Investigation of the Possibility to Detect Ventricular Late Potentials by a High-Resolution Electrocardiographic Hardware-Software Complex based on Nanosensors using Simson’s Method

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Abstract

According to the World Health Organization (WHO), cardiovascular diseases (CVD) are the leading cause for death worldwide. Over the past 20 years, the effectiveness of sudden cardiac death (SCD) prevention has not virtually changed, so the development of new methods to identify the groups at risk of SCDs is of crucial importance. One of the promising directions to improve the method of electrocardiographic diagnostics of SCD signs is the development of tools that can measure the low-amplitude components of electrocardiogram (ECG), the so-called micropotentials (MPs) of the heart. High-resolution hardware-software complex (HSC) based on nanosensors has been developed to record MPs of the heart in real time without filtering and averaging. The software component provides estimation of ECG low-amplitude components in order to detect early signs of SCD. The application of low-noise high-stability nonpolarizable noise-immune nanosensors enables the elimination of filters from the hardware. HSC is based on the algorithm of ventricular late potential (VLP) detection according to Simson’s method both in the averaged signal (within 30 s) and single cardiac impulses. The article presents the results of high-resolution ECG processing according to Simson’s method for a healthy person and for a patient who had undergone two heart attacks and heart failure. This high-resolution apparatus based on nanosensors will serve a high potential role in the ECG diagnostic rooms of the primary healthcare for the majority of patients.

Keywords

Hardware-software complex; Nanosensor; Ventricular late potentials (VLPs); High resolution; Micropotential; Real time; Sudden cardiac death (SCD)

Introduction

According to the World Health Organization (WHO), cardiovascular diseases (CVD) are the leading cause of death worldwide: more people die annually from CVDs than from any other disease. As reported by WHO [1], in 2012, 17.5 million people died from CVDs, representing 31% of all the global deaths. Of these, 7.4 million deaths were due to coronary heart disease and 6.7 million deaths were due to stroke. Over 75% of CVD deaths occur in low- and middle-income countries.

Mortality from CVD in Russia is one of the highest in the world and amounts to 1,462 per 100,000 inhabitants per year [2-4]. The main causes of death from CVD are the progression of chronic heart failure (which accounts for about half the number of all deaths) and SCD (which is the reason for the other half). According to the calculated data, in Russia, 200,000-250,000 people die from SCD each year [2,4]. Since SCDs tend to increase in number [4,5-10], they are highly relevant to the national healthcare.

The analysis of literature shows that the figures obtained almost 20 years ago are valid till today. They show, on the one hand, that the effectiveness of SCD prevention methods over this time has changed insufficiently, and, on the other hand, search for new criteria that would identify high-risk groups in the general population is of the utmost importance [2-11].

Over the past 15 years, the mortality rate from CVD has not virtually changed [2-11]. The development of new methods to identify groups at risk of SCDs is of crucial importance.

Methods

Any disease can most easily be cured at its early stage. We need special tools for the early detection of diseases.

All this marked the modern advances in electrocardiography—high-resolution ECG (HR ECG), ECG-mapping, tele-ECG and others. The accuracy of the diagnosis depends on the quality and quantity of the initial data. Improving these parameters is the challenge of the modern electrocardiography.

Modern methods most commonly benefit from the amount of information obtained, that is, the number of experiments and their various combination in complex processing.

The quality of the information is determined mainly by the signal-to-noise ratio, and it can be improved through better hardware and primary medical electrodes. Earlier, the use of chlorine-silver electrodes was a good solution, but they no longer meet the increasing requirements.

To address the problem, research has been underway toward the development of high-resolution electrocardiographic apparatus in the
laboratory of Medical Instrument at the Institute of Non-Destructive Testing, Tomsk Polytechnic University. The use of nanoscale silver particles in the electrode design allowed considerable improvement of metrological characteristics and creation of nanosensors with noise immunity and low level of self-noise [12]. The resolution of the apparatus based on nanosensors is in the range of several hundreds of nanovolts.

The practically available (100-200) nanovolt signal resolution provides a significant increase in the diagnostic value of the electrocardiography.

A particularly important goal is to develop software to allow implementation of a high technical potential and the advantages of the hardware to create a unified hardware-software complex.

The primary focus is on the detection of early heart abnormalities of the patient under dynamic life-time monitoring of the cardiovascular system. Diagnosis with regard to the heart rhythm frequency is insufficient only for early diagnosis. It is necessary to measure low-amplitude EGG waves, small early S-T segment shifts, to develop new technologies to measure weak signals in any investigated frequency range and to measure constant potentials of the heart. Measurement of micropotentials (MPs) in electrocardiosignal (ECS) and its statistical processing will improve the diagnostic accuracy of heart condition.

Electrocardiographs currently used in general practice have a coarse scale; the sensitivity of the majority of electrocardiographs with data acquisition on thermal recording paper is 10 mm/1 mV and 20 mm/1 mV. This coarse measurement scale does not detect the early changes in heart functioning which are small shifts of microvolt and nanovolt ECS in a broad frequency range. However, it is this type of the electrocardiograph with ECS recordings on thermal paper that has become the most widely used in primary care, that is, in outpatient clinics and polyclinics where the patient flow is most intense.

This situation can be changed through the creation of a next-generation high-performance computerized apparatus of high resolution based on nanosensors with a microvolt and nanovolt scale with data transmission via telecommunication channels and data storage in an automated database with the price affordable for health facilities and common people.

According to [13-15], there is a relationship between MPs of ECS and life-threatening heart rhythm disorders. It is crucial to develop a hardware-software complex for the analysis of high-resolution MPs that will improve the quality of diagnosis in the early stages of heart diseases, allow prediction of the disease dynamics and provide treatment monitoring [16].

MPs are classified according to the place and time of their occurrence as follows: specialized conduction system, ventricles of heart or potentials of different phases of the cardiac cycle [9,14,17,18].

Best-known ECS MPs are VLPs of heart which are high-frequency (25-250) Hz oscillations with a duration of several tens of milliseconds that occur immediately after the end of the QRS complex: in the ST-segment interval and at the beginning of the T-wave. The occurrence of these ECG signs may be the marker of susceptibility for the development of life-threatening cardiac arrhythmias, particularly in patients with myocardial ischemia or myocardial infarction. When identifying SCD electrophysiological markers, the most difficult problem is practical detection and clinical interpretation of ECS MPs for an individual patient [19,20].

When recording standard electrocardiogram, the root mean square value of the additive noise reaches 20 [μV], while VLP values vary from 5 to 20 [μV] [14]. Therefore, it is necessary to develop a sufficiently precise tool to identify a probable pathological sign in ECS and to measure its parameters, namely, the low-amplitude components of ECG.

The analysis of publications addressing the existing methods of the heart micropotential analysis revealed a set of key methodological techniques for the analysis of ECG MPs: elimination of network disturbances, baseline drift, cardiac cycle recording and averaging, determination of spectral components, amplitude-time analysis and others [14,15].

When developing approaches for the identification of low-amplitude components, we should consider that ECG MPs may appear at different timepoints. Regular MPs [21] can be found in all the cardiac cycles with a constant time bias relative to the reference point, for example, R-wave. Irregular MPs [21] occur in a specific part of the cardiac cycle at random time relative to high-amplitude ECG components.

The most widely studied are VLPs. Their occurrence is caused by the elongation of the electrical impulse path due to differences in the speed and the level of the recovery of the electrical potential of cardiomyocyte membranes during ischemia, separation of cardiomyocytes by the connective tissue and disorientation of the muscle fiber [18]. By analogy with the VLPs, activation through the atria in patients with atrial fibrillation was found to decelerate. In patients with atrial fibrillation, MPs are recorded at the end of the P-wave, which are called atrial late potentials (ALP). VLPs and ALPs detected on ECS are the signs of SCD [22].

According to [17,23,24], the results of Holter monitoring or electrophysiologic testing with programmable stimulation revealed that in patients after myocardial infarction with no susceptibility to ventricular tachycardia, VLPs were either not detected or were observed in individual cases (2%), and in patients with susceptibility to ventricular tachycardia and a positive test, VLPs were found in (26-44)% of cases. Exercise ECG testing with a bicycle ergometer did not identify correlation between the occurrence of symptoms of myocardial ischemia and VLPs; however, the signs of VLPs grew in number during transient ischemia induced by transient coronary artery occlusion during balloon angioplasty.

The VLP detection method was proposed by Simson in 1981 [25]. The method implies frequency filtering of the averaged cardiac impulses in 3 Frank orthogonal leads and evaluation of the change of the vector module over time. However, this method of micropotential analysis on ECS has been criticized as it bears not much relation to the phenomenon of the presence of high-frequency components in the ECG, especially TQRSF—the duration of the filtered complex and conventions of the two-component decision rule in VLP diagnostics [14].

The current challenge in implementing the methods of ECS micropotential recording and evaluation of High-resolution ECG in clinical practice is low resolution of electrocardiographs used in medical practice [15,16]. High-resolution electrocardiographs operating via averaging 100-400 ECG complexes are used only in major cardiac centers and clinics. In these devices, the main technique to eliminate noise is the signal averaging method. The disadvantage of this method is loss of information which indicates the instability of the myocardium due to ECS parameter averaging and signal filtering.
Thus, the development of the hardware-software complex to record high-resolution ECG with low noise level which will record the maximum useful signal without filtering distortion is critically important [16]. This type of the electrocardiograph enables high-resolution recording of heart MPs in patients with specific myocardium pathology and provides screening to detect highly predictive signs of sudden cardiac arrhythmias and SCD development. To address these issues, further investigations in this direction are to be conducted. In this regard, a high-resolution electrocardiograph on nanosensors is considered to be promising. The analysis showed that at the present time there are no hardware-software complexes for mass use (in hospitals, clinics, ambulances, at home, in the ever-wearable devices) to perform noninvasive testing of the electrical activity of the heart in real time and to record MPs that lead to the development of life-threatening cardiac arrhythmias.

The development of such hardware-software complex and its practical testing in patients at high risk for SCD to detect informative prognostic signs seems a reliable means to verify the theoretical basis of the diagnostic algorithm development. Upon confirmation of the predictive value of the method, the physicians will have a new diagnostic tool for preclinical diagnosis of heart diseases, and consequently, the ability to conduct primary prevention of SCD. The field of the electrocardiograph application should be not only the cohort of cardiac patients in the hospital, but also ambulatory (outpatient) survey of population.

High-resolution hardware-software complex (HSC) based on nanosensors to record MPs of the heart in real time without filtering and averaging has been developed in Tomsk Polytechnic University.

HSC consists of hardware and software. The hardware provides recording of the low-amplitude ECG components without filtering. The software provides estimation of the low-amplitude ECG components in order to early detect the signs of SCD.

The hardware implementation is based on the metrological properties of nanosensors. The low-noise high-stability nonpolarizable noise-immune nanosensors enable the elimination of some standard hardware components, primarily filters. Figure 1 shows the hardware for detection changes in the electrocardiographic signal of nanovolt and microvolt levels.

Nanosensors (11−13) are placed on the patient’s chest. Electrocardiographic signals travel from nanosensors to the inverting and noninverting inputs of instrumentation amplifiers (2−2). The signals from the instrumentation amplifier output travel to the noninverting inputs of operational amplifiers (3−3). The signals from the operational amplifier outputs travel to the inputs of analog-digital converters (4−4) and then, after digitization, to the input of microcontroller 5, which measures the input signal. In case of a zero-frequency component, the microcontroller sends a signal to digital-to-analog converters (6−6) to eliminate a zero-frequency signal at the input by compensating voltage supply to the inverting inputs of operational amplifiers (3−3). Insulator 7 isolates the patient from computer 8. The signals travel to the computer input via USB.

Simson’s method is used to evaluate regular MPs [25]. The following computing operations are performed: ECG averaging and bidirectional filtering in the frequency range of 25-250 Hz. Temporary averaging of the sequential 200-500 cardiac cycles with a correlation coefficient of at least 98% is the most common approach. When a narrow-band filter with the lower cut-off frequency of 25 Hz is used, the noise level should be reduced up to 1 [µV]; when the filter lower cut-off frequency is 40 Hz, the noise level is to be less than 0.7 [µV].

The signal-averaged ECG of three Frank orthogonal leads X, Y, Z is used to obtain the informative curve according to Simson’s method.

Then, the averaged signal is filtered by a bandpass filter (25-250) Hz, and the total value of the vectors is determined:

$$ F(X, Y, Z) = \sqrt{X^2 + Y^2 + Z^2}. $$

Since the method was developed about 30 years ago, its application for a single cardiac impulse was impossible at that time because of the noise components. The equipment for recording a qualitative ECG signal with the noise level lower than that of MPs enables VLP investigation in a single cardiac cycle.

The presence or absence of VLP signs is confirmed through the resultant curve. For this purpose, the following quantitative indicators are analyzed:

1. The duration of the filtered QRS complex (TotQRSF);
2. The duration of the low-amplitude (less than 40 [µV]) signals at the end of the QRS complex (LAS40);
3. The root mean square value of the last 40 ms of the filtered QRS complex (RMS40).

Table 2 presents the parameters to detect the warning signs of VLPs.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Input voltage range during recording</td>
<td>from ± 0.3 [µV]</td>
</tr>
<tr>
<td>ECG</td>
<td>up to ± 10 mV</td>
</tr>
<tr>
<td>Relative divergence in the range of 0.3 [µV]/5.0 [µV]</td>
<td>± 15%</td>
</tr>
<tr>
<td>Relative divergence in the range of 50 [µV]/10000 [µV]</td>
<td>± 10%</td>
</tr>
<tr>
<td>Recording time</td>
<td>30 s</td>
</tr>
<tr>
<td>Frequency range</td>
<td>from 0 to 10000 Hz</td>
</tr>
<tr>
<td>Sensitivity of channels, [µV]/10 mm</td>
<td>0.1; 0.2; 0.5; 1; 5; 10; 15; 20; 30; 50; 70; 100; 150; 200; 300; 500; 700; 1000</td>
</tr>
<tr>
<td>Input impedance</td>
<td>no less than 10MOm</td>
</tr>
<tr>
<td>Common-mode rejection</td>
<td>no less than 120 dB</td>
</tr>
<tr>
<td>Relative error of ST-segment displacement measurement:</td>
<td></td>
</tr>
<tr>
<td>- in the range of 0.010-0.051 mV</td>
<td>no more than ± 30%</td>
</tr>
<tr>
<td>- in the range of 0.51-2.05 mV</td>
<td>no more than ± 10%</td>
</tr>
</tbody>
</table>

Table 1: Basic parameters of the developed HSC
The developed program "Simson's method" for a high-resolution HSC presented in Figure 1 is based on the algorithm of VLP investigation both in the averaged signal and single cardiac impulses. The averaging is implemented with the support points located on the R-wave. If the correlation coefficient is less than that of the specified in the program settings, the cardiac impulse is excluded from the averaged signal formation. Bidirectional filtering is performed in the positive direction from the beginning of the cardiac impulse to the R-wave center, and from the end of the cardiac impulse to the R-wave centre if filtering is performed in the opposite direction. To update time intervals, the support points can be defined manually or automatically on the resultant Simson's curve to calculate the parameters, which are then compared with the criteria to detect the presence or absence of VLPs.

The algorithm of the program is presented in Figure 2.

The methods used in the program “Simson’s method” are as follows:
- R-wave center averaging;
- Bidirectional bandpass filtering (25-250 Hz);
- Estimation of parameters according to the criteria to make a preliminary diagnosis.

The files with the recorded data on the patients’ ECGs are opened in the first tab using the download button, and then the data are displayed in the first graph in the form of 3 signals (3 leads) (Figure 3).

The program includes the elements to control the data display such as scaling or allocation of a specific lead. When the scale is chosen properly, ECG can be visually assessed or a cardiac impulse can be selected to verify the presence of VLPs using Simson’s method. The time interval can be selected manually, and the signal can also be processed automatically in the form of signal averaging. In addition, the correlation between cardiac impulses is assessed and a search for the cardiac impulse with minimal noise is performed. If the correlation coefficient is below normal, the cardiac impulse is excluded from processing since it considerably differs from other impulses.

When the signal averaging is successfully executed or the cardiac impulse is selected for the analysis, the fragment of the time interval is processed: bandpass filtering with a high-frequency filter used in positive and negative directions to eliminate ringing after the QRS complex, so the R-wave center is defined, bidirectional filtering is performed up to the center; Simson’s curve is calculated after filtration
An example is processing the ECG of patient P, 56 years old, diagnosed with a coronary heart disease, occasional posterior myocardial infarction (02.03.15), postinfarction cardiosclerosis after the initial myocardial infarction (31.12.14), coronary atherosclerosis with stenosis of the main arteries of the heart. The infrequent ventricular extrasystoles were recorded on a standard ECG of the patient.

Figures 5a-c show the electrocardiogram of patient P and its spectrum in each channel recorded by a high-resolution HSC based on nanosensors.

The MPs of units of microvolts to a few tens of microvolts, which are irregular signals changing from cycle to cycle both in level and duration, were recorded on the electrocardiogram of patient P in real time without filtering. The peak value of the equipment noise for a single impulse is 0.25 μV, and it is $\sqrt{L}$ times smaller, where $L$ is the number of averaged cardiac impulses, for the cardiac impulse averaged within 30 s, that is, 0.05 μV.

The developed program implementing Simson's method both in the cycle averaged within 30 s and single cardiac cycles of patient P was employed to detect the signs of SCD in patient P with respect to the late ventricular MPs. The results are presented in Figures 6 and 7.

Figures 6a, b show the results of the analysis in the averaged cycle. Figure 7 shows the results of single cardiac impulse processing.

The identified changes of the electrophysiological parameters of the heart of patient P with a high prognostic risk of life-threatening arrhythmias were confirmed by the ventricular fibrillation with circulatory arrest and clinical death (13.03.2015) followed by cardioversion and cardiopulmonary resuscitation.

The patient’s life was saved. The cardioverter defibrillator was implanted in the patient and a surgical myocardial revascularization was performed at the subsequent stages of treatment.
On the basis of the research conducted, the following conclusion can be drawn:

1. The developed hardware and software make it possible to detect VLPs according to Simon's method within 30 s both in the cardiac impulse and in single cardiac impulses.

2. This high-resolution apparatus based on nanosensors will serve a high potential role in the ECG diagnostic rooms of the primary healthcare for the majority of patients.

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