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COMPLEX SYSTEMS BIOPHYSICS

Electrocardiographic Image of Myocardial Ischemia: Real Measurements and Biophysical Models

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Abstract—The peculiarities of the genesis of electrocardiosignal under myocardial ischemia in connection with an increase of its electrical inhomogeneity, as well as the electrophysiological mechanisms of morphological changes of the T wave of the electrocardiogram, including its "symmetrization" have been considered. A systemic approach to the problem has been used, which combines the mathematical, computer, and physiological modeling of the cardiac electrical activity with studies of the electric field of the human heart in terms of biophysical models. A database for the repolarization parameters of experimental electrocardiosignals ("Norm" and "Ischemia" samples) has been formed. The parameters of the ST–T interval and T wave, which could characterize the symmetry of the latter, and some additional properties of the repolarization process have been obtained. The methods of mathematical modeling were used also. Computer experiments were carried out on a system for 3D modeling of the cardiac electrical activity at different structural levels of the object. By the results of preliminary analysis, the β_T index, which is calculated as the ratio of two maximum absolute values of the derivative of the cardiosignal at the left and right of the T wave apex, has been chosen as one of the main diagnostic markers of ischemia. There is reason to believe that the use of the β_T index allows one to recognize those deviations from the norm that are usually hidden from a physician in traditional ECG analysis. The ratios of repolarization intervals inside of the generalized QT interval have also appeared potentially informative. With the purpose to test and correct the hypotheses for conducting further investigations, some preliminary experiments on a low-resolution model for several alternatives of the degree, localization, and extensiveness of ischemia have been carried out. The results obtained at the first stage of the team-work are essential to the understanding of mechanisms of the genesis of an electrocardiographic image for myocardial ischemia and of interest for the biophysically sound development of new algorithms for computer cardiodiagnostics.

Keywords: myocardial ischemia, electrical inhomogeneity, repolarization, transmembrane action potential, electrocardiogram, shape of the T wave, mathematical and computer modeling

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INTRODUCTION

The mechanisms of emergence, the diagnosis and prognosis of the development of cardiac pathologies are constantly in the focus of attention of modern medical science. One of the leading places among the biomedical problems of the present is occupied by coronary heart disease (CHD). A most important risk factor of sudden death of CHD patients is myocardial ischemia, i.e. a state of relative deficit of oxygen supply with blood as related to the global or local demands of the heart [1]. The consequences of ischemia are, in particular, development in the myocardium of anomalous electrical activity, which may lead to emergence of arrhythmias, and gradual damage of the structure of cells up to an irreversible phase of their death, i.e. myocardial infarction [2].

The main noninvasive method of recognition and study of many heart pathologies, among them ischemia and ventricular arrhythmia as its consequence, is electrocardiography in the broad interpretation of this method, i.e. study of the patterns of the distribution of cardiopotentials on the surface of the trunk and changes of their parameters in time. The

Abbreviations: CHD, coronary heart disease; ECG, electrocardiogram; ECS, electrocardiosignal(s); TAP, transmembrane action potential; MC, Minnesota Code; LVH, left ventricle hypertrophy.

Editor's Note: I certify that this is the closest possible equivalent of the original publication in all aspects, including concision and lucidity. *A.G.*

electrophysiological state of the heart is characterized therewith by numerous physicophysiological factors, which condition the emergence in the heart muscle of electric currents as a basis of its functioning and as a source of diagnostic information.

At the same time the routine electrocardiography, used in all places in its narrower existing stereotype, i.e. registration of 12 standard and/or three orthogonal leads of an electrocardiogram (ECG) with subsequent interpretation thereof in terms of physician's logic, while remaining the most widespread, available and cheap method of examination of the heart, does not possess for many problems of contemporary electrocardiology sufficiently high indices of sensitivity and specificity. Thus for example, it has been convincingly shown that the ECG at rest evaluated by generally accepted criteria remains normal approximately in 50% of patients with chronic CHD, among these even during episodes of discomfort in the chest [3].

An important task therefore is development of modern computer technologies that allow revealing pathological alterations at early stages of ischemia, when standard ECG methods are uninformative.

The social side of the problem, connected with the epidemiological (in its mass) character of CHD and the necessity of regular examinations, requires employment of new computer technologies, development of algorithms of automatic evaluation of the state of the heart by measurements of its physical fields, and also creation of specialized databases of electrocardiosignals (ECS) [4]. Let us note also that the term ECS can be regarded as an analog of the term ECG, although it has a broader interpretation.

Investigations of the basic and applied aspects of the biophysics and physiology of the electrical activity of the heart in myocardial ischemia receive much attention. Along with traditional physician's algorithms of verbal description of the shape of the ST–T interval of ECG, there appear modern computer technologies of registration and analysis of ECS, which permit increasing the worth of ECG examination. In the most recent time in experimental cardiology intensive studies are made of the electrophysiological mechanisms of morphological changes of the T wave of ECG, in particular its "symmetrization" in various pathologies including ischemia [5]. The diagnostic significance of the T wave symmetry and rate of change of the signal in the period of repolarization for recognition of myocardial ischemia was demonstrated by E.Sh. Khalfen with coauthors as far back as the 80s of the last century [6, 7].

The used methods of description of the T wave shape have a common pathophysiological basis and are directed in principle toward estimation by various means of the electrical homogeneity of the myocardium. This homogeneity (or inhomogeneity) is determined by a series of physical and physiological factors and manifests itself in that in the myocardium there exists some distribution of transmembrane action potentials (TAPs) generated in amplitude and duration [8]. It is customary to think that the more nonuniform the myocardium in the indicated sense, the greater the probability of emergence in the given patient of a grave cardiovascular "event" [9].

For this reason a topical problem of heart biophysics is elucidation of the regularities of the passing in the heart ventricles of repolarization processes, including mechanisms of attenuation of their stability in ischemia and mechanisms of alteration of some initial, characteristic of the norm, level of inhomogeneity of repolarization upon a change of the conditions of the normal work of the heart.

Many sides of this problem do not yet have a unified interpretation. The matter is that the majority of conclusions about the character of heterogeneity of repolarization processes in heart ventricles are made at the present time, in the main, on the basis of works on the study of ECS on the body surface, when analysis is conducted in terms of the so-called "indices of inhomogeneity of repolarization processes"—dispersions of the distribution over ECG leads of the durations of QT intervals and their constituent intervals QTa and TpTe—the prognostic significance of which, the mechanism of genesis and even the possibility of existence raise discussion ([10–12] etc.). To add, parameters characterizing cell repolarization at various stages of ischemia may strongly vary; in a series of investigations mentioned in [2], they observed both elongation and shortening of the repolarization process.

The heart as a complex biological object having an hierarchical structural-functional organization calls in the given case for a complex approach to the study of the relationship of the processes of de- and repolarization, which would combine measurements of the electrical activity of ventricles at least on the surface of the epicardium and on the surface of the trunk. This, in its turn, requires employment of the modern technique of an electrophysiological experiment and methods of mathematical description of the measured parameters, and also further development of the models of the electrical activity of the heart.

Prospective methods of investigations in the given field of knowledge are therefore the methods of mathematical and computer modeling [13, 14]. It should be noted, however, that there exists a noticeable gap between the models of the electrical activity of the heart on a high level of structural resolution of the object and the empirical, in most cases, models that are used to explain the connection of electrophysiological phenomena in the heart at the visceral level with the observed changes of ECS [14]. This pertains also to the problems of studying the mechanism of the genesis of pathological ECS patterns in myocardial ischemia in connection with an increase of its electrical inhomogeneity and, as a consequence, its instability.

Taking into account the contradictoriness of a number of experimental data, such a situation complicates the development of new algorithms of diagnostics of ischemia at its early stages, and also methods of quantitative description of some manifestations on ECS of disturbances in the processes of activation and repolarization of the heart muscle in terms of a unified model.

Analysis of the work on investigation of the mechanisms of pathological alterations of ECG parameters prompts one to think that practically the only possibility of studying in a problem-oriented way the hypotheses about the connection of parameters of the heart with the parameters of myocardial depolarization and repolarizationè measured on ECS is presented by the use of adequate biophysical models of ECS genesis in the framework of specially designed scenario hypotheses of the development of ischemia. In evaluation of the results of modeling one should apply, as far as it is possible, the methods of search for analogs on the material of verified samples of ECS of real patients. Necessary, in our opinion, is a systemic approach to the problem, combining mathematical, computer, and physiological modeling of the electrical activity of the heart with investigations of the electric field of the human heart in laboratory conditions and in clinic on the basis of adequate models of the studied phenomenon. Also required is refinement of the models of myocardial ischemia in terms of the dynamics of distribution in the ventricles of various forms of TAPs generated in the course of propagation of the excitation wave.

The most interesting, electrophysiologically substantiated and prospective, as it appears to us, is analysis of the morphology of the T wave of ECG in terms of various models—from simple indices of symmetry of the ascending and descending parts of the T wave to decomposition of ECS in eigenvalues at singular points with analysis of principal components and computation of the "coefficients of complexity" of the T wave [15]. A certain reserve of raising the diagnostic information value of the observed repolarization patterns may be associated also with development of models of mathematical description of the ST segment and the T wave by some approximating functions.

Speaking of reserves, it should be taken into account that apart of the electrical component the electromagnetic field of the heart has also a magnetic constituent, the behavior of which in time is registered in a contactless way in the form of a magnetocardiogram (MCG) intensely studied by many scientific groups. In the presence of relative advantages and shortcomings, ECG and MCG methods, which possess fundamental distinctions, must in principle allow obtaining in a systemic approach the mutually complementary diagnostic information about the electrophysiological state of the heart [16–18].

The given cooperative investigation is conducted in the framework of the Agreement on Scientific Collaboration between the Institute of Theoretical and Experimental Biophysics (ITEB), RAS and the International Research & Training Center for Information Technologies and Systems (IRTC ITaS), National Academy of Sciences of Ukraine for the years 2010–2012. The goal of collaboration is to obtain experimental and model comparative estimates of various parameters of the repolarization part of the cardiocycle that are connected, supposedly, with ischemia of the myocardium and increase of its electrical inhomogeneity, and also to study the electrophysiological mechanisms of morphological changes in the T wave of ECG in terms of biophysical models. In this paper (the first in the series planned on the given problem) we present the results of calculation and analysis of the parameters of description of the repolarization part of the cardiocycle for two databases of real ECS verified by different means; we consider also some methodological questions of modeling and show the results of benchmark tests on a small-resolution model.

DATA AND METHODS

The material for work was served by databases of real ECS, on the basis of which we obtained verified samples of ECG in standard and/or orthogonal lead systems for various groups of patients (more than 500 people each from IRTC ITaS and ITEB databases), including healthy individuals and persons with CHD, arterial hypertension and left ventricle hypertrophy (LVH).

Registration and analysis of ECS, including calculation of special parameters of the repolarization part of the cardiocycle, were conducted both on standard equipment (12-channel electrocardiographs, Schiller and IDK EKG 12-1.1 from firm Geolink) as well as with the aid of the Fazagraf device [9] developed in IRTC ITaS and the Uran system [10] created earlier in ITEB and exploited in the department of mass surveys of the State SRCenter for Preventive Medicine of Rosmedtechnologies.

For verification of the results obtained on the IRTC ITaS sample, a coronary-angiographic examination was conducted on all patients with the object to reveal stenosis. The degree of stenosis in the main coronary arteries was evaluated by two experienced experts independently of each other.

Formation of the ECS samples "Norm" and "Ischemia" from the Uran system database, where verifying was performed only by the ECG method of revealing LVH and ECG classification was conducted in terms of the Minnesota Code (MC), was actualized for the given investigation in the following way (for each patient we analyzed four or five cardiocycles): (1) group "Norm" (N) was constituted by patients for whom in all available cardiocycles in accordance with MC we obtained only code "1–0" (207 patients); (2) group "Ischemia" (MC4_5) was entered by patients who at least in one cardiocycle had MC code "4" (ST depression) and/or MC code "5" (T wave inversion) of lateral (L) localization (148 patients), at that we used for analysis the cardiocycles with only these codes, while in the remaining cardiocycles there must have been no other MC except "1–0" (norm); (3) a special group "Quasinorm" ($\tilde{N}$) was entered by patients from the group of lateral ischemia, but for analysis we used only those cardiocycles which did not have codes of ischemia, showing only code "1–0" (cardiocycles of 86 patients). In this way we imitated cases when a doctor (in our case, MC) "does not see" ischemia on ECG, while it possibly does exist, i.e. there may take place an error of first order (or "target miss"), at which the results of recognition would be false negative.

Earlier, with an aim to study the dynamics of ECG parameters in the phase space of ECS in the process of development of myocardial ischemia we have conducted experiments on laboratory animals (dogs) with the use of catheterization of coronary arteries and heart cavity without opening the chest with preservation of natural respiration [9]. Myocardial ischemia of duration up to 90 min was modeled by way of introducing into one of the branches of the left coronary artery a plastic embolus (ball) 2.0–2.5 mm in diameter.

Use was also made of the methods of mathematical modeling. Computer experiments have been performed on a system of 3D modeling of the electrical activity of the heart that is being created in ITEB RAS [14]. The foundation of the system is the earlier proposed and modified biophysical model of ECS genesis. Model parameters: electrophysiological, anatomical and biophysical characteristics of the heart. The methodological peculiarity of the system: work with modeled heart as with a real object, including processing of model cardiograms with the aid of the program package Uran_Model' by the algorithms that are used for real ECS in the Uran system.

In the work with real and model signals we determined the amplitude and temporal parameters of the chosen cardiocycle, and also the value of dispersion of the duration of the QT interval and its constituents; on the basis of synchronous measurements of all ECS leads we calculated the "generalized" durations of de- and repolarization intervals (the concept of generalized intervals see in [10, 19]).

Processing of ECS in a phase space of coordinates was conducted in accord with the original method developed in IRTC ITaS [9]. The gist of the method consists in that in every time point of the initial signal $u(t)$, which itself represents an ECG recording in the chosen lead, its derivative $du(t)/dt$ is determined, and all the subsequent processing and analysis of the signal are actualized on the phase plane in coordinates (u, du/dt). This method permits simultaneously estimating both amplitude and velocity parameters of ECG on any parts of the cardiocycle. For every cardiocycle, and also as a mean over cardiocycles, in all groups we calculated the maximal values of the derivative modulus, D_2 and D_1, at the left and at the right of the extremum of T wave amplitude at its apex. By the results of preliminary investigations in the capacity of the main diagnostic trait of ischemia we chose the index β_T, which is calculated as $\beta_T = D_2/D_1$.

RESULTS AND DISCUSSION

On the material of real ECS (IRTC ITaS database) it is shown that the mean values of parameter β_T differ substantially for CHD patients and for healthy subjects of the control group (respectively 0.963 ± 0.17 and 0.665 ± 0.12; $p < 0.001$). Examples of ECG cardiocycles and their phase portraits for CHD and "Norm" are shown, respectively, in Fig. 1a,b. We propose a decision rule in the form of implication: (if $\beta_T \geq \beta_0$, then "Ischemia"). The choice with the aid of a ROC curve (receiver operating characteristic) of an optimal value $\beta_0 = 0.72$ provides the given algorithm with 81% sensitivity and 78% specificity, which appears to be a high index of "usefulness" of the test [15]. For patients of different groups we obtained the following estimates of the mean values of parameter β_T: chronic CHD patients, 0.963 ± 0.47; control, 0.665 ± 0.12; acute coronary syndrome patients, 1.11 ± 0.49; myocardial infarction patients (nitroglycerin test), 0.98 ± 0.09; hypertension, 0.86 ± 0.15.

On the Uran system sample we obtained the following, averaged over cardiocycles, values of parameter β_T for groups: "Norm", 0.70 ± 0.14; "Codes MC4_5 (lateral localization)", 0.91 ± 0.28; "Code MC 5 (lateral localization)", 0.91 ± 0.29; "Quasinorm", 0.84 ± 0.2.

We calculated also other parameters of the T wave that could have characterized its symmetry and/or some additional properties of reflection in ECS of the repolarization process. Table 1 along with β_T presents the cardiocycles-averaged values of the investigated parameters for patients of the four mentioned groups, where the following designations are used: $V_{av}L/V_{av}R$, ratio of mean velocities of signal left and right of Twave peak; $t(am)L/t(am)R$, ratio of time intervals between T wave peak and points were derivatives at the left (L) and at the right (R) are maximal; JTa/JT, JTa/QT, $TpTe$ and $TpTe/JTa$, values and/or ratios of the corresponding cardiocycle intervals (J, "junction" point, i.e. generalized time of the end of the QRS complex; Ta, time of T wave reaching its maximum in lead I); SL/SR, ratio of left and right (relative to

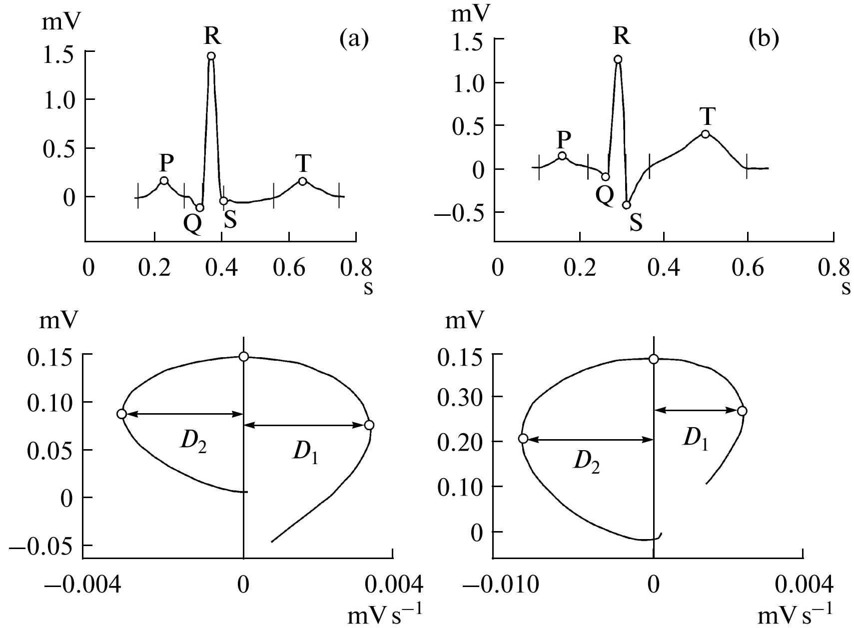

Fig. 1. Examples of ECG cardiocycles (upper panel) and their phase portraits for cases "CHD" (a) and "Norm" (b).

Twave apex) parts of T wave area; $Symm_T$, index of axial mirror symmetry of the left and right sides of the T wave relative to a vertical axis passing through the wave apex. The $Symm_T$ value is calculated as the difference between *SL* and *SR* related to their sum (the simplest of the possible variants of integral quantitative description of axial symmetry; if $Symm_T = 0$, then the wave is fully symmetrical).

Checking of the hypothesis of equality of the mean values of parameters from Table 1 in pairwise comparison of all groups of patients (N-MC4_5; N-Ñ; N-MC_5; MC4_5-N; MC4_5-MC4; Ñ-MC5) in accordance with the Student's *t*-test has shown that the best results are provided by the use of parameter β_T: the probability of coincidence of the mean β_T values of group "Norm" with means of groups "Ischemia" and "Quasinorm" $p < 0.0001$. Reliably distinguished are also the mean values of β_T for pairs of groups MC4_5-N and Ñ-MC5. Not distinguished by β_T are only groups MC4_5 and MC4 ($p = 0.7$), which is quite

Table 1. The values of parameters of the ST–T interval averaged over cardiocycles ($M \pm s$) for patients of four groups of the Uran system

Parameter	Groups			
	Norm	MC_5(L)	MC4_5(L)	Ñ
β_T	0.70 ± 0.14	0.91 ± 0.29	0.91 ± 0.28	0.84 ± 0.2
$V_{av}L/V_{av}R$	0.82 ± 0.16	0.64 ± 0.34	0.66 ± 0.32	0.73 ± 0.32
$t(am)L/t(am)R$	1.23 ± 1.3	1.7 ± 1.2	1.57 ± 1.1	1.30 ± 0.72
JTa/JT	0.68 ± 0.03	0.76 ± 0.06	0.72 ± 0.05	0.74 ± 0.05
JTa/QT	0.49 ± 0.03	0.59 ± 0.06	0.53 ± 0.052	0.58 ± 0.05
TpTe (ms)	87 ± 9	80 ± 20	81 ± 18	83 ± 18
$TpTe/JTa$	0.46 ± 0.07	0.38 ± 0.13	0.38 ± 0.12	0.41 ± 0.13
SL/SR	1.38 ± 0.21	1.7 ± 2.0	1.61 ± 1.75	1.33 ± 0.36
$Symm_T$	0.15 ± 0.07	0.16 ± 0.17	0.15 ± 0.16	0.12 ± 0.14

explainable, because in both groups account is taken of the same patients with displacement of the ST segment.

Practically the same *p* values as for β_T upon pairwise group comparison are given also by the ratios of the durations of time intervals within the QT intervals (*JTa*/*JT* and *JTa*/*QT* in lead I). At the same time the index of axial symmetry for two sides of the T wave, $Symm_T$, has shown the worst results—the mean values of this parameter statistically do not differ for patients of all groups, which turned out to be somewhat unexpected. Analysis of the procedure of calculating parameter $Symm_T$ for several patients of the sample in automatic and manual modes has shown that in connection with the importance of principle of the question of a quantitative connection of the degree of ischemia with the T wave morphology it is necessary to conduct a special investigation for checking the adequacy and stability of the used algorithms of automatic calculation of the $Symm_T$ value in conditions of practical measurements, and also for testing the hypotheses regarding the degree of diagnostic value of this parameter or its modifications, which is planned to be executed at the second stage of the work.

In this way, comparison of the results of identification of the state of myocardial ischemia by excess of the threshold for β_T with the results of operation of MC algorithms and formalized physician's algorithms gives grounds for stating that the use of parameter β_T permits disclosing such deviations from the norm as are usually hidden from the physician upon traditional analysis of ECG in the time domain. The results of studying the peculiarities of the ECG alterations in the phase space in the process of development of myocardial ischemia in experiments on animals [9] also confirm the fact that the dynamics of the β_T index presents an early and trustworthy criterion of development of acute myocardial ischemia.

As regards parameters *JTa*/*QT* and *JTa*/*JT*, each of them was tested in an algorithm, analogous to the diagnostic rule for β_T (excess of some threshold), for recognition of ischemia in the group of patients {N, MC4_5(L)} and separately in group {N, MC5(L)} (N – 207 patients, presence of MC codes "L4 and/or L5" – 146 patients, presence of only code "L5" – 104 patients).

The comparative results of calculating the sensitivity *Sn* (%) of recognition of ischemia by a threshold algorithm with the use of each of the three supposedly most informative parameters (β_T, *JTa*/*QT*, *JTa*/*JT*) are brought together in Table 2. Sensitivity was calculated for specificity equal to 60%.

It is necessary, of course, to remember that for verification of the presence or absence of ischemia in patients in the given case use was made only of the MC.

Upon analysis of the ST interval in MC terms it can be noted that the vague descriptions of the ST segment

Table 2. Values of sensitivity, *Sn* (%), of a threshold algorithm of recognition of ischemia in groups {N, MC4_5(L)} and {N, MC5(L)} in three most informative parameters at a specificity equal to 60%

Parameter/Groups	N – MC4_5	N – MC5
β_T	75.2	75
JTa/*JT*	75.3	88
JTa/*QT*	72	92

pattern used in medical practice like "depressed and upward sloping", "arcuate with downward convexity", "elevated and trough-shaped" and all that hamper observation of the quantitative dynamics of disturbances of the repolarization process [20, 21]. Therefore on the ECS sample from the Uran database we studied the possibility of approximating the ST segment with a parabolic curve $u(t) = at^2 + bt + c$ on the interval "generalized point 4 – generalized point 5" with the origin of coordinates in point *J*. The peculiarities of the process of formation of the ST–T interval were traced therwith on the basis of a model scheme of the contribution of the TAP set into ECS (see Fig. 1 in work [22]). In Fig. 2 as an example we present large-scale ECS for several characteristic ST patterns with the corresponding values of quadratic approximation

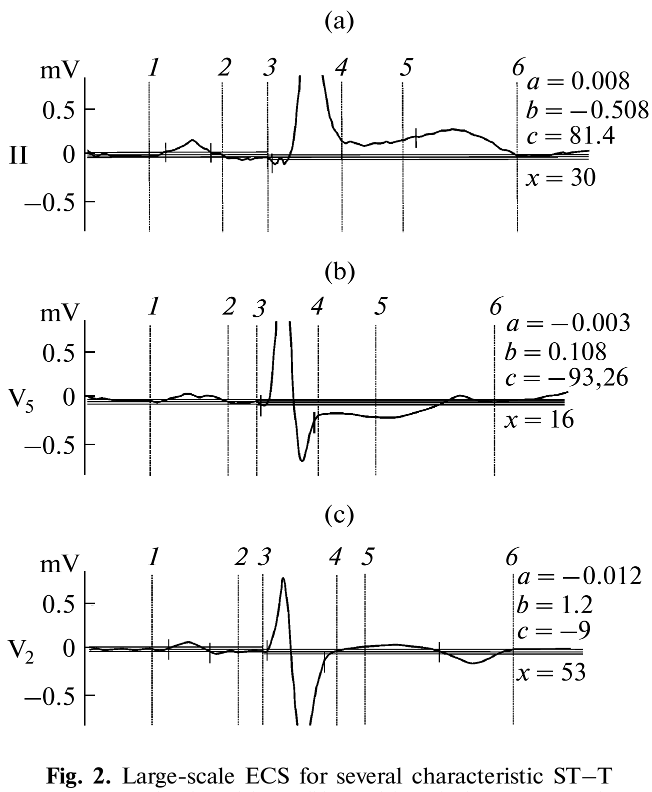

Fig. 2. Large-scale ECS for several characteristic ST–T patterns in leads II (a), V_5 (b), V_2 (c) with the corresponding values of parameters (*a*, *b*, *c*, *x*) of quadratic approximation of the ST segment.

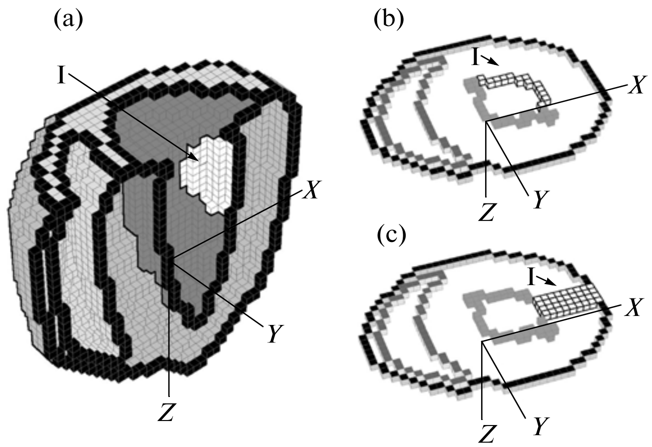

Fig. 3. General 3D view of ventricles for low-resolution model (a) with lateral ischemic focus (I) and examples of sections of the surface of electrically active myocardium in the horizontal plane for subendocardial (b) and transmural (c) ischemia.

parameters (a, b, c, x), where x is the abscissa of the parabola vertex. The proposed approximation practically always adequately (in terms of root mean square error) describes the shape of the ST interval and can be put into the basis of refining physician's statements on the shape of ST and building algorithms of quantitative description of ST patterns (displacement of the J point, slope of ST and its shape).

Modeling of ischemia in the space of model parameters. Ischemia causes complicated changes of the electrophysiological properties of cardiomyocytes, which proceed in several phases and include in themselves: (1) change of durations of action potentials; (2) redistribution of these durations on the surface of electrically active myocardium; (3) local reduction of the resting potential and emergence of currents of injury. In connection with the great scatter of opinions and hypotheses regarding the behavior of TAP parameters in development of ischemia (see, for example, [2, 23–26] and many other works), its modeling presents a complicated task, rather a problem, when methods and means necessary for solution are "brought up to" in the course of obtaining results at each of the consecutive stages of the work. An important aspect of solving the problem is development of the corresponding methodology.

Methodologically the center of gravity of theoretical investigations must lie in the field of computer experiment on studying the influence of myocardial heterogeneity (i.e. local distinctions of shape and duration of model TAPs) on the output characteristics of the model. The model states of the heart and the tested hypotheses must be defined and formulated in the model parameter space. The main aim of computer experiments is revealing the tendencies of change in the characteristics of model ECS upon changing the biophysical parameters of the heart with the aim of building adequate models of the studied phenomenon.

For conducting the next stage of the work—model investigations of the mechanisms of change of T wave shape in ischemia—we developed several versions of the first approximation for "scenarios" of the development of ischemia [27], and also the corresponding protocols of model experiments.

Taking into account the literature data and the results of own model investigations [10–12, 28], the considered hypotheses are formulated in terms of the dynamics of changes in the ischemic zone of such TAP parameters as duration and expressedness of the plateau phase, and also the shape of the terminal phase of fast repolarization. It should be said that as far back as 1983, while solving a 2D-model problem on the propagation of phases of the repolarization process in the ventricular wall with taking into account the field of temperatures in the myocardium, we observed changes of T wave shape and its symmetry, and also changes in the duration of QTa and JTa intervals upon a change in the transmural difference of TAP durations and the steepness of the second phase of fast repolarization on the epicardium relative to endocardium (see Fig. 1 in work [28]).

With the aim of testing hypotheses and their correction for conducting further investigations we fulfilled preliminary experiments on a low-resolution model sized 40^3 msu (msu, model space unit [22]) for several variants of the degree of ischemia, its localization and expanse, and also variants of the anatomical position of the heart. We obtained model ECS in orthogonal and standard lead systems for subendocardial and epicardial ischemia of the free wall of the left ventricle as compared with "conventional norm". Results have been analyzed with the aid of the Model'_Uran program, correction of the initial data has been performed.

As an illustration of the work with the small-resolution model Fig. 3 presents the general 3D view of modeled ventricles with a lateral (in development of ischemia, posterolateral) ischemic focus (a), the localization and dimensions of which can be varied, and also examples of separate sections of the surface of electrically active myocardium of the model (elements of "surf" type [22]) in the horizontal plane for subendocardial (b) and transmural (c) ischemia of the lateral wall. In Fig. 4 one can see one of the variants of the shapes of action potentials for endocardium (*1*) and epicardium (*2*) of the model, and also TAP for the region of ischemia (*3*), the shape and duration of which change in accordance with the protocol of the computer experiment.

Shown in Fig. 5a are the initial signals for leads X, Y, Z of the orthogonal system, which are identified by the Model'_Uran program as "Norm", and in Fig. 5b,

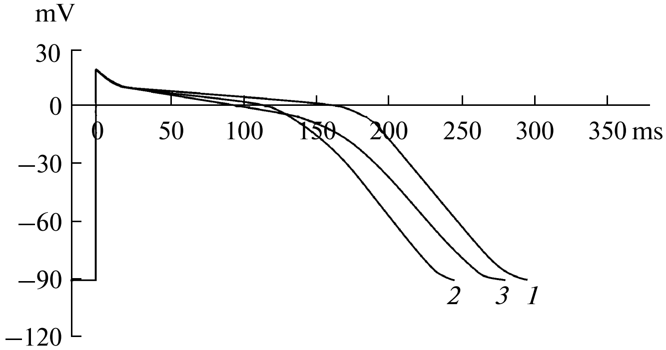

Fig. 4. One of the variants of the shapes of action potentials for endocardium (*1*) and epicardium (*2*) of the model, and also TAP for the region of ischemia (*3*), the shape and duration of which change in accordance with the protocol of the computer experiment.

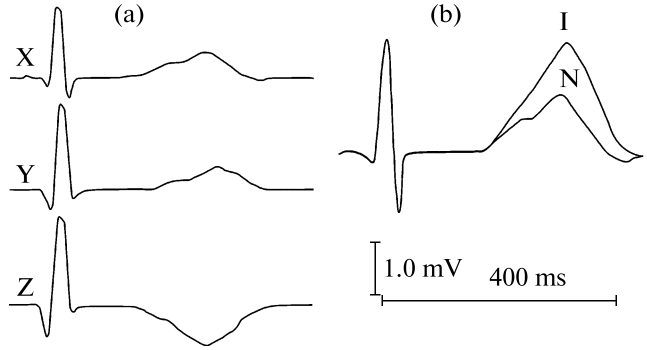

Fig. 5. Initial conventionally normal signals of the orthogonal lead X, Y, Z system (a) and ischemic changes of the T wave as compared with the norm in one of the leads of the standard system ((b) curves I and N respectively).

ischemic alterations of the T wave as compared with the norm in one of the leads of a standard system (respectively, curves I and N).

In Fig. 6a we see "petty," i.e. low-amplitude changes of ECS on the ascending and descending slopes of the T wave in lead V_2 for one of the simplified versions of the "scenario" of the development of ischemia. The area of ischemia, S_I, constituted 0 (initial norm) 40, 87, 173, 235 elements with linear dimension msu ≈ 2 mm (respectively, curves *1–5* in the figure) at a fixed duration of ischemic TAP, as in Fig. 4. The peak value of the T wave therewith slowly and nonlinearly grew to its maximum (at $S_I = 235$ elements), and then declined in accordance with a complicated mechanism of the sum influence of the curvature of ischemized surface, direction of the external normals of its elements relative to the point of "measurement" of ECS and shape of the fast repolarization phase. Changes in the signal in the vicinity of the T wave apex are shown at a larger scale in Fig. 6b. The MC did not react to these changes; for all curves except one MC yielded value "1–0". Whereas the curve with the smallest T wave amplitude, standing "by itself" on this figure (curve *6*), where MC showed code "4_5 (change of T wave and/or ST segment)", pertains to a hypothetical case of ischemia of the entire endocardial surface of the left ventricle, when the T wave amplitude, having had passed its maximum, has reached upon further increase of S_I its minimal magnitude. At the same time parameter β_T, staying within the limits of the norm for small areas of ischemia (values of β_T from 0.612 to 0.625), had a tendency to its augmentation upon growth of the ischemic "spot" and reached a magnitude of 1.08 at "general subendocardial ischemia."

For investigation of the mechanisms of complex changes in T wave morphology in the model there is a possibility of separate representation and visualization of partial contributions into the signal of any lead from elements of myocardium with different types of TAP (which, according to [22], constitute a set $\{U_{j(i)}(t)\}$), and also, in another variant, from elements belonging to different regions of the surface of electrically active

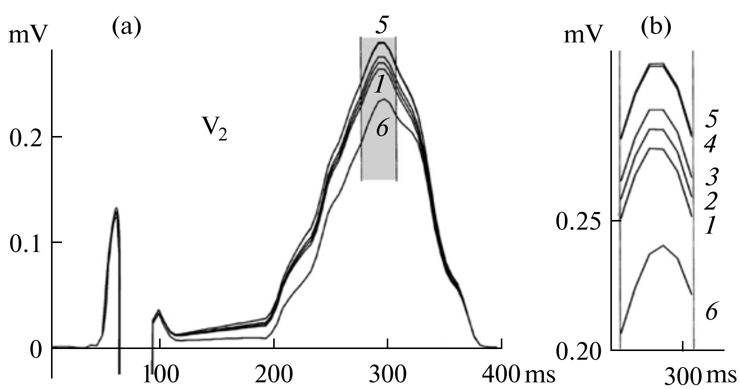

Fig. 6. Low-amplitude changes of ECS on the ascending and descending slopes of the T wave for one of the versions of modeling the development of ischemia. The curve with the smallest T wave amplitude pertains to a hypothetical case of ischemia of the entire endocardial surface of the left ventricle.

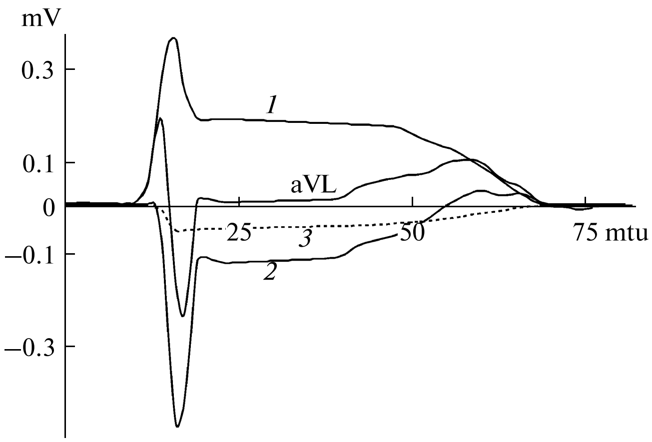

Fig. 7. Model signal in lead aVL and its components: contributions into ECG from endocardium (*1*), epicardium (*2*) and from the ischemic region (*3*); the area of the ischemized region of surface Surf, S_I, constitutes 173 elements.

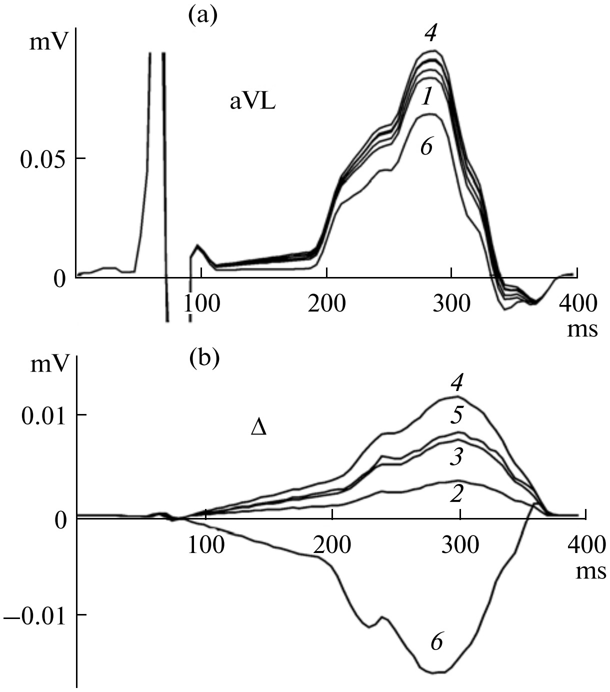

Fig. 8. Change in T wave shape depending on the expanse (S_I) of the subendocardial ischemic focus (a, curves *1–6*) and difference signals Δ for each of the dimensions of the "spot" in relation to the conventional norm (b).

myocardium. Figure 7, for example, demonstrates ECS in lead aVL and its components for the case S_I = 173 elements (i.e. about 6.8 cm^2): shown are contributions into ECG from endocardium (*1*), epicardium (*2*) and from the ischemic region (*3*); graduations on the time axis are given in units of mtu (model time unit), for the small-resolution model 1 mtu ≈ 5 ms.

In Fig. 8 we show the shapes of T wave in lead aVL upon changes of the expanse of the ischemic focus (a), similar to those presented in Fig. 6 (curve numbers correspond to the same S_I values), and present the difference signals, Δ, for each of the dimensions of the "spot" in relation to the conventional norm (b). One can see that upon transition to another lead the change of positional factors leads to that the maximum of the T wave amplitude is reached at another S_I value.

CONCLUSIONS

The developed model has turned out to be a convenient tool for investigation of the dependence of the measured and calculated parameters of the electric field of the heart on the change of the electrophysiological characteristics of the myocardium. The results obtained at the first stage of joint work are important for understanding the mechanisms of formation of an electrocardiographic image of ischemia and are of interest for biophysically substantiated development of new algorithms of computer cardiodiagnostics.

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