Research into spontaneous activity of myocardial cells under normal and pathological conditions using the hardware and software complex based on nanosensors

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Abstract. Cardiovascular diseases are the leading cause of death in the world. The paper focuses on the capability of a nanosensor-based hardware and software complex (HSC) developed at Tomsk Polytechnic University to measure the activity of myocardial cells from the surface of the human body. A comparative study of nanosensors used in the HSC and conventional AgCl electrodes by FIAB Spa (Florence, Italy) was carried out. It is shown that the value of electromagnetic interference in conventional electrodes is several times higher compared to nanosensors. ECG was recorded using the developed HSC in order to show the possibility to control the activity of myocardial cells.

1. Introduction

One of the most common pathologies encountered in medicine is the heart pathology leading to death. Out of the total deaths worldwide, diseases of cardiovascular system occupy leading positions [1]. World Health Organization statistics 2015 showed that 17,866,560 people died from diseases of the cardiovascular system. Among all the causes of death from cardiovascular diseases, the phenomenon of sudden cardiac death (SCD) is prevailing. SCD is an unexpected death due to cardiac causes. The phenomenon occurs within a short period of time and manifests itself in immediate and severe symptoms that hinder effective treatment and prophylaxis [2]. In this regard, the study of spontaneous activity of myocardial cells is an important area of research. The analysis of the sources shows that the methods of SCD prevention has not changed considerably over the last 35 years [3–6].

Given the importance of this problem, a lot of attention has recently been paid to finding risk markers for SCD. These risk markers include demographic indicators, low left ventricular ejection fraction, decreased heart rate variability, ventricular rhythm disturbances: stable ventricular tachycardia, frequent ventricular extrasystole (> 10 per hour), short paroxysms of ventricular tachycardia, late ventricular potentials [6], microvolt T-wave alternans, high-resolution electrocardiography indicators such as the filtered QRS interval (fQRS) and late ventricular potentials, variance and daily dynamics of the QT interval, variability, heart rate turbulence, and baroreflex sensitivity [3]. At the same time, different literature sources give different data on the prognostic significance of these markers. The significance of some markers is disputable [7].
Due to the fact that the positive predictive value of each risk marker for SCD is not high, a combination of features is proposed to be used [6]. Unfortunately, at the moment there is no generally accepted algorithm for examining patients, which makes it possible to assess the risk of SCD.

This suggests that it is necessary to look for new features and criteria that will allow us to identify high-risk groups of SCD.

2. Methods and Materials
Currently, efforts of many scientists and specialists are aimed at solving problems of automatic analysis and recognition of cardiovascular pathologies. For this, various methods and algorithms for processing and analyzing ECG are used. This is evident from a large number of publications and scientific papers devoted to this problem [8–11]. A number of methods have been developed. The most common methods for identifying R-peaks are based on the analysis of the first derivative of ECG [9]. The methods are aimed to provide the user with the most accurate data of measurements taken after their processing. This is extremely important in view of the fact that any transformation of a measuring signal implies its distortion depending on the method chosen. Filtering significantly distorts the signal [12].

Tomsk Polytechnic University in collaboration with Tomsk Cardiology Research Institute (TCRI) have developed a high-resolution nanosensor-based hardware and software complex (HSC) for real-time recording of micropotentials of the heart without filtering and averaging. HSC comprises nanosensors developed at Tomsk Polytechnic University [13]. Nanosensors are of high stability, low noise and noise immunity of unpolarized electrodes. Using these nanosensors, ECG can be recorded without the use of filtering units in the frequency range from 0 to 10,000 Hz. In addition to standard metrological measures, a series of experiments was conducted to confirm a high quality of recording of physiological signals from the body surface performed using nanosensors. For this purpose, AgCl electrodes by "FIAB Spa (Florence, Italy)" were used as a reference for comparison. The measurements were carried out under similar environmental conditions. The same patient was taken for measuring, and the study method was also unchanged.

The preliminary studies to verify the quality of HCS were carried out in volunteers and patients of TCRI. Each volunteer signed the informed consent form for clinical trials (clinical trials were approved by the local ethical committee for biomedical ethics, TCRI, protocol No. 147 dated June 28, 2016). The volunteers were provided with sufficient information on the procedures of examination and treatment, according to the internal regulations on the procedure for hospitalization in TCRI. The results of the study maintain confidentiality of the patients and volunteers surveyed.

3. Results and considerations
The results of comparison of nanosensors and conventional AgCl electrodes by FIAB Spa (Florence, Italy) is presented in Figure 1. These results show that AgCl electrodes exhibit significant interference of 50 Hz and its harmonics under the same measurement conditions. Conventional electrodes can only be used with filters (including power-line filters). The interference is usually random, both in terms of the level and the width of the spectrum in a 50 Hz region. A power-line filter may significantly distort micropotentials of the heart [12], and dynamic observation will not provide reliable results.
Figure 1. Comparison of electromagnetic pickups of (a) the nanosensor (sensitivity 200 µV/div) and (b) the conventional AgCl electrodes by FIAB Spa (Florence, Italy) (sensitivity 200 µV/div).

Figure 2a-c presents patient electrocardiogram #178 records in the frequency range from 0 to 10,000 Hz. Registration was carried out in the medical ward away from sources of electromagnetic interference (including medical equipment).

Figure 2. High-resolution ECG recording of patient #178, frequency range from 0 to 10,000 Hz. (a) - 1 lead; (b) - 2 lead; (c) - 3 lead.
4. Conclusion
Figure 1 shows that nanosensors have a higher sensitivity and improved signal-to-noise ratio. Noise in the ECG recorded using nanosensors is less significant than that recorded by conventional electrodes. ECG recorded far from the sources of interference does not contain electromagnetic interference in the range from 0 to 10,000 Hz. As can be seen from Figure 2, ECG recording performed by the HSC (including spontaneous activity of myocardial cells) does not require any filtering and averaging.

References
[1] Mahanani W R 2013 Projections of mortality and causes of death, 2015 and 2030 World Heal. Organ
[2] Zipes D P and Wellens H J J 1998 Sudden Cardiac Death Circulation 98 2334–51
[3] Golukhova E Z et al 2017 Kardiologiya 57 73–81
[4] Spirito P and Maron B J 1990 J. Am. Coll. Cardiol. 15 1521–1526
[5] Maron B J et al 1982 Circulation 65 1388–1394
[6] Priori S G et al 2001 Eur. Heart J. 22 1374–1450
[7] Malik M 2001 Risk of Arrhythmia and Sudden Death (London: BMJ)
[8] Elgendi M 2013 PLoS One 8 e73557
[9] Djohan A et al 1995 Proceedings of 17th International Conference of the Engineering in Medicine and Biology Society 1 167–168
[10] Martis R J et al 2013 Biomed. Signal Process. Control 8 437–448
[11] Rybalka S et al 2018 MATEC Web Conf. 155 1008
[12] Avdeeva D K et al 2014 Biol. Med. 6 BM-025
[13] Mishchenko K V et al 2016 Eur. J. Nanomedicine 8 195-202