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OPPORTUNITY AND PLANNING BIM-ANALYSIS FOR MONITORING BLOOD

Results of the study of the possibility of using the results of the bioimpedance method for monitoring hidden and spontaneous bleeding are presented. The current problem of accounting for blood loss during resuscitation, surgery and rehabilitation activities is shown. The use, as informative parameters, of the spectral properties of the bioimpedance signal, namely, the coefficient of inter-spectral correlation of the original measurement signal and its linear transformation is proposed. In work, the existing models substantiating the prospects of using the bioimpedance method for such problems are considered in detail, and the calculated empirical expressions for determining the volume of liquid segments of the human body are given. The mathematical substantiation of the method of inter-spectral correlation based on the calculation of the correlation coefficients of the wavelet-decomposition coefficients of the original signal and its linear transformation is given. The results of experimental studies on the approbation of this method for fixed venous blood sampling are presented in the work. Using criterial T-statistics, a quantitative evaluation of the effectiveness of the options for choosing the spatial placement of measuring electrodes in bioimpedanceometry was carried out. The obtained results allow to draw a conclusion about the possibility and prospects of the proposed method for real-time monitoring of the onset of latent and spontaneous hemorrhages, and also make it possible to formulate recommendations for placement of measuring electrodes on the patient's body.

Keywords: blood loss; active monitoring; bioimpedance analysis; wavelet transformation; inter-spectral correlation; T-statistics.

Introduction

Statement of problem. The problem of taking into account the volume of blood loss is of exceptional importance not only for choosing a strategy for any resuscitation in traumatic amputations, but also for diagnosing closed trauma and postoperative complications. The existing methods [1-2] of monitoring such blood loss are imperfect and exclude the possibility of monitoring in real time, which is critical, especially for cases of acute blood loss.

The analysis of literature sources [3-4] showed great promise of using the bioimpedanceometry method for studying the state of the vascular bed and liquid media of the organism, which gives definite hopes for the effective application of this method to control hidden blood loss.

The aim of work is development of a method for active monitoring of hidden and spontaneous blood loss in the process of postoperative rehabilitation based on bioimpedance analysis of the patient's body.

Analysis of literature sources and recent research. According to the generally accepted classification, three degrees of blood loss are distinguished: mild, moderate and severe [2, 5]. Their main characteristics are given in Table 1.

Usually, when calculating the estimated volume of blood loss, a shock index is calculated that is equal to the ratio of the heart rate value to the systolic blood pressure value. Table 2 shows the correspondence of the calculated indices to the estimated values of blood loss.

The method of assessing the volume of blood loss, based on a comprehensive approach that takes into account both the nomogram for determining hemorrhagic hemorrhage, is more accurate (table 3).

With gastrointestinal bleeding, the deficit of volume of circulating blood can be determined by the parameters of hematocrit (table 4).

<table>
<thead>
<tr>
<th>Rate of blood loss</th>
<th>The degree of hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume deficit, %</td>
<td>Up to 20</td>
</tr>
<tr>
<td>Number of erythrocytes, 10^12/l</td>
<td>3.5 or higher</td>
</tr>
<tr>
<td>Hemoglobin level, g/l</td>
<td>More than 100</td>
</tr>
<tr>
<td>Pulse rate, number of beats per minute</td>
<td>Up to 80</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>100 or higher</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>More than 30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Index</th>
<th>Blood loss volume, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0,4</td>
<td>0</td>
</tr>
<tr>
<td>0,78</td>
<td>10-20</td>
</tr>
<tr>
<td>0,99</td>
<td>20-30</td>
</tr>
<tr>
<td>1,11</td>
<td>30-40</td>
</tr>
<tr>
<td>1,38</td>
<td>40-50</td>
</tr>
<tr>
<td>More than 1,5</td>
<td>More than 50</td>
</tr>
</tbody>
</table>
Bioimpedance analysis of the body composition is to estimate the amount of fluid in the bioobject, since it is the liquid medium that creates the active constituent of conductivity [3-4, 16-18].

Equivalent scheme of the bioobject, also called the Fricke-Morse model, contains the resistance of the extracellular fluid $R_E$, the resistance of the cell fluid $R_C$ and the capacity $C_M$ of the membranes. To determine the volume of extracellular fluid, it is necessary to measure the impedance at a constant current, since in this case the cell membranes remain impermeable, and the intracellular fluid does not affect the measurement result. To determine the total body fluid, it is necessary to measure the impedance at an infinitely large frequency when the current passes through the cell [19-25].

In the classical representation for bioimpedanceometry (BIM), there are several physical models of the body composition (Fig. 1), the main ones of which are the model of a homogeneous body (Fig. 1, a) and the model of the mixture (Fig. 1, b) [14, 26-27].

The cylinder is divided into two sectors, one of which fills all cells of the body, the other - a conductive electrolyte of extracellular fluid.

The resistance of a cylindrical body is given by

$$R = \frac{\rho L}{S} = \frac{\rho \ell^2}{V},$$

and the capacity

$$V = \frac{\rho \ell^2}{R}.$$  

The homogeneous body model does not take into account the fact that nonconducting components are distributed inside the volume of the conducting medium and therefore the current density is spatially nonuniform. Hanai (1968) proposed a model for a mixture in which biological tissue is represented as a suspension of nonconducting particles in a liquid conducting medium (Fig. 1, b) [31]. This model is valid only if the organism is sensed by currents of low frequency.

The average resistivity $\rho$ in the mixture model is described by the expression:

$$\rho = \frac{\rho_0}{(1-P)^{3/2}},$$

where $\rho_0$ – resistivity of liquid conducting medium, $P$ – percentages of nonconducting particles in the total body volume.

Bioimpedance measurement is of three types:

- local - the measurement of the impedance of an individual part of the body;
- segmental - measurement of bioimpedance of a separate part of the body;
- integral - the measurement of the bioimpedance of the whole organism.

In addition, according to the number of frequencies used in measuring the bioimpedance of the body, there are: single-frequency BIM, two-frequency, multifrequency and spectroscopy [32].

It is of interest to use the time-frequency properties of BIM signals correlated with the dynamics of the blood supply to the organism [33]. Such signals make it possible to obtain control information in real time, monitoring the time-dependent nonstationarity of the blood flow with random factorial influence (change in the volume of the vascular bed).

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Table 3. Assessment of the volume of blood loss

<table>
<thead>
<tr>
<th>The volume of blood loss (in dm³) with body weight kg</th>
<th>Volume of circulating blood %</th>
<th>Systolic blood pressure, mmHg</th>
<th>Shock index</th>
<th>Systolic blood pressure, mmHg</th>
<th>Volume of circulating blood %</th>
<th>The volume of blood loss (in dm³) with body weight kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>70</td>
<td>80</td>
<td></td>
<td>3,0</td>
<td>0</td>
<td>55</td>
</tr>
<tr>
<td>2,8</td>
<td>2,5</td>
<td>2,1</td>
<td>50</td>
<td>40</td>
<td>3,5</td>
<td>40</td>
</tr>
<tr>
<td>1,5</td>
<td>2,2</td>
<td>1,9</td>
<td>45</td>
<td>50</td>
<td>3,5</td>
<td>40</td>
</tr>
<tr>
<td>2,1</td>
<td>1,9</td>
<td>1,6</td>
<td>38</td>
<td>70</td>
<td>2,0</td>
<td>50</td>
</tr>
<tr>
<td>1,7</td>
<td>1,5</td>
<td>1,3</td>
<td>30</td>
<td>80</td>
<td>1,5</td>
<td>70</td>
</tr>
<tr>
<td>1,0</td>
<td>0,9</td>
<td>0,8</td>
<td>18</td>
<td>90</td>
<td>1,0</td>
<td>90</td>
</tr>
</tbody>
</table>

Table 4. Volume of circulating blood shortage estimation

<table>
<thead>
<tr>
<th>Hematocrit value, %</th>
<th>Deficiency of volume of circulating blood, ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>50</td>
</tr>
<tr>
<td>16</td>
<td>35</td>
</tr>
<tr>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>28</td>
<td>17</td>
</tr>
<tr>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>36</td>
<td>12</td>
</tr>
</tbody>
</table>
Mathematical justification of the method of inter-spectral correlation

Consider the result of measuring bioimpedanometry at several frequencies as random processes. It is known that when the harmonics of the original processes are correlated, the latter become spectrally nonstationary [34]. Such non-stationarity can be identified by calculating the coherence function [35], which is determined by the expression [36].

\[ \gamma_{xy}(\omega) = \frac{|f_{xy}(\omega)|}{\left[ f_x(\omega) \cdot f_y(\omega) \right]^{1/2}}, \]  

(4)

\( f_{xy}(\omega) \) – mutual spectral density of stationary coupled signals \( x(t) \) and \( y(t) \); \( f_x(\omega) ; f_y(\omega) \) – spectral densities of nonstationarity of any of the processes \( x(t) \) and \( y(t) \). Hence, a condition is obtained

\[ 0 < \gamma_{xy}(\omega) < 1 \]  

(5)

Let us now consider some random measuring signal existing on a finite interval \( T \) of its observation time. To reveal the spectral properties of such a signal, we use its two-dimensional time-frequency (on the scale "a" and the shift "b") wavelet transform, carrying out the convolution of the signal \( x(t) \) with a certain basis wavelet function \( \psi(t) \) [36].

\[ W_x(a,b) = \frac{1}{\sqrt{|a|}} \int_{-\infty}^{\infty} x(t) \cdot \psi^{(b-a)}_\omega dt \]  

(6)

For a discrete continuous wavelet transform, the convolution results will be represented by a set of wavelet coefficients \( W_{ij}(a,b) = \eta_{ij}, j = 1, \ldots, m \) \[ h \] where \( h \) is the number of scales, \( m \) is the number of shifts. It is known that such a model of a continuous wavelet transform increases the mutual correlation of the wavelet coefficients obtained [35]. To reduce the latter, we differentiate (for example, \( k \) times) the analyzing wavelet \( W[x(t)] \), which is equivalent, based on the properties of the wavelet transform, to differentiating the realization of the signal \( X(t) \).

\[ \frac{d^k}{dt^k} W[x(t)] = W \left[ \frac{d^k}{dt^k} x(t) \right]. \]  

(7)

We denote the wavelet coefficients obtained with this differentiation as \( W_{ij}(a,b) \). We will consider the basic and differentiated spectra, both realizations \( V_{ji} = W_x(a_j,b_t) \) and \( U_{ji} = W_y(a_j,b_t) \) of system \( (V,U) \) for random variables \( V \) and \( U \).

For processes \( x(t) \) and \( y(t) \), condition (5) for the coherence function (4) leads to the condition

\[ 0 < R_{VU} < 1, \]  

(8)

where

\[ R_{VU} = \frac{|K_{VU} \sqrt{\sigma_{UU} \sigma_{VV}}|^{1/2}}, \]  

(9)

\( K_{VU} \) – covariance (a joint second-order central moment) between the spectra \( V_{ji} \) and \( U_{ji} \);

\( \sigma_V^2, \sigma_U^2 \) – dispersion of spectra \( V_{ji} \) and \( U_{ji} \).

Taking into account that the coefficient of linear pair correlation \( R_{VU} \), normalized \((-1 < R_{VU} < 1)\), makes sense to remove the modulus constraint for this coefficient.

In this case, the restriction on the sign of covariance \( K_{VU} \), which is defined by expression

\[ K_{VU} = (N - 1)^{-1} \sum_{j=1}^{h} \sum_{i=1}^{m} (V_{ji} - \bar{V})(U_{ji} - \bar{U}), \]  

(10)

where \( N = h \cdot m \), \( \bar{V}, \bar{U} \) – average values of wavelet spectra \( V_{ji} = W_x(a_j,b_t) \) and \( U_{ji} = W_y(a_j,b_t) \).

Taking into account the two-dimensionality of the wavelet spectrum with respect to the frequency \( \omega \) (given by the scale) and in time \( t \) (given by a shift), we introduce factor models of the spectral nonstationarity of the process \( x(t) \).

1. Frequency nonstationarity (in scale)

\[ V_{ji}^{(t)} = \bar{V} + \delta_{ji}^{(t)} + z_{ji}^{(t)}, \]  

(11)

where \( \delta_{ji}^{(t)} \) – functional spectrum change \( V_{ji} \) along the scale axis, caused by the influence of the spectral nonstationarity factor (for a fixed observation time);

\( z_{ji}^{(t)} \) – random (residual) changes in harmonics \( W_{ji}(a_j,b_t) \) spectrum over time (for a fixed scale).

2. Temporary non-stationarity (by shift):

\[ V_{ji}^{(t)} = \bar{V} + \delta_{ji}^{(t)} + z_{ji}^{(t)} \]  

(12)

where \( \delta_{ji}^{(t)} \) – functional change in the spectrum along the shift axis (due to the nonstationarity factor);

\( z_{ji}^{(t)} \) – random (residual) changes in the spectrum \( V_{ji} \) by frequency (shift - fixed).

In the models (11) and (12) for deviations \( \delta_{ji}^{(t)}, \delta_{ji}^{(t)}, z_{ji}^{(t)} \) we can impose conditions

\[ \sum_{i=1}^{h} \delta_{ji}^{(t)} = 0, \sum_{j=1}^{m} z_{ji}^{(t)} = 0, \sum_{i=1}^{h} \sum_{j=1}^{m} z_{ji}^{(t)} = 0, \sum_{i=1}^{h} \sum_{j=1}^{m} z_{ji}^{(t)} = 0, \]  

and the conditions for the constancy of residual dispersions

\[ M \left[ z_{ji}^{(t)} \right] = \sigma_{zji}^2, \]  

\[ M \left[ z_{ji}^{(t)} \right] = \sigma_{zji}^2. \]  

(13)

Where \( M \) – sign of mathematical expectation.

With respect to the spectra \( \nu(a,b) \) and \( \nu(t,a) \) of signal \( U(t) \) and its linear transformation \( V_{ji}^{(t)} \) the coherence function can be transformed into a coefficient of normalized inter-spectral correlation (as an analog of the auto-coherence function [35]):
use of inter-spectral correlation coefficients (ISCC) for active monitoring of blood loss

The input signal when using ISCC for active monitoring of blood loss will be a sampled BIM signal \( x_i \) at several frequencies, for example, \( 20\,\text{kHz}, 100\,\text{kHz}, 500\,\text{kHz} \). In this case, \( k \) is the time reference number, \( i = 0..n \). The linearly transformed signal, in our case the first derivative, is denoted by \( dx_i \).

We perform a wavelet transformation of a signal with a window of width \( b \). The choice of the parent wavelet and the width of the window will be carried out in subsequent work. In this paper we used a Morley wavelet with a window width of 30. The results of the wavelet transform of the signal and its linear transformation will be two coefficient matrices \( X_{i,j} \) and \( dx_{i,j} \). The coefficient of spectral nonstationarity by the shift will have the form:

\[
RSM_j = \frac{\sum_{i=0}^{a-1} \left( X_{i,j} - Mx_i \right) \cdot \left( dx_{i,j} - Mdx_i \right)}{\sqrt{\sum_{i=0}^{a-1} \left( X_{i,j} - Mx_i \right)^2} \cdot \sqrt{\sum_{i=0}^{a-1} \left( dx_{i,j} - Mdx_i \right)^2}}
\]  

(14)

where \( Mx_i = \frac{1}{b} \sum_{j=0}^{b-1} X_i \), \( Mdx_i = \frac{1}{b} \sum_{j=0}^{b-1} dx_i \) - mathematical expectations on the scale of the wavelet coefficients of the signal \( X_{i,j} \) and its linear transformation \( dx_{i,j} \).

The developed method makes it possible to obtain additional information on the nonstationarity of higher-order spectra.

For example, for a second-order spectrum (a power spectrum), the spectral non-stationarity by shift will have the form

\[
RSD_j = \frac{\sum_{i=0}^{a-1} \left( X_{i,j} - Ddx_i \right) \cdot \left( dx_{i,j} - Ddx_i \right)}{\sqrt{\sum_{i=0}^{a-1} \left( X_{i,j} - Ddx_i \right)^2} \cdot \sqrt{\sum_{i=0}^{a-1} \left( dx_{i,j} - Ddx_i \right)^2}}
\]  

(15)

where \( Ddx_i = \frac{1}{b} \sum_{j=0}^{b-1} \left( X_i - Mx_i \right) \), \( Ddx_i = \frac{1}{b} \sum_{j=0}^{b-1} \left( dx_i - Mdx_i \right) \).

As an integral indicator, we can use the average value of the correlation coefficient on the observation window for the spectrum of the first

\[
RSM = \frac{\sum_{i=0}^{a-1} \left( (Mx_i - Mx) \cdot (Mdx_i - Mdx) \right)}{\sqrt{\sum_{i=0}^{a-1} (Mx_i - Mx)^2} \cdot \sqrt{\sum_{i=0}^{a-1} (Mdx_i - Mdx)^2}}
\]

(16)

and of the second order

\[
RSD = \frac{\sum_{i=0}^{a-1} \left( (Ddx_i - Bdx_i) \cdot (Bdx_i - Bdx) \right)}{\sqrt{\sum_{i=0}^{a-1} (Ddx_i - Bdx)^2} \cdot \sqrt{\sum_{i=0}^{a-1} (Bdx_i - Bdx)^2}}
\]

(17)

A significant change in the hemodynamics of the vascular bed, which can be interpreted as an external factor, can be estimated from a significant change in the coefficient of inter-spectral correlation (in the temporal region). Checking the significance of the differences in the coefficients is possible according to one of the standard statistical tests (for example, T-statistics) taking into account the given level of risk.

Approval of the developed method.

The discussion of the results.

To achieve this goal, a series of test active (with deterministic moments of the beginning and end of the selection of a fixed volume of blood) experiments was carried out. The experiment was conducted on the basis of the Military Medical Clinical Center of the Northern Region. A series of 9 measurements with different patients was performed. Selection of blood was carried out by medical personnel, volume fixed - 450 ml. Measurements of the BIM signals were carried out at 2 frequencies - 20 and 500 kHz. To obtain the primary signal, we used a four-electrode circuit for obtaining a BIM signal with four different electrode deposition options. Fig. 2 shows typical implementations of BIM signals for frequencies of 20, 100 and 500 kHz. This figure shows the boundaries separating the complete period of the patient's observation into three phases: phase 1 - absence of blood loss (initial phase); phase 2 - the presence of blood loss (active phase); phase 3 - no blood loss (end phase).

Fig. 3 shows the results of estimating ISCC (RSM, RSD) for 20 kHz, calculated from Eqs. (14, 15).

Table 5 presents the results of ISCC (RSM and RSD) estimation for the four spatial arrangements of the BIM transducers on the patient's body.
Table 6. Values of T-statistics for four options for spatial separation of electrodes on the patient’s body (frequency - 20 kHz, RSM)

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrode location</td>
<td>A third of the left forearm is the shoulder of the left arm</td>
<td>Palm-the middle of the shoulder of the left hand</td>
<td>Wrist of left hand - left ankle</td>
<td>Wrist of left hand - ankle of right foot</td>
</tr>
<tr>
<td>Conditional distance</td>
<td>d1</td>
<td>d2</td>
<td>d3</td>
<td>d4</td>
</tr>
<tr>
<td>The value of T-statistics. Phase 1-2</td>
<td>0,5711</td>
<td>0,8139</td>
<td>3,3348</td>
<td>4,4575</td>
</tr>
<tr>
<td>The value of T-statistics. Phase 2-3</td>
<td>-0,6101</td>
<td>1,9693</td>
<td>-0,5372</td>
<td>-0,5974</td>
</tr>
</tbody>
</table>

Table 6 clearly shows the decrease in ISCC for phase 2 with respect to phase 1 (T-statistics is positive). This indicates an increase in the dynamics of the spectral nonstationarity of the BIM signal over a time interval corresponding to this phase. In fact, the onset of blood loss is accompanied by a decrease in ISCC with respect to the previous phase (phase 1), and the end of blood loss leads to an increase in ISCC with respect to phase 2. In Table 6, only one (smoothed) T-statistics can be considered a miss, since its sign for phase 2-3 is positive. For Table 6, the RSM coefficient was used, because it was for him, in contrast to the RSD coefficient, of Table 5, that there was a qualitative dynamics of the change in the ISCC during the transitions from phase 1 to phase 2 and from phase 2 to phase 3. Table 6 is compiled taking into account the ranking (by increasing the value) of the geometric distances between the electrodes, which corresponds to the condition

\[ d_1 < d_2 < ... < d_4. \] (18)

It can be seen from Table 6 that the maximum value of the T-statistic carrying information on the change in the ISCC at the boundary of the two phases is maximal for the distance \( d_4 \) (\( T = 4.4575 \)). This distance is geometrically maximized and allows us to justify the choice of the sensor placement option on the patient’s body. In fact, this is the task of planning the metrological component, associated with the conditional optimization of the variant with the maximum of the objective function in the form of T-statistics. This optimization is conditional, since the number of initial conditions is limited in this variant by the number of patients, although the total number of variants tends to infinity. However, any restriction of the options makes it possible, for example, on the basis of Table 6 to choose a variant that is close to known biophysical models, supported by maximizing T-statistics. Analysis of the results presented in the second line of Table 6 indicates their ambiguity, which allows us to conclude that the use of ISCC is effective only in problems of detecting the beginning of blood loss. Table 6 gives the possibility of not only a qualitative (on the sign of T-statistics) but also a quantitative (by its magnitude) analysis of the options for choosing one of the two solutions:

\[ \gamma_0: \text{there is no difference between the ISCC of the compared phases;} \] (19)

\[ \gamma_1: \text{ISCC of neighboring phases are statistically different.} \] (20)
In the case of a positive T-statistic, the validity of the choice of the solution \( y_1 \) (the onset of hemorrhage) is based on the normative requirements of the theory of statistical decisions \([37, 38]\). When T-statistics exceed the critical value for a given level of significance. For the level of significance \( \alpha = 0.05 \) The value of the critical statistics is 1.645.

Thus, the planning of an experiment for active monitoring of the appearance of blood loss should provide the maximum length of the path for the passage of the scanning current of the BIM signal, by selecting the locations for fixing the electrodes according to the variant "left hand-right foot".

**Conclusions**

The conducted studies indicate the prospects of an information-measuring procedure for monitoring dynamic parameters of non-stationarity of BIM signals in problems of detecting hidden bleeding. Particularly important is the possibility of automating active monitoring in the framework of already existing computerized medical information systems. Such automation is based on the construction of a plan for a biomedical experiment in which a sliding observation of the BIM signal using a dual observation window is used. This window represents two consecutive time intervals for each of which an independent value of the ISCC is calculated (for example RSD), and a comparison of these ISCCs is performed using T-statistics. If in the course of the comparison a solution \( y_1 \) is obtained according to the models (19, 20), then the beginning of the blood loss corresponds to the positive sign of the T-statistic. In this case, the statistical significance of a reliable solution will not be less than 0.95.

**Reference**

Можливості застосування і планування біометричного дослідження для визначення об'єму витрат воды

В майбутньому може бути використано біоімпеданський метод для визначення об'єму витрат воды. Відомо, що при випадках водяних витрат інтенсивними витратами води в організмі, біоімпеданський метод може бути ефективним інструментом для оцінки об'єму витрат відшкодування. Проте, до цього періоду, необхідно здійснити додаткові дослідження в цій галузі для підвищення ефективності методу.

Враховуючи ці обставини, можемо зробити висновок, що біоімпеданський метод може бути ефективним інструментом для визначення об'єму витрат воды. Проте, до цього періоду, необхідно здійснити додаткові дослідження в цій галузі для підвищення ефективності методу.