Method for Determining the Projection of an Arrhythmogenic Focus on the Heart Surface, Based on Solving the Inverse Electrocardiography Problem

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Abstract—The problem of determining the point on the heart surface (projection) nearest to the arrhythmogenic focus, which is located inside the heart, is considered. Localization of this point is crucial for a successful cardiac ablation procedure. The sought projection is calculated on the basis of solving the inverse electrocardiography problem, which is a generalization of the Cauchy problem for the Laplace equation. The inverse electrocardiography problem is solved by the boundary integral equation and Tikhonov regularization methods. Examples of test computations are demonstrated, and the results of processing real electrophysiological data are presented and compared with the medical observation data.

Keywords: cardiac arrhythmias diagnostics, inverse problem of electrocardiography, Cauchy problem for the Laplace equation, boundary integral equations method, Tikhonov regularization method, hypersingular integral equations

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1. INTRODUCTION

Heart rhythm disturbance is one of the main reasons of sudden death and significant reduction in the quality and duration of life. At the present time, the most effective method for healing cardiac arrhythmia is the minimally invasive catheter surgery, as a result of which the arrhythmogenic focus is removed by a radio-frequency pulse or cold action. The success of such an operation significantly depends on the accu racy of determining the projection of the arrhythmogenic focus on the heart surface.

The medical experiment aimed at finding the projection of the arrhythmogenic focus consists in the following. A bipolar electrode is brought to the heart surface, and the potential difference of the heart's electric field is measured across the poles of the electrode at different instants of time for different direc tions of the electrode. Processing this data enables one to find the point on the heart surface (projection) nearest to the arrhythmogenic focus, which is situated inside the heart. The description of these methods used in medicine can be found, e.g., in [1] and the literature cited there.

Unfortunately, this type of diagnostics has its drawbacks. The first one is the necessity to insert a bipolar electrode in the region of the heart. The second one is the X-ray fluoroscopic control of the intracardiac bipolar electrode, which causes high irradiation doses both on the patient and the medical personnel.

In this work, we consider a numerical method for finding the arrhythmogenic focus on the heart sur face only from measurements of the heart's electric field potential on the trunk surface. The sought pro jection is calculated by solving the inverse electrocardiography problems for different instants of time. These problems are solved by the boundary integral equations and Tikhonov regularization methods.

The algorithm developed in this work agrees with the medical experiment used for determining the projection of the arrhythmogenic focus on the heart surface.

2. THE INVERSE ELECTROCARDIOGRAPHY PROBLEM

The inverse electrocardiography problem in the potential form consists in calculating the heart's elec tric field potential on the heart surface from this field detected on the surface of the human breast. The inverse cardiography problem is solved independently for each fixed instant of time t_k , $k = 1, 2, ..., N$, corresponding to measurements made at these moments on the breast surface.

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Let us consider a region Ω in space R^3 , bounded outside by surface Γ_B and, inside, by a closed surface Γ _{*H*}. The surface Γ _{*B*} is a union of two surfaces Γ _{*T*} and Γ _{*E*}. Two nonintersecting regions Ω _{*i*} \subset Ω with boundaries Γ_i , $i = 1, 2$, are defined in Ω . This geometric configuration is interpreted as follows: Γ_H is the heart surface, Γ_E is the part of the trunk surface on which the potential of the electric field is measu upper and lower cuts of the trunk, and Ω_i , $i = 1, 2$, are the regions of inhomogeneity of human breast (the left and right lungs). Γ_i , $i = 1, 2$,

Having defined $\Omega_0 = \Omega \setminus (\overline{\Omega}_1 \cup \overline{\Omega}_2)$, $\Gamma_0 = \Gamma_E$, and $\Gamma_3 = \Gamma_H \cup \Gamma_T$, let us consider the following boundary value problem: find a function $u(x)$, $x \in \overline{\Omega}$, such that $u(x) = u_i(x)$, $x \in \overline{\Omega}_i$, $i = 0, 1, 2$,

$$
\Delta u_i = 0, \quad x \in \Omega_i, \quad i = 0, 1, 2,
$$
\n
$$
(1)
$$

$$
u_i = 0, \quad x \in \mathbb{R}_i, \quad i = 0, 1, 2,
$$

$$
u_0(x) = \varphi(x), \quad x \in \Gamma_3,
$$
 (2)

$$
\frac{\partial u_0(x)}{\partial n} = 0, \quad x \in \Gamma_0,\tag{3}
$$

on

$$
u_0(x) = u_i(x), \quad x \in \Gamma_i, \quad i = 1, 2,
$$
 (4)

$$
\sigma_0 \frac{\partial u_0(x)}{\partial n} = \sigma_i \frac{\partial u_i(x)}{\partial n}, \quad x \in \Gamma_i, \quad i = 1, 2. \tag{5}
$$

Here, $\varphi(x)$ is a given function and σ_i , $i = 0, 1, 2$ are given positive constants. Function $\varphi(x)$ is the potential on surface Γ_3 , and σ_i is the quantity determining the electric conductivity of tissue occupying region Ω_i . Problem (1)–(5) defines operator *A* mapping potential $\varphi(x)$ on surface Γ_3 onto its values $u_0(x)$ on surface Γ_0 .

The inverse electrocardiography problem is formulated as follows: find a function $u(x)$, $x \in \overline{\Omega}$, such that $u(x) = u_i(x), x \in \overline{\Omega}_i, i = 0, 1, 2,$

$$
\Delta u_i = 0, \ x \in \Omega_i, \ i = 0, 1, 2,
$$
\n(6)

$$
u_0(x) = \psi(x), \quad x \in \Gamma_0,
$$
\n(7)

$$
\frac{\partial u_0(x)}{\partial n} = 0, \quad x \in \Gamma_0,\tag{8}
$$

on

$$
u_0(x) = u_i(x), \quad x \in \Gamma_i, \quad i = 1, 2,
$$
 (9)

$$
\sigma_0 \frac{\partial u_0(x)}{\partial n} = \sigma_i \frac{\partial u_i(x)}{\partial n}, \quad x \in \Gamma_i, \quad i = 1, 2,
$$
\n(10)

where $\psi(x)$ is a known function obtained from measurements on the trunk surface.

Problem (6) – (10) is a generalization of the Cauchy problem for the Laplace equation and is ill-posed. One of the most significant manifestations of its ill-posedness is the instability of the potential $u(x)$ with respect to small variations in the initial data $\psi(x)$.

Problem (6)–(10) can be reformulated as a problem of finding function $u(x)$ on surface Γ_3 under the condition that $u(x)$ satisfies (6)–(10). It can also be written as a problem of solving the operator equation of the first kind

$$
A\varphi = \psi,\tag{11}
$$

where ψ is a given function and the operator *A* is defined by problem (1)–(5) and function $\varphi(x)$ is unknown.

The inverse electrocardiography problem is solved by the boundary integral equations and Tikhonov regularization methods. After writing the system of boundary integral equations for solving problem (1)– (5) and discretization, we obtain a system of linear algebraic equations that is a discrete analog of operator equation (11). Applying the Tikhonov regularization method for solving this system of linear algebraic equations, we find the approximate value of potential φ on the heart surface. The numerical method for solving the inverse electrocardiography problem is described in more detail in [6, 7].

3. FINDING THE PROJECTION OF AN ARRHYTHMOGENIC FOCUS

The projection of the arrhythmogenic focus on the heart surface is found from the values of the gradient of potential $u_0(x)$ on this surface. For solving the problem of calculating the gradient, it is sufficient to use the method of boundary integral equations, because this method was used for solving the inverse electro cardiography problem.

Potential $u_0(x)$, $x \in \Gamma_H$, in region Ω_0 with boundary $\partial \Omega = \Gamma_T \cup \Gamma_H \cup \Gamma_E \cup \Gamma_1 \cup \Gamma_2$ satisfies Green's third formula

$$
c_P u_0(P) = \int_{\partial \Omega_0} \left(\frac{\partial u_0(Q)}{\partial n} G(P,Q) - u_0(Q) \frac{\partial G(P,Q)}{\partial n} \right) dS_Q, \quad P \in \Gamma_H, \quad Q \in \partial \Omega_0,
$$
\n(12)

where c_p is the coefficient depending on the solid angle at point *P* and $G(P, Q)$ is the fundamental solution of the Laplace equation:

$$
G(P,Q) = \frac{1}{4\pi} \frac{1}{|P - Q|}.
$$
\n(13)

Denote by e_k , $k = 1, 2, 3$, the unit coordinate vectors and take the partial derivatives of the function $u_0(p)$ in (12)

$$
c_P \frac{\partial u_0(P)}{\partial \mathbf{e}_k} = \frac{\partial}{\partial \mathbf{e}_k} \int_{\partial \Omega_0} \left(\frac{\partial u_0(Q)}{\partial n} G(P,Q) - u_0(Q) \frac{\partial G(P,Q)}{\partial n} \right) dS_Q, \quad P \in \Gamma_H, \quad k = 1,2,3.
$$
 (14)

When points P and Q coincide, the integrals with the kernels $G(P,Q)$ and $\frac{\partial G(P,Q)}{\partial q}$ are improper. The integral with kernel $G(P, Q)$ has a weak singularity and exists for points $P = Q$, and the integral with kernel $\frac{\partial G(P,Q)}{\partial \rho}$ must be replaced by Cauchy's principal value. We will define Cauchy's principal value as the limit when *P* tends to the surface $\partial \Omega_0$ along the internal normal: *n* ∂ ∂ *n* ∂

$$
\int_{\partial\Omega_0} u_0(x) \frac{\partial G(P,Q)}{\partial n} dS_Q = \lim_{P_I \to P} \int_{\partial\Omega_0} u_0(Q) \frac{\partial G(P_I,Q)}{\partial n} dS_Q = \lim_{\varepsilon \to 0} \int_{\partial\Omega_0} u_0(Q) \frac{\partial G(P - \varepsilon n, Q)}{\partial n} dS_Q, \tag{15}
$$

or along the external normal:

$$
\int_{\partial\Omega_0} u_0(x) \frac{\partial G(P,Q)}{\partial n} dS_Q = \lim_{P_E \to P} \int_{\partial\Omega_0} u_0(Q) \frac{\partial G(P_E,Q)}{\partial n} dS_Q = \lim_{\varepsilon \to 0} \int_{\partial\Omega_0} u_0(Q) \frac{\partial G(P + \varepsilon n,Q)}{\partial n} dS_Q.
$$
 (16)

In [8, 12], it was proved that definition (15) and (16) is equivalent to the following definition [11]:

$$
\int_{\partial\Omega_0} u_0(x) \frac{\partial G(P,Q)}{\partial n} dS_Q = \lim_{\varepsilon \to 0} \int_{\partial\Omega_0 \setminus \Gamma_\varepsilon} u_0(Q) \frac{\partial G(P,Q)}{\partial n} dS_Q.
$$
 (17)

Using formulas (15) and (16) and the method proposed in [10], we obtain

$$
\frac{\partial u_0(P)}{\partial \mathbf{e}_k} = \lim_{P_I \to P} \int_{\partial \Omega_0} \left(\frac{\partial u_0(Q)}{\partial n} \frac{\partial G(P_I, Q)}{\partial e_k} - u_0(Q) \frac{\partial^2 G(P_I, Q)}{\partial n \partial e_k} \right) dS_Q
$$
\n
$$
- \lim_{P_E \to P} \int_{\partial \Omega_0} \left(\frac{\partial u_0(Q)}{\partial n} \frac{\partial G(P_E, Q)}{\partial e_k} - u_0(Q) \frac{\partial^2 G(P_E, Q)}{\partial n \partial e_k} \right) dS_Q, \quad P \in \Gamma_H, \quad k = 1, 2, 3.
$$
\n(18)

Therefore, for calculating the gradient, it suffices to find the singular and hypersingular integrals.

In order to calculate the components of the gradient, we will construct the integral relationships based on the Galerkin projection method [10]:

$$
\int_{\partial\Omega_{0}} \varphi_{j}(P) \frac{\partial u_{0}(P)}{\partial \mathbf{e}_{k}} dS_{P} = \lim_{P_{i} \to P} \int_{\partial\Omega_{0}} \varphi_{j}(P) \int_{\partial\Omega_{0}} \left(\frac{\partial u_{0}(Q)}{\partial n} \frac{\partial G(P_{i}, Q)}{\partial \mathbf{e}_{k}} - u_{0}(Q) \frac{\partial^{2} G(P_{i}, Q)}{\partial n \partial \mathbf{e}_{k}} \right) dS_{Q} dS_{P}
$$
\n
$$
- \lim_{P_{E} \to P} \int_{\partial\Omega_{0}} \varphi_{j}(P) \int_{\partial\Omega_{0}} \left(\frac{\partial u_{0}(Q)}{\partial n} \frac{\partial G(P_{E}, Q)}{\partial \mathbf{e}_{k}} - u_{0}(Q) \frac{\partial^{2} G(P_{E}, Q)}{\partial n \partial \mathbf{e}_{k}} \right) dS_{Q} dS_{P},
$$
\n
$$
P \in \Gamma_{H}, \quad k = 1, 2, 3, \quad j = 1, 2, ..., M,
$$
\n(19)

where $\varphi_j(P)$ is the interpolating basis functions. The use of the Galerkin method substantially simplifies the calculation of the singular and hypersingular integrals, because, in many cases, we obtain simple ana lytic expressions.

Let us turn to finding the projection of the arrhythmogenic focus on the heart surface. As a result of solving the inverse electrocardiography problem at different instants of time t_k and calculating the gradi-

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No.	Number of nodes/elements	ϵ , min	ε , max	ε, average	Computation time, s
	247/490	0.0205	0.3212	0.0510	11.02
2	504/1004	0.0055	0.2576	0.0432	23.25
3	1023/2042	0.0112	0.3521	0.0398	48.12
4	1542/3080	0.0025	0.2243	0.0291	74.99
	2585/5166	0.0019	0.2498	0.0251	139.15

Table 1. Results of the first numerical experiment

ent, we know grad $u_0(x, t_k)$, $x \in \Gamma_H$, $k = 1, 2, ..., N$. Let us consider function $\vec{g}(x, t_k)$ for $x \in \Gamma_H$, which is the projection of $\text{grad } u_0(x, t_k)$ onto the tangent plane.

Then, we calculate on the heart surface the vector function $\vec{A}(z)$ such that, for an arbitrary point $z \in \Gamma_H$,

$$
\vec{A}(z) = \vec{g}(z, t_{k_1}),
$$
\n(20)

where

$$
t_{k_1} = \arg \max_{t_k} |\vec{\mathbf{g}}(z, t_k)|, \ \ k = 1, 2, ..., N.
$$
 (21)

From the known function $\vec{A}(x)$, we find the scalar function $a(x)$, $x \in \Gamma_H$, that minimizes the functional

$$
I = \int_{\Gamma_H} \left| \vec{\mathbf{A}}(x) - \vec{\mathbf{g}}_a(x) \right| ds,
$$
 (22)

where $\vec{g}_a(x)$ is the gradient of the function $a(x)$ calculated at the point *x* of the tangent plane. The point x^* at which function $a(x)$ attains its maximum is taken as the sought projection of the arrhythmogenic focus.

The above-described algorithm corresponds to the medical experiments on finding the arrhyth mogenic focus on the heart surface. In this experiment, in order to find the function $a(x)$, an electrode is brought to the heart surface; its position varies in time. This mathematical algorithm enables one to find the projection of the arrhythmogenic focus on the heart surface only from measurements of the potential of the electric field on the human trunk surface.

4. EXAMPLES OF COMPUTATIONS AND THEIR COMPARISON WITH MEDICAL EXPERIMENTS

Let us consider the results of some numerical experiments. The details of the numerical implementa tion of the method of boundary integral equations are the following. Each surface Γ_l was approximated by a polygonal surface $\hat{\Gamma}_l$ consisting of plane triangles. Each such triangle is termed a boundary element. In

Results of the second numerical experiment.

each element, linear interpolating basis functions $\varphi_j(x)$, $j =$ 1,2, …, *M*, with the nodes at the vertices of the triangle are introduced. The potential and the normal derivative of the potential were approximated by the expansion in the sys tem of basis functions $\varphi_j(x)$. The normals at the vertices of the triangle were averaged. The integrals of the product of the fundamental solution by the basis functions in ele ments in which the collocation and integration points do not coincide were calculated by the Gauss quadrature for mulas of the 4th order. The singular and hypersingular integrals were calculated by the analytic expressions obtained in [10].

In the first numerical experiment, we used the real trunk and heart geometries. On surface Γ_3 , the electric field potential $\varphi(x)$ corresponding to the potential produced by a quadruple situated inside the heart, at its geo metrical center was specified. The direct electrocardio graphy problem was solved with this value, and potential

No.	Type of arrythmia	Number of patients	Maximum distance, mm
	Ventricular extrasystoles, basal regions		
2	Ventricular extrasystoles, free wall		
3	Auricular extrasystoles		
$\overline{4}$	WPW syndrome		

Table 2. Results of processing medical experiments

 $\psi(x)$ on surface Γ_0 was calculated. An error was introduced into the potential on surface Γ_0 , which gave function $\psi_{\delta}(x)$ with which the inverse problem was solved. The direct and inverse problems were solved for a piecewise-homogeneous model of a breast with $\sigma_0 = 1$ and $\sigma_1 = \sigma_2 = 5$. After solving the inverse electrocardiography problem on the heart surface, the gradient was numerically calculated at each node of the triangulation polygonal grid and compared with the analytically calculated gradient of the potential pro duced by a quadruple. The experiment was performed for polygonal grids with different numbers of nodes and elements. For each polygonal grid, the minimum relative error (ε min), the maximum relative error (ε max), and the average value (ε average) over all nodes were calculated. The results of the numerical experiment are summarized in Table 1.

The second numerical experiment was aimed at comparing functions $a(x)$ and $\hat{a}(x)$. The first function was directly measured in the medical experiment, and the second one was calculated by the method pro posed in this work from the data of measuring the potential on the trunk surface only. The details of the experiment are the following. A patient was subjected to the above-described procedure of determining the position of the projection of the arrhythmogenic focus. Simultaneously, the heart's electric field potential was detected on the trunk surface. The geometries of the trunk and heart were reconstructed from the computer tomography data. Then, on the basis of measurements on the trunk surface only, func tion $\hat{a}(x)$ was numerically calculated and compared with the directly measured function.

Figure 1 shows the values of the measured function $a(x)$ and the numerically determined function $\hat{a}(x)$ on a contour comprising the cross section of the heart passing through the found projection of the arrhyth mogenic focus at an angle of 35 degrees to the vertical axis of the heart.

The aim of the third experiment was to compare the results of determining the projection of the arrhythmogenic focus from the medical experiment and by the numerical method from the data of mea surements on the trunk surface only. For some types of arrhythmia, a medical experiment on determining the position of the projection of the arrhythmogenic focus was conducted for a group of patients. Simultaneously, the patients' heart's electric field potential on the trunk surface was detected and the projection of the arrhythmogenic focus was determined by the above-described numerical method. After that, the minimum distance over the heart surface between the found points was calculated.

Table 2 presents the results of comparison between the projections of the arrhythmogenic focus for dif ferent types of arrhythmia. For each type of arrhythmia, the number of patients subjected to the above described procedure is presented and the distance between the two found projections of the arrhyth mogenic focus of the patient for whom the error of determining the focus was maximal is given.

The results of this work lead to the conclusion that our algorithm enables one to determine the position of the arrhythmogenic focus on the heart surface with sufficient accuracy.

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REFERENCES

- 1. S. K. Stephen Huang and M. A. Wood, *Catheter Ablation of Cardiac Arrhythmias* (Elsevier, 2010).
- 2. R. Barr and M. Spek, *Solutions of the Inverse Problems Expresses Directly in the Form of a Potential* (Meditsina, Moscow, 1979) [in Russian].
- 3. A. M. Denisov, E. V. Zakharov, A. V. Kalinin, and V. V. Kalinin, "Application of the Tikhonov Regularization Method for Numerical Solution of the Inverse Electrocardiography Problem," *Vestn. Mosk. Univ., Ser.* **15** (2), 5–10 (2008).
- 4. A. M. Denisov, E. V. Zakharov, A. V. Kalinin, and V. V. Kalinin, "Numerical Methods for Solving Some Inverse Problems of Cardiac Electrophysiology," Differents. Uravn. **45** (7), 1014–1022 (2009).
- 5. E. V. Zakharov and A. V. Kalinin, "Numerical Solution of the Three-Dimensional Dirichlet Problem in Piece wise-Homogeneous Medium by the Method of Boundary Integral Equations," Zh. Vychisl. Mat. Mat. Fiz*.* **49** (7), 1197–1206 (2009).
- 6. A. M. Denisov, E. V. Zakharov, A. V. Kalinin, and V. V. Kalinin, "Numerical Solution of the Inverse Electro cardiography Problem in a Medium with a Piecewise-Constant Conductivity," Zh. Vychisl. Mat. Mat. Fiz*.* **7**, 1233–1239 (2010).
- 7. A. V. Kalinin, "An Iterative Algorithm for Solving the Inverse electrocardiography Problem with a Piecewise- Constant Conductivity," in *Applied Mathematics and Informatics*, no. 34 (Izd-vo MGU, Moscow, 2010), pp. 35–40.
- 8. E. V. Zakharov, A. G. Davydov, and I. V. Khaleeva, "Integral Equations with Hadamard Kernels in Diffractrion Problems," in *Urgent Problems of Applied Mathematics* (Moscow: Izd-vo MGU, Moscow, 1989), pp. 118-127.
- 9. A. N. Tikhonov and V. Ya. Arsenin, *Solution of Ill-Posed Problems* (Nauka, Moscow, 1986) [in Russian].
- 10. A. Sutradhar, G. H. Paulino, and L. J. Gray, *Symmetric Galerkin Boundary Element Method* (Springer, 2008).
- 11. A. N. Tikhonov and A. A. Samarskii, *Equations of Mathematical Physics* (Izd-vo MGU, Moscow, 1998) [in Russian].
- 12. G. M. Vainikko, I. K. Lifanov, and L. N. Poltavskii*, Numerical Methods in Hypersingular Integral Equations and their Applications* (Yanus, Moscow, 2001) [in Russian].