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Experimental Studies of Non-Invasive Evaluation of Kinematic Activity of an Intact Left Ventricle

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The research is aimed at studying the topology of energy-efficient areas on the epicardial surface. The data enable determination of optimal areas for implantation of microelectromechanical systems (MEMS), including for their application for electrotherapy of the heart. A non-invasive method of assessing epicardium kinematic activity of the left ventricle of the heart in patients with various cardiovascular diseases was used for predicting the localization of implanted devices.

Introduction

Nowadays in high-tech medicine implantable devices are widely used to replace the functions of certain organs, e.g., pacemakers [1]. Implantation of pacemakers in Russia in 2012 amounted to 33827 operations, which is a 61% increase (12868 operations) compared to 2007. The pacemaker implantation rate in children in 2012 amounted to 386 transactions [2]. The service life of modern pacemakers is limited by the battery life and is on average 5-7 years before pacemaker replacement, i.e., a second operation, is needed. Therefore, increasing the service life of implantable devices is both medically and economically necessary. At the same time, the dimensions and service life of a pacemaker largely depend on the capacity of the power supply. This is especially critical for implantable devices located on the surface of the heart, where the weight should not exceed 15 g. A new power source, a battery with a service life of more than 10-15 years, is the key to solving the problem [3, 4]. Current research is aimed at methods and apparatuses for generating electric power using the energy of reciprocating, oscillating, or vibrating movement of objects [5]. Development of microelectromechanical devices for conversion of heartbeats into electricity is a promising method to improve epicardial pacing systems [6].

Modern microelectromechanical systems (MEMS) have the theoretical capability to be used in implantable devices for cardiac electrotherapy. Such MEMS are integrated micro devices or systems combining electrical and mechanical components compatible with integrated circuit technology and having a size of several micrometers to several millimeters. To expand application of MEMS in medical electronics, development of new scientific approaches for studying the energy of the heart function is required.

Application of a MEMS transducer in cardiac surgery is possible in epicardial pacemakers that are implanted directly on the wall of the left ventricle of the heart. The kinematic energy of the heart is enough to increase the service life of the pacemaker battery by at least two times. Due to the application of pacemakers with a MEMS transducer in humans and the fact that the effectiveness of a MEMS transducer is dependent on its location, it is necessary to conduct a non-invasive analysis of the amount of kinematic energy generated by different portions of the left ventricle.

Modern non-invasive methods of electrocardiography and echocardiography of the heart, according to our assumptions, can be used for non-invasive assessment of the kinematic activity of the myocardium using motion vector analysis for various sections of the myocardium according to echocardiography. This approach enables

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both qualitative and quantitative non-invasive assessment of the kinematics of the left ventricular wall.

The aim of our research was to study the topology of energy-efficient areas on the epicardial surface using non-invasive methods to localize the most energy-efficient regions sufficient for the implantation of medical devices for different purposes. The research was based on assessment of the kinematic activity of the epicardium in laboratory animals.

Materials and Methods

Materials

Domestic pigs were used as laboratory animals. A total of 15 animals at the age of 6-9 months were examined; the average weight was 56 ± 5 kg. The study was conducted at the Bakulev Scientific Center for Cardiovascular Surgery, Moscow. Ethical review approved use of laboratory animals (domestic pigs). The plan and design of the research was finalized and approved by the Ethics Committee of the Bakulev Scientific Center for Cardiovascular Surgery, Protocol No. 325 of September 6, 2014.

Laboratory animals were prepared for the study by intramuscular administration of 1.5 ml of a 2% Zoletil solution and 3 ml of a 20% xylazine solution (premedication). After 15 min the animals were placed on an operating table on their right side.

Electrocardiography (ECG) was performed on a Nihon Kohden ECG-1350K machine. The electrocardiogram was recorded in six standard and six chest leads to determine the electrical axis of the heart (heart axis). The heart axis was determined by a standard technique using the α angle.

Echocardiography was performed on a Siemens ACUSON X300 apparatus in the two-chamber and four-chamber positions along the long and short axes with a standard procedure of assessment of the valvular and contractile functions. Recording was done for 20-30 min. Echocardiograms were saved on CD.

The kinematic activity of the epicardium was assessed by velocity vector analysis of a 2D VVI image using a Siemens workstation and the *syngo* US Workplace 3.5 software (version 3.5.6.34). The method of moving particle analysis was the basis for determining the amplitude and velocity of movement of the left ventricular wall at different levels. The vector analysis was performed in postprocessing stages at the level of the epicardium, contrary to standard procedures. The following parameters were measured: radial displacement of the epicardium, longitudinal displacement of the epicardium, and deformation of the myocardium. These data were recorded at three levels: basal, middle, and apical. For the analysis a QRS loop of standard projections was selected: along the short axis at three levels: the level of the mitral valve (basal), the level of the papillary muscles (middle), and the apical level; an apical loop was selected in a position of two-, four-, and five-chamber images. Two indicators were registered at the front, side, and rear walls at each level. Movement parameters were assessed in the epicardium region. The following parameters were analyzed: longitudinal and radial displacement, and deformation of the myocardium. Displacement characterizes the distance (in centimeters) by which the point moves between two consecutive frames, estimated along the long and short axes (longitudinal and radial, respectively). Deformation of the myocardium is the percentile fraction of change in length of a myocardial segment (for a length increase from 10 to 13 mm, the deformation is 30%).

Statistical analysis was performed using the STATISTICA 10.0 software (StatSoft, USA).

Data description used mean (M) and standard deviation (SD), M ± SD (for a normal distribution), as well as median (Me) and interquartile range (Q1; Q3), i.e., the 25th and 75th percentiles (for a distribution different from normal). Normality was tested using the Shapiro–Wilk test.

Two independent samples were compared using the non-parametric Mann–Whitney *U* test and the parametric two-sided Student's *t*-test (for a normal distribution). Two dependent samples were compared using the non-parametric Wilcoxon test. Several independent samples were compared using the non-parametric Kruskal–Wallis test with Bonferroni correction.

Differences were considered statistically significant at $p < 0.05$.

Theoretical calculations

Inertial converters of energy moving along different trajectories give different values of the energy yield. Without a rigorous mathematical model for a particular example of the converter, it is impossible to predict the absolute values of the energy produced by the converter; however, in terms of comparing the energy potential of the regions, it is sufficient to compare the values to which the generated energy is proportional. As a rule, the power generated by the converter is directly proportional to the product of the amplitude of motion (trajectory form) and the contraction frequency. At a fixed contraction frequency the power is proportional to the amplitude. Thus, since for all heart compartments the contraction frequency is similar, the magnitudes of the displacements should be compared to evaluate the energetic potential, i.e., the amount of energy that can be obtained using the inertial converter positioned on the surface of the region.

It is known that for a heart rate of 40 bpm an energy of up to 6 μW can be obtained, at 60 bpm the power is up to 17 μW, and after 200 bpm the power begins to decline. Accordingly, when the heart rate is below 40 or above 160 bpm the capacity of the kinematic energy of the heart is greatly reduced and the work of the MEMS transducer becomes ineffective [7].

Results

The ECG study conducted on 15 animals showed that 13 animals had a horizontal heart axis (α = 0°-30°), while in 2 animals the heart axis was normal (α = 30°-70°). According to the ECG data, the average α angle for the entire group was 29° (28°; 30°).

Depending on the direction of the heart axis, the animals were divided into two groups, with normal (group 1) and horizontal (group 2) heart axes. The splitting into two groups was due to the need to exclude a mutual influence of the heart axes. All laboratory animals during echocardiography showed no congenital anomalies of the heart structure, valve disease, or presence of local and/or diffuse reduction of the contractility of the left ventricle. Given the normal distribution of echocardiographic parameters, the parameters of motion of the left ventricle of the animals from group 1 were described by calculating the mean values and the standard deviation of the mean square.

Group 2 included data of the animals with a normal heart axis (n = 2). Given the normal distribution of echocardiographic parameters, wall displacement of the left ventricle in group 2 was described by calculating the mean values and the standard deviation of the mean square.

Considering the absence of significant differences between the echocardiogram data in the two groups, the analysis of echocardiographic parameters was conducted on a sample of 15 animals.

Comparison of the radial and longitudinal displacement and deformation of the myocardium in laboratory animals with a horizontal heart axis (<30°) and a normal heart axis (>30°) using the t-test for independent groups resulted in $p > 0.05$, which testifies to the absence of statistically significant differences between the groups in the above parameters.

The echocardiographic data were analyzed using vector analysis. In comparing the parameters of radial displacement at the three different levels, statistically significant differences were revealed: $x^2 = 30.1$, $p = 0.000$ (Kruskal–Wallis test with Bonferroni correction). Pairwise comparison of the basal level to the middle, the middle to the apical, and the apical to the basal revealed that the indicators of radial displacement at the apical level differ significantly from the indicators at the basal and middle levels: the heart apex versus the middle segment, 1.3 ± 0.18 vs. 3.69 ± 0.17, $p = 0.000$, and the apical level versus the basal segment, 1.3 ± 0.18 vs. 4.01 ± 0.26, $p = 0.000$. The indicators at the basal and middle levels do not have significant differences: 4.01 ± 0.26 vs. 3.69 ± 0.17, $p = 0.443$. The results are shown in Fig. 1.

Comparison of the indicators of the longitudinal displacement at the same levels revealed statistically significant differences: $x^2 = 22.05$, $p = 0.000$. Pairwise comparison (the basal level vs. the middle, the middle vs. the apical, and the apical vs. the basal) proved that these indicators differ significantly at all levels. Thus, the indicators differ according to the respective levels as follows: the apical level versus the middle segment, 1.8 ± 0.21 vs. 5.7 ± 0.16, $p = 0.000$; the apical level versus the basal segment, 1.8 ± 0.21 vs. 6.81 ± 0.27, $p = 0.000$; the basal level versus the middle level, 6.81 ± 0.27 vs. 5.7 ± 0.16, $p = 0.000$ (Fig. 2).

Indicators of the myocardial deformation according to the three levels of distinction were statistically significant: $x^2 = 22.05$, $p = 0.000$. Pairwise comparisons (the basal level vs. the middle, the middle vs. the apical, and the apical vs. the basal) also indicated the presence of sig-

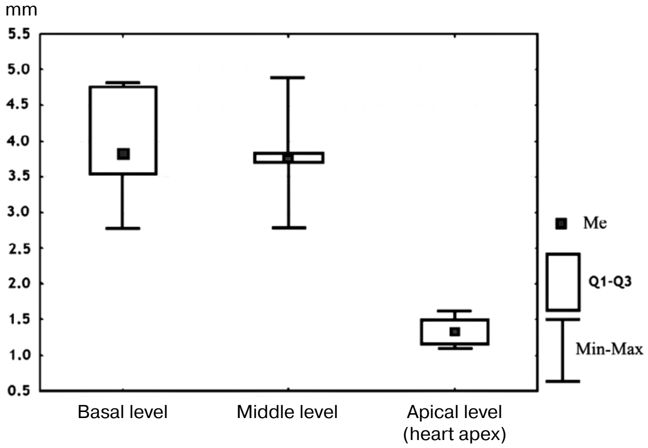

Fig. 1. Radial displacement of the epicardium at three levels: basal, middle, and apical. Statistical analysis was performed on 15 laboratory animals.

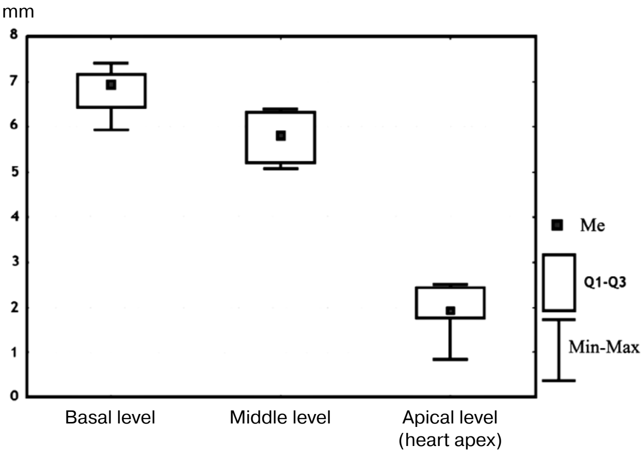

Fig. 2. Longitudinal displacement of the epicardium at three levels: basal, middle, and apical. Statistical analysis was performed on 15 laboratory animals.

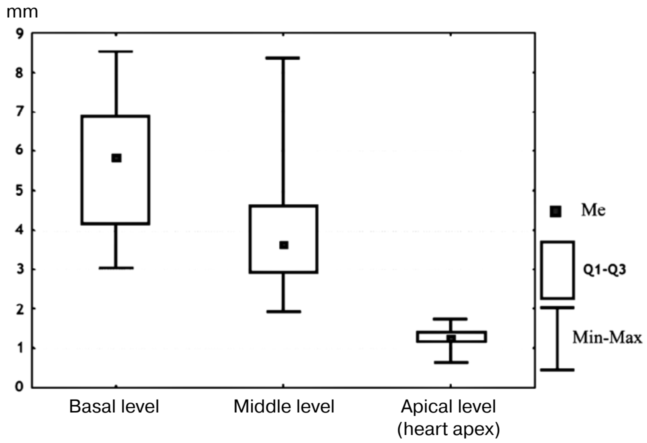

Fig. 3. Deformation of the myocardium at three levels: basal, middle, and apical. Statistical analysis was performed on 15 laboratory animals.

nificant differences at all levels together: myocardial deformation at the basal and middle levels, $p = 0.017$, and at the heart apex and the basal level as well as at the heart apex and the middle level, $p = 0.000$ (Fig. 3).

Due to the fact that in terms of comparison of the energy potential of the regions, it is enough to compare the magnitudes to which the produced energy is proportional, in the first place, when comparing the magnitudes of displacements, it can be stated that the basal compartments of the left ventricle in the studied laboratory animals are the most energy-efficient area for implantation of a MEMS transducer.

Discussion

The application of pacemakers with a MEMS transducer in cardiac surgery raises the issue of identifying the most energy-efficient region of the left ventricular wall for pacemaker implantation. Zurbuchen et al. [8] conducted cardiac MRI in one healthy patient, followed by an analysis of the movement of selected points of the left ventricle. The range of motion was analyzed on three walls at three levels. The greatest range of motion was observed on the side wall at the basal level and reached a maximum of 47.6 mm. Analysis of the heart rotation revealed that the highest degree of rotation was on the rear wall at the apex with a maximum value of 27.3° [8].

In our study we selected a different non-invasive way to assess the movement of the heart, echocardiography and ECG. Echocardiography enables objective judgment on the movement of the heart wall at different levels, including the movement and velocity of movement of the epicardium. Calculating the amplitude and velocity of the movement, it becomes possible to calculate the amount of kinematic energy which can be transformed into electricity using a MEMS transducer. Both ECG and echocardiography are widely implemented in clinics around the world and are safe for patients. The proposed methodology for determining the kinematic activity on the surface of the epicardium can be performed by any doctor of functional diagnostics, since many such methodologies are used in clinical practice today, but only at the level of the myocardium. The longitudinal and radial displacements were evaluated at the level of the epicardium. The myocardial deformation, which reflects the movement of the left ventricle wall, was measured as well. The advantages of this method are its wide availability and absence of any contraindications to the use of standard echocardiography, as well as the lower cost of the study. Given the fact that echocardiography is widely performed, it will be possible in the future to remotely evaluate the data of each individual patient.

The methodology was tested on animals with an intact heart. The maximum values of epicardial longitudinal displacement of the heart were registered at the basal level and on average were 6.81 mm; epicardial radial displacement at the same level was 4.01 mm, and the degree of myocardial strain was 5.6%.

This methodology can be applied to individual patients with different diseases of the cardiovascular system. Data of the non-invasive methodology would facilitate identifying the most energy-efficient locus for implantation of a MEMS transducer into patients.

Conclusions

The results show that the basal compartment of the left ventricle in the test animals is the most energy-efficient area for implantation of the MEMS transducer. The non-invasiveness of this approach allows it to be used for individual evaluation of the kinematic activity of the left ventricular epicardium in patients with various cardiovascular diseases and to predict the place of device implantation.

The first results of the research indicated enough energy potential of the heart for pacemaker operation. The most movable region of the left ventricle from the epicardium side was located: the basal level of the lateral wall of the left ventricle.

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