — a set of functions equal to:

$$\widehat{T}_{mi}(t) = \{k_{mi} \bullet t + b_{mi}, t \in W_{mi}, m \in Z, i = 1, N, 0, t \notin W_{mi}. \quad (6)$$

The area $W_{mi} = [\widetilde{t}_{mi}, \widetilde{t}_{m,i+1})$ corresponds to the i -th zone in the m -th cycle of arterial oscillogram. If $i = N$ then $\widetilde{t}_{m,N+1} = \widetilde{t}_{m+1,1}$. Of course, in practice m takes its values from a finite subset of integers.

Therefore, when piecewise-linear interpolation of the rhythm function, it is necessary to find sets of coefficients $\{k_{mi}, m \in Z, i = 1, N\}$ and $\{b_{mi}, m \in Z, i = 1, N\}$ which will completely determine the interpolation function $\widehat{T}(t, 1)$. Find the expressions for calculating the required coefficients of the interpolation function. To do this, write the equation of the segment connecting the points with the coordinates $(\widetilde{t}_{m,i}, T(\widetilde{t}_{m,i}, 1))$ and $(\widetilde{t}_{m,i+1}, T(\widetilde{t}_{m,i+1}, 1))$, that is, it combines the readings of a discrete rhythm function $T(\widetilde{t}_{m,i}, 1)$ at times $\widetilde{t}_{m,i}$ and $\widetilde{t}_{m,i+1}$:

$$\frac{\widehat{T}_{mi}(t) - T(\widetilde{t}_{m,i+1}, 1)}{T(\widetilde{t}_{m,i+1}, 1) - T(\widetilde{t}_{m,i}, 1)} = \frac{t - \widetilde{t}_{m,i+1}}{\widetilde{t}_{m,i+1} - \widetilde{t}_{m,i}}, t \in W_{mi}, m \in Z, i = 1, N. \quad (7)$$

It is easy to show that these equations can be reduced to the following equations:

$$\begin{aligned}
 \widehat{T}_{mi}(t) = &\frac{T(\widetilde{t}_{m,i+1}, 1) - T(\widetilde{t}_{m,i}, 1)}{\widetilde{t}_{m,i+1} - \widetilde{t}_{m,i}} \cdot t + T(\widetilde{t}_{m,i+1}, 1) \\
 &- \frac{T(\widetilde{t}_{m,i+1}, 1) - T(\widetilde{t}_{m,i}, 1)}{\widetilde{t}_{m,i+1} - \widetilde{t}_{m,i}} \cdot \widetilde{t}_{m,i+1}, \quad (8)
 \end{aligned}$$

$$t \in W_{mi}, m \in Z, i = 1, N.$$

Or similarly:

$$\begin{aligned}
 \widehat{T}_{mi}(t) = &\frac{T(\widetilde{t}_{m,i+1}, 1) - T(\widetilde{t}_{m,i}, 1)}{\widetilde{t}_{m,i+1} - \widetilde{t}_{m,i}} \cdot (t - \widetilde{t}_{m,i+1}) \\
 &+ T(\widetilde{t}_{m,i+1}, 1), t \in W_{mi}, m \in Z, i = 1, N. \quad (9)
 \end{aligned}$$

Therefore, the coefficients $\{k_{mi}, m \in Z, i = 1, N\}$ and $\{b_{mi}, m \in Z, i = 1, N\}$ will be determinate by the ratios:

$$k_{mi} = \frac{T(\widetilde{t}_{m,i+1}, 1) - T(\widetilde{t}_{m,i}, 1)}{\widetilde{t}_{m,i+1} - \widetilde{t}_{m,i}}, m \in Z, i = 1, N. \quad (10)$$

$$\begin{aligned}
 b_{mi} = &T(\widetilde{t}_{m,i+1}, 1) - \frac{T(\widetilde{t}_{m,i+1}, 1) - T(\widetilde{t}_{m,i}, 1)}{\widetilde{t}_{m,i+1} - \widetilde{t}_{m,i}} \cdot \widetilde{t}_{m,i+1}, m \\
 &\in Z, i = 1, N. \quad (11)
 \end{aligned}$$

3.4 Statistical methods for estimating the probabilistic characteristics of arterial oscillograms

Let's write down formulas for calculation of realizations of the corresponding statistical estimations of probabilistic characteristics of cyclic casual process in a case when some its long realization is set $\xi_\omega(t), t \in W$ which contains a sufficiently large number of its complete cycles.

Implementation of statistical evaluation of mathematical expectation:

$$\widehat{m}_\xi(t) = \frac{1}{M} \sum_{n=0}^{M-1} \xi_\omega(t + T(t, n)), t \in W_{c_1} = [\widetilde{t}_1, \widetilde{t}_2), \quad (12)$$

where $t_1 \neq 0$ in the general case.

Implementation of statistical estimation of variance:

$$\begin{aligned}
 \widehat{d}_\xi(t) = &\frac{1}{M-1} \\
 &\cdot \sum_{n=0}^{M-1} [\xi_\omega(t + T(t, n)) - \widehat{m}_\xi(t + T(t, n))]^2, t \\
 &\in W_{c_1} = [\widetilde{t}_1, \widetilde{t}_2). \quad (13)
 \end{aligned}$$

Implementation of statistical estimation of the initial moment function k -th order:

$$\widehat{m}_\xi^k(t) = \frac{1}{M} \cdot \sum_{n=0}^{M-1} \xi_\omega^k(t + T(t, n)), t \in W_{c_1} = [\widetilde{t}_1, \widetilde{t}_2). \quad (14)$$

Implementation of statistical estimation of the central moment function

k -th order:

$$\begin{aligned} \widehat{d}_{\xi}^k(t) &= \frac{1}{M-1} \\ &\cdot \sum_{n=0}^{M-1} [\xi_{\omega}(t+T(t,n)) - \widehat{m}_{\xi}(t+T(t,n))]^k, t \\ &\in W_{c_1} = \widetilde{t}_1, \widetilde{t}_2. \end{aligned} \quad (15)$$

Implementation of statistical estimation of mixed initial instantaneous order function $p = \sum_{i=1}^k R_i$

$$\begin{aligned} \widehat{c}_{p_{\xi}}(t_1, \dots, t_k) &= \frac{1}{M - M_1 + 1} \\ &\cdot \sum_{n=0}^{M-1} [\xi_{\omega}^{R_1}(t_1 + T(t_1, n)) \cdot \dots \cdot \xi_{\omega}^{R_k}(t_k + T(t_k, n))], t \\ &\in W_{c_1}, t_2, \dots, t_k \in \bigcup_{m=1}^{M_1} W_{c_m}, \end{aligned} \quad (16)$$

where $M_1 (M_1 \ll M)$ —the number of cycles in which arguments gain value t_2, \dots, t_k .

Implementations of statistical estimation of mixed central moment function of order: $p = \sum_{i=1}^k R_i$

$$\begin{aligned} \widehat{r}_{p_{\xi}}(t_1, \dots, t_k) &= \frac{1}{M - M_1} \\ &\cdot \sum_{n=0}^{M-M_1} [(\xi_{\omega}(t_1 + T(t_1, n)) - \widehat{m}_{\xi}(t_1 + T(t_1, n)))^{R_1} \\ &\cdot \dots \cdot (\xi_{\omega}(t_k + T(t_k, n)) - \widehat{m}_{\xi}(t_k + T(t_k, n)))^{R_k}], t_1 \\ &\in W_{c_1}, t_2, \dots, t_k \in \bigcup_{m=1}^{M_1} W_{c_m}. \end{aligned} \quad (17)$$

To obtain additional information about the nature and the mechanisms involved in the adaptation to various influences in the studies, the indicators are further subjected to correlation analysis for further inclusion in the Expert System. The block diagram of the applied methods in Oranta-AO software is given in Fig. 1.

Morphological analysis (10 indicators), temporal (37 indicators) and spectral analysis (485 indicators) of oscillograms are used for the analysis of arterial oscillograms. The spectral analysis calculates the spectral power of the intervalogram (45 indicators), the arterial oscillogram according to the Fourier transform (340 indicators) and the instantaneous frequency and phase according to the Hilbert-Huang transformation (90 indicators). The arterial oscillogram is divided into 5 parts: until diastolic pressure is reached, from diastolic pressure to 70% of the amplitude of the oscillogram, from 70 to 100% of the amplitude of the oscillogram, from 100 to

70% of the amplitude and from 70% to the end of the measurement. For each of these AO intervals, Fourier transform (68 indicators) and the instantaneous frequency and phase of the Hilbert-Huang transformation (18 indicators) was used [34–42].

3.5 Spectral analysis

Spectral analysis methods have been widely used in various fields of signal analysis. A detailed substantiation of the biological content of the Fourier transform is performed, which indicates the power of participation of a certain adaptation mechanism in the researched process. The Hilbert-Huang transformation has become less widespread, the biological content of the obtained indicators reflects the instantaneous adaptation mechanisms involved in the researched phenomenon.

3.5.1 Discrete Fourier transform

Spectral analysis Rapid Fourier transform (RFT) methods have been used to analyze biosignals in the frequency spectrum [17, 43]. The discrete Fourier transform for a vector x consisting of N elements has the form:

$$X_m = \sum_{n=0}^{M-1} x_{2n} a_M^{mn} + \exp\left(-2\pi i \frac{m}{N}\right) \sum_{n=0}^{M-1} x_{2n+1} a_N^{nm}. \quad (18)$$

3.5.2 The Hilbert–Huang transform (HHT) use for the vital indicators of frequency and phase in the spectrum of biosignals research

To study the vital signs of frequency and phase in the spectrum of biosignals Hilbert–Huang transform (HHT) was used. It means the method of empirical mode decomposition (Empirical Mode Decomposition, EMD) of nonlinear and nonstationary processes and Hilbert spectral analysis (Hilbert Spectral Analysis, HSA) [39]. HHT is a frequency-time analysis of data and does not require a priori functional basis of transformation. Instantaneous frequencies (IFs) are calculated from derivatives of Hilbert phase functions by transforming basis functions.

The next step in the Hilbert–Huang transformation is the Hilbert transformation. Using the transformation for each signal allows to get the values of instantaneous frequency and amplitude for each time moment.

Spectral methods of arterial oscillogram analysis are used directly for the values of the pressure change in the cuff during the compression of the shoulder, without the pressure component that creates the compressor in the cuff. For the curve reflecting mechanical activity of an arterial wall in the course of a shoulder compression the visual analysis on quan-

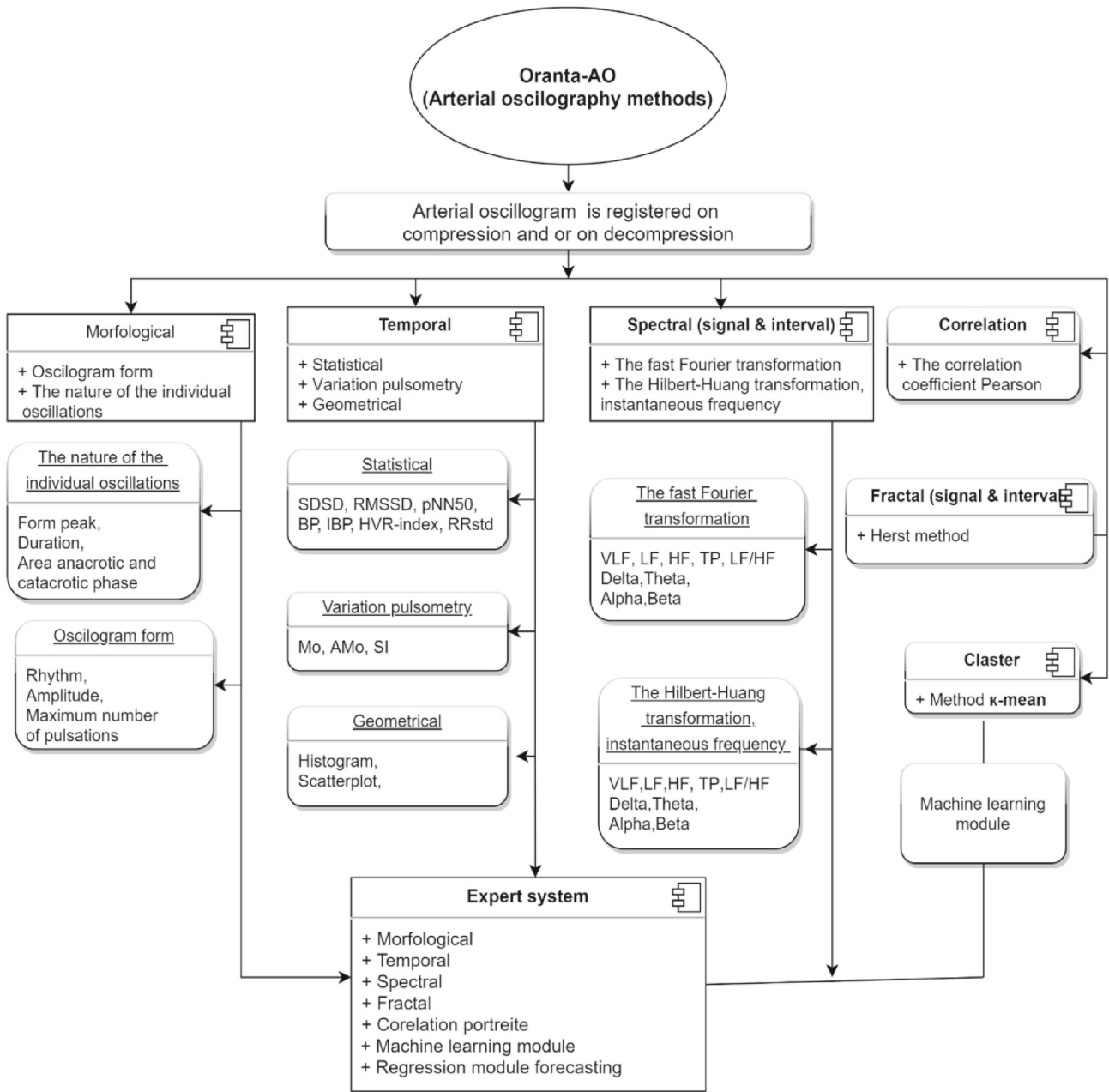


Fig. 1 Block diagram of the methods used for the arterial oscillogram analysis

titative signs, localization, and small fluctuations existence is applied.

3.6 k-Means clustering

The minimum-sum-of-squared clustering problem [44]

$$\left\{ \sum_{j=1}^m \min_{c \in C} \|a^j - c\|^2, |C| = k \right\} \quad (19)$$

is to find k cluster centers $c^i \in R^n, i \in I\{1, \dots, k\}$ so as to minimize the overall sum of squared Euclidean distances between data items and their closest centers [45]. It can be cast as the following mixed integer programming problem:

$$\sum_{i=1}^k \sum_{j=1}^m x_{ij} \|y^i - a^j\|^2 \rightarrow \min_{(x,y)} \quad (20)$$

$$\sum_{i=1}^k x_{ij} = 1, \forall j = 1, \dots, m, \quad (21)$$

$$x_{ij} \in \{0, 1\}, \forall i = 1, \dots, k, \forall j = 1, \dots, m. \quad (22)$$

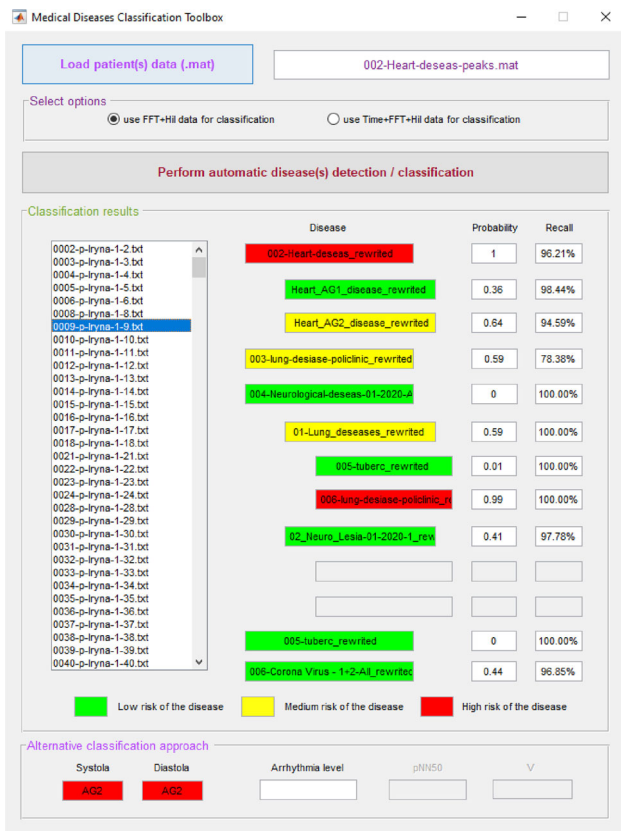


Fig. 2 Interface classification tasks (Health—Cardiovascular disease, Health—Pulmonary disease, Health—Mental disease) in the Matlab 2020 environment with probability and recall value

To solve problem (19) and (20)–(22) the k -means (Lloyd's algorithm) algorithm is used. The k -means algorithm works in two repetitive steps: assigning each data item to the closest cluster centers and computing the new cluster centers as the means of the data items assigned to the same clusters.

Despite the efficiency and simplicity of k -means algorithm, it has some disadvantages. It requires $O(mnk)$ time, which is rather much in the worst case. Moreover, it converges to local optima only and depends a lot on the choice of the initial point. One of the modifications of the k -means algorithm, fighting this problem is k -means++ algorithm [46]. It permits to set better initial points and obtain (log k) competitive solutions. The k -means++ algorithm is built in many libraries of various programming languages. For instance, MATLAB has a k -means implementation that uses k -means++ as default for seeding [47], as well as Scikit-learn library for Python.

3.7 Solving classification problem with decision tree induction method as part of expert system

The goal is to apply the decision tree induction method for software implementation in the decision-making sys-

tem regarding classification and forecasting risks of diseases appearance based on arterial oscillogram analysis.

A study of almost healthy patients and patients with abnormalities in health (14 nosological conditions), at rest and under the influence of various external factors was conducted. Among them are diseases of various stages and clinical manifestations: coronary heart disease (303 patients), hypertension (160), psychoneurological diseases (294), patients diagnosed with tuberculosis (204), COVID-19 (74 patients, 287 measurements) and others.

To solve the classification problem, a forest of decision trees was built on the basis of machine-learning methods [14]. The matrix of states of each sample (Cardiovascular, Pulmonary, Mental Illness, Covid-19 and others) includes indicators of morphological, temporal, spectral, cluster analysis, based on the model in the form of a cyclic random process and statistical methods for estimating the probabilistic characteristics of arterial oscillograms.

Using machine-learning methods: problems classification and regression analysis methods, training and analysis of the results is made. The results are integrated into the computing kernel of Oranta-AO information system to calculate the probabilistic risk assessment of diseases (Cardiovascular, Pulmonary, Mental Illness, Covid-19 and others).

The main stages of data analysis using decision trees.

4 1. Problem statement and data preparation (from.mat files).

Since a patient can have several diseases at the same time, this task is formed as a "Multi-label classification problem". A transformation of the initial task is made to solve it, namely:

1. the initial Multi-label classification problem is transformed into a set of binary classification problems such as "sick-healthy" for each pair of appropriate classes;
2. each of the newly formed problems is solved separately by building an appropriate algorithm (model) for it;
3. for each of the binary classification problems its own training and test data sets is formed;
4. independent training of models for each task on the corresponding training data set is done;
5. an independent assessment of the models quality for each task on the appropriate test data set is done;
6. trained models are tested on new (future) data;
7. the results of all models form the overall result.

5 2. Choice of data analysis model/algorithm.

In this case, the random forest classifier is chosen as a model. It is an ensemble algorithm formed as a composition of decision trees that act as basic (elementary) algorithms. Each tree in such an ensemble studies independently and on its own data set (training sample). Such a training sample is formed by sampling the data of the available complete training data set (statistical sample). It should be noted that the structure of each tree is formed on the basis of various attributes analysis (features, parameters) available in the training set. In general case, the optimal number of such attributes (features, parameters) for the construction of trees is determined either experimentally or on the basis of available heuristic data.

6 3. Selection of model/algorithm parameters

Selection of model parameters is a rather difficult task that can be solved in one of the following ways:

- go through all possible parameters combinations (it is used very rarely due to resource intensity);
- use of optimization algorithms;
- use of heuristic data;
- use of own experiments.

As a result of the experiments the following basic parameters were selected for each model:

- number of trees in the ensemble is 100;
- the maximum number of branches (tiers) of the tree is 5;
- the maximum number of attributes for forming tree vertices is 10;
- algorithm for building a decision tree is CART.

7 4. Selection of strategy and metrics for assessing the model quality.

The evaluation of the quality of the model (s) is carried out using k -fold cross-validation ($k = 3$). Since there is an imbalance in the data, one of the criteria that gives an objective assessment of the model quality is the F -measure ($F1$ -measure).

8 An example of software research implementation in the Matlab 2020 environment

Figure 2 shows an example of software research implementation in the Matlab 2020 environment Classification tasks for the next pair: Health—Heart disease, Health—Lung disease, Health—psychoneurological disease.

The interface window of the constructed models of classification tasks for disease classes (Cardiovascular, Pulmonary, Mental disease and others). The left column displays a list of measurements of patients with Cardiovascular disease, the central column Disease presents a list of constructed models with color display, depending the magnitude of the disease probability. The next column shows the probability of belonging to the class and recall the quality of the built model. The lower part of the window shows the Alternative classification approach, which includes the probabilities of hypertension of the first and second type and some other indicators.

9 Oranta-AO information system

Oranta-AO information system does the following:

- gets measurements raw data from a pressure monitor;
- sends the measurement raw data to the computing kernel which computes a number of indicators that characterize the level of health, risks for heart and vessel, lung and mental diseases and predicts some indicators of blood, central hemodynamics and mental states;
- saves raw measurement data and computed indicators both in files and database;
- displays the measurement data and the computed indicators in a user-friendly form, that allows to qualitatively analyze the patient's state and make recommendations for further action to maintain/improve the patient's health.

Oranta-AO IS includes three main parts: Oranta-AO mobile application, computing kernel and Oranta-AO web system (Fig. 3).

To obtain arterial oscillograms on compression, a blood pressure monitor VAT 41-2 produced with Iks-Techno, Ukraine was used. Pressure monitors Omron, Japan and Dr. Frei, Switzerland were selected to obtain arterial oscillograms on compression and decompression. Since the

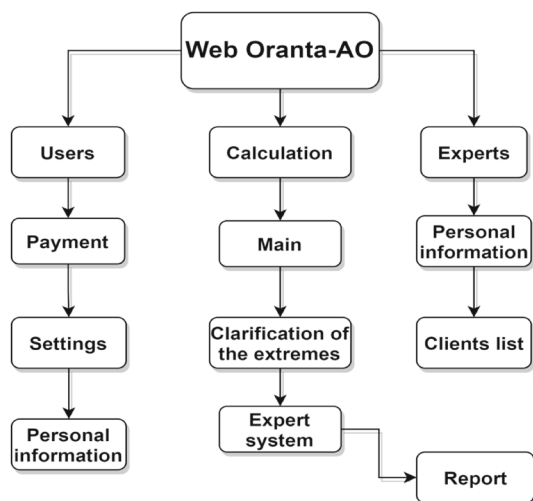


Fig. 4 Oranta-AO web system structure

The results are returned as a json file that can contain computed results for one or more measurements. The raw measurements data file is also sent to web system for storing.

The web system is designed to store the results of computations performed by the computing kernel, and display these results in a way convenient for analysis by the patients or consulting doctors (Fig. 4). The web system consists of backend and frontend parts.

The backend part provides the REST API for the frontend part. It is developed using nodejs 12.16 [50] and express framework 4.16 [51]. Also mongodb 4.2 [52] database server and mongoose ORM 5.9 were used. The frontend is developed using Angular 11 [53] framework with TypeScript programming language. The web system functions structure is presented in Fig. 4.

Both patients and experts or consultants (doctors) can be the web system users. A patient can upload his or her personal measurements data and view the calculated indicators. They also can select consultants to help them with interpreting the data. A consultant can upload his patients measurements data and view the calculated indicators for them. A consultant can also use patient functions for himself.

Both the computing kernel and web system are deployed on AWS servers and are available in test mode now.

10 Results

In previous research some concepts, substantiation, methods, algorithms, and tools of the new blood pressure monitor application were developed (described in Sect. 2 of this paper). Also, Oranta-AO information system was developed which implemented the methods and algorithms.

In this work, for the first time, a new model for arterial oscillograms was applied in the form of a cyclic random process, which made it possible to take into account stochasticity, cyclicity of probabilistic indicators and rhythm variability in the arterial oscillograms analysis methods.

The detailed substantiation of the biological content for arterial oscillograms spectral analysis methods of the Fourier and Hilbert–Huang transform is provided. The Fourier transform is performed, which indicates the power of participation of a certain adaptation mechanism in the researched process. The Hilbert–Huang transform has become less widespread, the biological content of the obtained indicators reflects the instantaneous adaptation mechanisms involved in the researched phenomenon.

The classification problem was solved as a part of the expert system using the k -means (Lloyd's) algorithm. To obtain better local optima the modification of the k -means algorithm was applied (known as k -means++), which permits to set better initial points for selecting the most informative indicators for the following solution in the decision tree induction method. As a platform for solving the classification problem the MATLAB was used, which uses the k -means++ algorithm as default. It is also planned to develop non-smooth optimization and combinatorial algorithms for solving the classification problem.

The decision tree induction method for software implementation in the decision-making system regarding classification and forecasting risks of diseases appearance based on arterial oscillogram analysis is applied. Machine learning methods like problems classification and regression analysis methods were used, training and analysis of the results was made.

The use of the following was substantiated for the implementation of the problems: the main stages of data analysis using decision trees; choice of data analysis model/algorithm; selection of model/algorithm parameters; selection of strategy and metrics for assessing the model quality are done.

The model(s) quality evaluation is carried out using k -FOLD cross-validation ($k = 3$). Since there is an imbalance in the data, one of the criteria that gives an objective assessment of the model quality is the F -measure ($F1$ -measure). An example of the research is implemented in the Matlab 2020 environment.

The methods are integrated into the computing kernel of Oranta-AO information system to calculate the probabilistic risk assessment of diseases (Cardiovascular, Pulmonary, Mental Illness, Covid-19 and others).

The methods and algorithms developed, adapted and tested in this work for a specific type of biosignal (arterial oscillogram), which is distinguished by its dynamics, duration and specific artifacts, are unique and the authors have not encountered similar applications for similar tasks.

The Oranta-AO information system was updated to include the above mentioned methods.

The research opens up new prospects for increasing the informativeness of arterial oscillograms analysis in the work of the disease risk forecasting module of the Oranta-AO Expert System. On the basis of preliminary testing for groups of patients with cardiovascular (480 patients), pulmonary (320 patients) and mental (370 patients) diseases and more than 2,000 patients without health problems, training and testing of built models was carried out to solve classification problems. The built models showed a high predictive efficiency (probability 90–98%), which indicates the significant value of the developed approach. For further improvement of the methods and algorithms presented in this paper, further clinical research and expertise of medical communities from narrower specializations are needed. It should be noted that the basic principles laid down in the analysis of the arterial oscillogram and implemented in Oranta-AO information system, which reflect the level of centralization of the autonomic nervous system, the heart and blood vessels functional capabilities, are extremely relevant and highly informative and can be used in medical practice after the completion of the necessary national certification procedures. The application of arterial oscillography methods and Oranta-AO algorithms was tested on the holter blood pressure monitors VAT41-2, and Omron and Dr. Frei. VAT41-2 measures during shoulder compression, but Omron and Dr. Frey during exhalation. These are the two main principles of registering pulsations by the oscillometric method. A method of recording pulsations in the sound range, known as the Korotkoff method, was also tested. The arterial oscillogram can be affected by the sensitivity of the sensor, the sampling rate during signal registration, so further research will help to better understand the limitations in the application of the developed methods and information system Oranta-AO.

11 Conclusion

The authors developed and substantiated the original methods of arterial oscillography, which were implemented in the Oranta-AO information system. The application the methods to the arterial oscillogram registered at arterial pressure measurement gives the possibility to make the supplementary systematic assessment of human health in general, the functional state of cardiovascular system, its reserve possibilities; get information from 4 levels of regulation of CVS activity (peripheral-autonomous, autonomic, hypothalamic-pituitary, central nervous system); to study the condition of blood vessels: their tone, elasticity, quality of adaptation to different levels of compression when measuring blood pressure; identify the state of a disease, the effectiveness of therapeutic, preventive and rehabilitative measures.

In this research, for the mathematical modeling of arterial oscillograms used cyclic random processes. Method of evaluation of the rhythm function of arterial oscillograms and statistical methods for estimating the probabilistic characteristics of arterial oscillograms was developed. Total and instantaneous spectral power of the signal was applied to estimate the total and instantaneous reaction of the body for the shoulder cuff compression. The authors also developed an Expert System (based on the clustering problem using the k -means and k -means++ algorithm and machine-learning methods) for the differential diagnosis of risks of heart, lung, mental illness and prognosis of some blood parameters.

The results of this research increase the informativeness of human health assessment in general, its reserve possibilities, data from 4 levels of regulation of CVS activity (peripheral-autonomous, autonomic, hypothalamic-pituitary, central nervous system), and the probability of right disease classification. The research results help to improve the effectiveness of a patient diagnostic, therapeutic, and rehabilitative trajectory.

Based on the methods and algorithms developed as a result of the authors work, Oranta-AO information system was designed and developed allowing the user to take measurements with an electronic blood pressure monitor, load them into the system, get calculated indicators, view them in a convenient way and see analytical information which is the basis for one to assess the state of the cardiovascular system and decide on further action.

Oranta-AO information system consists of three interrelated parts: mobile application, computing kernel and web system. Computing kernel and web system are deployed on AWS servers and are being tested now. Versions in Ukrainian and English are available.

The software developed will significantly expand the scope of electronic pressure monitors. The developed environment aims to be integrated into every new model of electronic meters in the world. Certification (EN 62304:2014, ISO 13485: 2018) in Ukraine is completed, PCT priority is completed. The next step will be to establish cooperation with manufacturers of electronic pressure monitors, patenting and certification in the world.

The activities of Oranta-AO information system provides the ability to integrate into patient monitoring systems and other information systems as well.

No approaches similar to the arterial oscillography was found. This conclusion is based on the analysis of publications in the world, visits to medical exhibitions in Ukraine, Austria and Germany, Dusseldorf, Medica 2016, 2018, 2020. Oranta-AO software is designed to supplement the informativeness of the dynamic adaptive properties of blood vessels in Doppler, rheographic, pulse examination and heart electrocardiographic examination.

Acknowledgements The work was performed with the support of the National Research Foundation of Ukraine (2021.01/0136 “Development of cloud platform for patient-centric telerehabilitation of cancer patients based on mathematical modeling”).

Data availability statement Arterial oscillograms obtained during blood pressure measurement (2000 AOGs for healthy people, 463 AOGs for people with cardiovascular disease, 204 AOGs for people with pulmonary disease, 294 AOGs for people with mental disease) were used for the conducted research. For each AOG 1030 indicators were calculated in the Oranta-AO research environment, which were grouped in MS Excel. Data is available only to the collaborating scientists from the respective Oranta-AO participating centers. The data may be available upon request for some of the participating centers but not for all due to relevant data protection laws.

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