«Digital Twin» technology in medical information systems

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Abstract. Given the high mortality rate from cardiovascular diseases and the need to transfer medicine to a more high-tech level of development, the authors propose the use of digital twin technology for the diagnosis and treatment of heart diseases. As a digital twin of the human heart, it is proposed to use the combination of an equivalent electric heart generator and the of D. Noble computer heart model within the subsystem for supporting medical decision-making. The use of such digital twin will make it possible to reliably conduct non-invasive cardiodiagnosis to select drugs within the treatment regimen.

1. Introduction

According to the World Health Organization, cardiovascular disease (CVD) is the leading cause of death worldwide: for no other reason as many people die every year as from CVD. It is estimated that in 2018, 17.9 million people died from CVD, which is 31% of all deaths worldwide, 85% of these deaths occurred as a result of a heart attack and stroke. People with CVD need early detection and personalized care through counseling and, if necessary, prescribing medications and procedures [1].

In the long-term “Forecast of the Scientific and Technological Development of Russia until 2030” [2], the medicine and healthcare section is identified as the first of seven priority areas of science, technology and engineering. In it, in the context of the problems associated with the prevalence of CVD and mortality from these causes, a number of research and development areas are identified that are recognized by experts as the most promising for Russia. They include research and development aimed at creating new experimental models of the most relevant human diseases, including diseases of the cardiovascular system (CVD).

2. Problem statement

The Russian healthcare system was created over a hundred years ago in other conditions. In recent decades, there has been a jump in the development of high-tech medical care, the creation of wearable means of the human body functional state monitoring, as well as implantable medical devices and remote control devices that do not fit into its traditional structure.

In the new healthcare model, according to the national project “Healthcare” [2], special attention should be paid to preventive medicine and a personalized approach based on the development of “digital” medicine, which allows collecting and processing, including remotely, large amounts of data to make informed optimal strategic decisions, identify new areas of development. In the Russian
According to [3], DT is a complex multidisciplinary mathematical model with a high level of adequacy to human organs and tissues, described by 3D non-stationary nonlinear partial differential equations, providing a difference between the results of virtual tests and full-scale tests within ±5%.

3. Materials and methods

The functioning of living cells is accompanied by the appearance of transmembrane electrical potentials. Cells, forming a holistic organ, form a complex image of its electrical activity. Electrical activity reflects the functional state of the heart and is different in the development of CVD. Registration and analysis of electrical activity allows to create mathematical models of the heart in order to study its functioning, conduct clinical diagnostics, and select a treatment regimen.

To assess the functional state of the heart by its electrical activity, an equivalent electric generator of the heart (EEGH) model is used, showing how the electric field changes on the surface of the body, depending on the change in the electrical activity of the heart with a change in the functional state of the human body [4].

There are two fundamental tasks in electrocardiography: the direct task is to calculate the distribution of the electric potential on a given surface of the body according to the given EEGH characteristics and the inverse problem is to determine the characteristics of the EEGH from the measured potentials on the body surface [4].

The inverse task is the task of clinical diagnosis: determine the functional state of the heart measuring and registering an electrocardiogram. The direct task is to use the mathematical model of the heart to select external influences (medical procedures, medications, diet, physical activity) and their levels,
which allow normalizing the functioning of the heart and ensuring optimal, for given conditions, functional state of the human body.

The implementation of the DT discipline in medicine is, first of all, the development and implementation of MDMSS, which allows solving direct and inverse tasks of diagnosing the CVS. The solution of these tasks is to conduct research on the patient’s CVS, carry out diagnostic measures based on EEGH - human heart DT, establish a diagnosis and, using the D. Noble computer model of the heart (CMH) [5] simulate the results of the treatment process in order to select the personalized treatment regimen containing medical procedures, medications, diet, exercise. The method proposed by the authors is given in figure 3.

![Figure 3. Implementation scheme of the digital twin in the study of the patient's CVS.](image)

D. Noble CMH is, like EEGH, a cardiac DT, the work of which is modeled by equations [5], and is designed to test various pharmacological and physical methods of CVD treating without contact with the patient, which allows to anticipate and exclude side effects of drugs and procedures and develop a personalized CVD treatment regimen.

The base of the D. Noble CMH is a modification of the Hodgkin-Huxley equations describing the distribution of excitation in the heart [5]:

\[
\frac{dV}{dt} = \Delta V - C^{-1}[(V - E_K) g_K n^4 + (V - E_{Na}) g_{Na} m^4 h + (V - E_0) g_0],
\]

\[
dn/dt = an(1 - n) - \beta_n n,
\]

\[
dm/dt = am(1 - m) - \beta_m m,
\]

\[
dh/dt = ah(1 - h) - \beta_h h.
\]

The D. Noble CMH consists of the basic equation for the potential and equations for the values \(n, m, h\) describing potassium and sodium currents, but the coefficients in them have a different meaning and, in addition, the potassium current in this case consists of two components. D. Noble CMH reliably reproduces the general form of the cardiac potential and a number of its other properties. For example, it is known that if the heart muscle is induced twice, and the time interval between these two stimuli is small enough, then the impulse arising in response to the second stimulus will be shorter than normal. The same phenomenon is found on the D. Noble CMH. A certain change in the coefficients of D. Noble equations leads to a system in which spontaneous rhythmic excitation of the membrane occurs, similar to the periodic activity of the sinus node of the heart.

4. Results and discussion

Creation of heart DT begins with the solution of the inverse task of diagnosing the state of CVS - the construction of EEGH (see figure 4a) [6, 7]. Based on the data obtained, a diagnosis is made (see figure 4b) [6, 7] and, using the D. Noble computer model of the heart, a treatment regimen is selected: drugs, doses, regimens [5].

The process of creating EEGH (a mathematical model for changing the electrical activity of the heart) is given in [8] and consists in the following. Electrodes are installed on the patient’s torso and an electrocardiogram (ECS) is recorded, the anthropometric parameters of the torso and the coordinates of the electrodes are determined in a three-dimensional coordinate system, the potentials are interpolated
on the torso surface, the potential distributions and its normal derivative are calculated on the surface of the auxiliary internal elliptical cylinder, and the spatial distribution of the electrical activity of the heart are determined - total over the entire cardiocycle and the interval of the P-wave, the coordinates of the center of the patient’s epicardial model and the center of the patient’s atrial model are calculated.

Based on the data obtained, the surface-type EEGH is first reconstructed as follows.

![Diagram of the method for non-invasive determination of electrophysiological characteristics of the heart.](image)

**Figure 4.** Method for non-invasive determination of electrophysiological characteristics of the heart.

The distribution of the potential and its normal derivative is calculated on the surface of the reconstructed model of the patient’s epicardium for temporary readings of the cardiocycle from the beginning of the P-wave to the end of the T-wave using the Seidel iteration method according to the formulas:

\[
[G_{eb}^e]_{ge} - [H_{eb}^e]_{\varphi e} = [H_{eb}^{bb}t]_{\varphi b}; \quad P_i c S_b; \quad i = 1 \ldots N_b;
\]

\[
[G_{ee}^e]_{be} - [H_{ee}^e]_{\varphi e} = [H_{be}^{be}t]_{\varphi b}; \quad P_i c S_e; \quad i = 1 \ldots N_e;
\]

where \( P_i \) is the point on the surface of the torso \( S_b \);

\( P_i \) is a point on the surface of the inner elliptical cylinder \( S_e \).

Potential vectors of the surface of the epicardial model and derivative potentials in the direction normal to the surface of the patient's epicardial model are determined by the formulas:

\[
\varphi^e = (\varphi_{1e}^e, ..., \varphi_{Ne}^e),
\]

\[
g^e = \left( d\varphi_{1e}^e/dn, ..., d\varphi_{Ne}^e/dn \right).
\]
Potential vectors on the torso surface are determined by the formulas:
\[ \varphi^b = (\varphi^b_1, ... \varphi^b_N), \]
\[ G^e_{ji} = (1/R_{ji}) \Delta S_i; \]
\[ H^e_{ji} = [d(1/R_{ji})/dn_e] \Delta S_i; \]
\[ G^b_{ji} = (1/R_{ji}) \Delta S_i; i \neq i', \]
\[ H^e_{ji} = [d(1/R_{ji})/dn_e] \Delta S_i; j \neq j', \]
\[ H^b_{ji} = [d(1/R_{ji})/dn_e] \Delta S_i; j \neq j'. \]

where \( R_{ji} = |P_j P_i| \) are elements of the matrices included in the system of linear matrix equations.

The convergence of the iterative process is monitored when calculating the potential distribution on the epicardium and the accuracy of the approximation of potentials on the torso for the \( m \)th iteration are monitored by the formulas:
\[ \frac{\|\varphi^{(m+1)} - \varphi^{(m)}\|}{\|\varphi^{(m+1)}\|} < \varepsilon, \]
\[ \frac{\|g^{(m+1)} - g^{(m)}\|}{\|g^{(m+1)}\|} < \varepsilon, \]
\[ \frac{\|\varphi^{(m+1)} - \varphi^{(m)}\|}{\|\varphi^{(m)}\|} < \delta, \]

where \( \varepsilon \) and \( \delta \) are small positive dimensionless quantities.
And \( \varphi^{(l+1)}, g^{(l+1)}, \varphi^{(l)} \) are determined by the formulas:
\[ \varphi^{(l+1)} = [H^{ee}]^{-1}([G^{ee}]g^{(l)} - [H^{be}]\varphi^{(l)}), \]
\[ g^{(l+1)} = [G^{eb}]^{-1}([H^{eb}]\varphi^{(l+1)} + [H^{bb}]\varphi^{(l)}), \]
\[ \varphi^{(l)} = [H^{bb}]^{-1}([G^{eb}]g^{(l)} - [H^{eb}]\varphi^{(l)}). \]

Then, the reconstruction of the EEGH of the dipole type is carried out. For that for all time samples of the cardiocycle \( t_k (k \in (k_{b0} \ldots k_0)) \) a preliminary estimate of the array of ECG parameters \( s_{0k} = (x_{s0k}, y_{s0k}, z_{s0k}, M_{x0k}, M_{y0k}, M_{z0k}) \) is obtained, where \( (x_s, y_s, z_s) \) are the coordinates of the EEGH, \( (M_x, M_y, M_z) \) are the projections of the vector of the dipole moment of the EEGH by searching for the minimum of the functional \( \Omega_0 = \| U - U(s_{0k}) \|^2 \), where \( U = (U_1, ..., U_n, ..., U_{N_1}); U_n \) is ECS of the \( n \)th electrode; \( U(s) = (U_{1s}, ..., U_{ns}, ..., U_{N_1s}); U_{ns} \) are the signal of the dipole EEGH with parameters \( s_{0k} \) calculated for the \( n \)th electrode.

Then an estimate of the regularization coefficient \( \alpha_k \) for each moment of time \( t_k \) is obtained by the formula:
\[ \alpha_k = C_M \left[ \| U_k - U_k(s_{0k}) \|^2 \right]^2 \frac{1}{(1/N_k) \sum_{k=k_{b0}}^{k_0} \| s'_{0k} \|^2} \]

where \( C_M \) is the scale coefficient of regularization \( C_M \in (0.5; 1.5); \)
\[ s'_{0k} = \left( \frac{x_{s0k} - x_{ce}}{R_H}, \frac{y_{s0k} - y_{ce}}{R_H}, \frac{z_{s0k} - z_{ce}}{R_H}, \frac{M_{x0k}}{M_H}, \frac{M_{y0k}}{M_H}, \frac{M_{z0k}}{M_H} \right) \]
is a normalized array of estimates of the EEGH parameters; \((x_{ce}, y_{ce}, z_{ce})\) are coordinates of the center of the patient’s epicardium model; \(R_H \approx 6 \text{ cm}\) is the average radius of the epicardium.

The module of the dipole moment vector of the EEGH is determined by the formula:

\[
M_H = \sqrt{(M_{x0R})^2 + (M_{y0R})^2 + (M_{z0R})^2},
\]

where \(M_H, M_{x0k}, M_{y0k}, M_{z0k}\), respectively, are the module and projections of the dipole moment vector of the EEGH of the dipole type for the time reference of the maximum of the R-wave of the cardiocycle.

Next, the search for the EEGH parameters of the dipole type for each moment of time \(t_k\) is carried out by minimizing the functional:

\[
\Omega_\alpha = \| U - \tilde{U}(s_k) \|^2 + \alpha_k \| s_k' \|^2,
\]

where

\[
s_k' = \left( \frac{x_{sk} - x_{ce}}{R_H}, \frac{y_{sk} - y_{ce}}{R_H}, \frac{z_{sk} - z_{ce}}{R_H}, \frac{M_{xk}}{M_H}, \frac{M_{yk}}{M_H}, \frac{M_{zk}}{M_H} \right)
\]

is the normalized array of EEGH parameters of the dipole type.

After that, the results of searching for EEGH parameters of dipole type are also controlled by checking the convergence of the EEGH parameters and the proximity of the array of ECS samples for dipole type to the array of samples of measured ECS by the formulas:

\[
\frac{\| \Omega^{(m)} - \Omega^{(m-1)} \|}{\| \Omega^{(m)} \|} < \epsilon_1,
\]

\[
\frac{\| u_n - u_n^{(m)}(s) \|}{\| u_n \|} < \delta_1,
\]

where \(m\) is the iteration number in the process of searching for the minimum of the functional \(\Omega_\alpha\); \(\epsilon_1\) and \(\delta_1\) are small positive dimensionless quantities.

Thus, the proposed method for reconstructing EEGH allows to obtain patterns of changes in the electric potential on the surface of the epicardium that change during the cardiocycle for a more effective diagnosis of CVD (see figure 3b).

5. Conclusion

The combination of D. Noble EEGH and CMH within the framework of MDMSS will allow for non-invasive diagnosis of CVD, selecting the names and dosage of drugs using DT, rather than a real patient, which eliminates side effects and worsening of the patient’s state. And thus, it takes healthcare to a new level of high-tech medical care.

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