

*artificial heart, ventricular assist device (VAD),  
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## **DETERMINATION OF STROKE VOLUME OF THE VENTRICULAR ASSIST DEVICE USING BIOIMPEDANCE METHOD**

The stroke volume of pulsatile ventricular assist device (VAD) is one of the key clinical indicators to evaluate the adequacy of the process of mechanical heart assistance and ensuring the patient's safety. In order to evaluate the volume changes in VAD blood chamber, a bioimpedance method was applied, based on volumetric electric conductivity of the blood. Periodic changes in VAD volume during its operation result in a pulsatile impedance waveform; its amplitude in the subperiods of filling and ejection correlates with blood volume in the chamber. The paper presents the method of analysis of the bioimpedance signal recorded in VAD blood chamber with a reference to the classical method of analysing the cardioimpedance signal from the patient's thorax. The paper also presents the results of determining stroke volume of blood chamber based on an empirical formula that has been developed.

### 1. INTRODUCTION

Natural heart assistance is applied in cases of serious heart injuries when efficiency of the heart is not enough to sustain vital functions of the body. Ventricular assist device (VAD) support is provided while the patient is waiting for transplantation or in order to regenerate the cardiac muscle [1]. At present, the most commonly used VAD is the extracorporeal pneumatically controlled pulsatile prosthesis. VAD contains a blood chamber - the space with blood; its volume changes periodically due to the movement of the flexible membrane. Membrane movement is forced by pressure change in the pneumatic part of VAD.

In order to be able to monitor VAD operation, it is of crucial importance to know pressure changes in VAD and the stroke volume, which are clinically significant indicators of blood pumping effectiveness [2].

Within the Program "Polish Artificial Heart", experimental and analytical research was conducted in order to develop methods of evaluating the hemodynamic parameters of the VAD. Apart from the acoustic method of measuring the degree of filling of the blood chamber [3] and ultrasonic measurement of blood flow in the aortic connector, the research also elaborated on the use of the bioimpedance method to determine the stroke volume in each working cycle of VAD.

The bioimpedance method, also called impedance rheography, is widely used in medical diagnosis, for example to evaluate body segments volume, in particular the circulatory system. Impedance cardiography

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(ICG) is becoming an increasingly reliable and more and more frequently used method for noninvasive determination of cardiac stroke volume (SV) [4].

The bioimpedance method is based on passive electrical properties of biological tissues. As tissue characterized by high conductivity, blood may be regarded as a suspension of erythrocytes and leukocytes in the plasma. Plasma and cytoplasm are characterized by resistance properties. The cell membrane of the erythrocytes with dielectric properties along with cytoplasm and plasma make capacitive structures [7]. The impedance of biological tissue can be measured by means of application current with the frequency of several dozen kHz and constant amplitude in the range  $100\mu A_{RMS} \div 2mA_{RMS}$ . The voltage generated as a result of electric current flow contains information about the value of impedance and its changes over time for the tested tissue. The measured impedance depends on blood volume in the tested area, temperature and blood resistivity, affected by spatial orientation of erythrocytes and by hematocrit (HCT) [5].

The bioimpedance method has been proposed to determine the stroke volume of the pulsatile heart prosthesis. Impedance is measured by means of the dual-electrode method. Metal rings of inlet and outlet valves are used as measuring electrodes. The periodic change of the cross-section of the conductor caused by a change in VAD volume during movements of the flexible membrane result in changes of the measured impedance. Impedance increases along with the decreasing blood volume in VAD. An assumption has been made that the bioimpedance signal in the period from the end of the filling phase until the end of the ejection phase, makes it possible to determine the stroke volume for each working cycle of VAD.

## 2. THE EXPERIMENTS

A series of tests were made on an in-vitro flow test stand with the use of animal blood. The experiments were primarily aimed at determining the impact of phenomena related to pulsatile blood flow through the VAD on the features of the bioimpedance signal [6].

The laboratory equipment provided by the Foundation of Cardiac Surgery Development in Zabrze, made it possible to introduce changes to the configuration of the flow test stand as well as to the spots where sensors for reference measurements were connected. Moreover, full analytical support was guaranteed, necessary to maintain the required blood parameters. Specially designed and dedicated measurement devices were used for the tests. The measuring module consisted of an application current source with high amplitude stability, as well as a circuit to receive input signal. A computer application enabled the visualization and recording of the bioimpedance signal, pressure signals and the signal from the reference volume flow meter Transonic TS206. The computer application was provided with analytical tools to determine the dependences between signals, the characteristic points, as well as to measure the amplitude and time parameters of the signals. The basic configuration of the flow test stand is shown in Fig. 1.

The following signals were recorded during the tests: the bioimpedance signal (REO), the pressure signal in the blood chamber (P2) and in the outlet cannula (P3), as well as the blood flow signal in the outlet cannula (FLOW) at various levels of VAD filling.

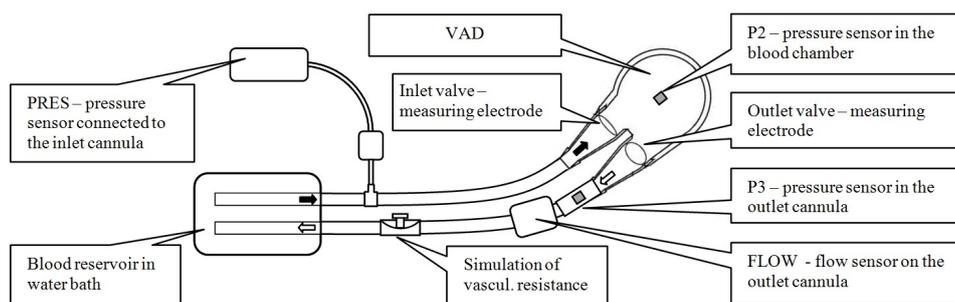


Fig. 1. Flow test stand.

During the measurements, animal blood with marked hematocrit (HCT) was used. HCT was changed in the entire range of physiologically occurring values. Reference values of VAD stroke volume were determined based on the flow waveform for assumed ejection periods. The beginning and the end of the ejection corresponded respectively to the opening and closing of the aortic outlet valve. The tests made it possible to get to know the features of the signals in characteristic modes of VAD operation: complete filling - complete ejection, complete filling - incomplete ejection and incomplete filling - complete ejection. A simulation was also made of the impact of the natural heart on the measured impedance values in VAD, as well as on the shape of the recorded bioimpedance waveforms.

The results of the experiments have confirmed the assumption that the amplitude of the impedance waveform from the end of the filling phase until the end of the ejection phase correlates with the blood volume in the chamber. However, during opening and closing of the valves, the bioimpedance signal is impacted by volume changes, as well as by changes in blood resistivity as a result of changed spatial orientation of erythrocytes. It is impossible to determine the chamber volume based on the analysis of the amplitude of the bioimpedance signal in these subperiods. The results of the tests also indicate that a reliable evaluation of chamber volume will be possible if the working cycles of the natural heart and VAD are synchronized and the ejection phases do not overlap for a while. Within the experiments on the flow test stand, 69 recordings of signals for various configurations of the flow system, various HCT values and various stroke volumes of the chamber measured as a reference were obtained altogether. The recordings provided a basis for defining the position of the characteristic points of the bioimpedance signal, as well as for developing an empirical formula to determine the value of VAD stroke volume.

### 3. ANALYSIS OF BIOIMPEDANCE SIGNALS AND DETERMINING THE STROKE VOLUME

#### 3.1. IMPEDANCE CARDIOGRAPHY (ICG)

The fundamentals of determining the stroke volume of the heart by means of impedance cardiography are based on models and dependences developed many years ago [10]. Nyboer was the first person to use the bioimpedance technique to examine tissue volume. He found out that periodic changes in the volume of arterial vessels in the arm, caused by pulsatile blood flow, cause changes of the measured impedance. In order to model the discovered properties, he made the following assumptions:

- the artery is modelled by means of a cylinder filled with blood with permanent resistivity,
- owing to the blood inflow, the volume of the artery changes, but only in the radial direction; its length remains the same,
- the diameter of the artery increases simultaneously in the entire examined area,
- the electric current is applied toward the axis of the cylinder, the current density is the same in the whole area.

Based on the aforementioned assumptions, Nyboer's formula was created, providing a basis for the bioimpedance method (1).

$$\Delta Z = \frac{\Delta V}{\rho \cdot \left(\frac{L}{Z_0}\right)^2} \quad (1)$$

The formula describes a change of impedance  $\Delta Z$  caused by a change of volume  $\Delta V$  as a result of blood inflow to the area of length  $L$ . Electrical parameters of the blood are taken into consideration in resistivity of plasma  $\rho$ ; its value is assumed to be  $0.63[\Omega m]$ .  $Z_0$ , so-called base impedance, stands for the impedance of blood in the examined area without any volume changes.

In order to determine the stroke volume of the heart, the bioimpedance measurement must be carried out in the thorax. The measuring electrodes should be placed at the basis of the neck and at the level of the xiphoid process and encompass the area of the heart, aorta and pulmonary artery. In the first attempts to determine the stroke volume with the bioimpedance method carried out by Kubicek, the simplest,

cylindric model of the thorax was used [8]. It was assumed that the obtained waveform of impedance change  $\Delta Z$  results only from volume changes in the heart and large vessels and that blood resistivity during flow is constant. However,  $\Delta Z$  in formula (1) is the value of impedance change that would occur if blood only flowed in to the tested area, without any outflow. In a real circulatory system, the pulse waveform spreads on a permanent basis. At the beginning of the ejection phase, the blood inflow is very strong, then subsides to give way to outflow. Hence, the maximum value of impedance change on the bioimpedance curve is understated [9]. In order to determine the actual impedance change, extrapolation of the rising slope of the bioimpedance curve was applied, based on the assumption that blood inflow during ejection has a dominating impact on the shape of the cardioimpedance cycle. Fig. 2 presents an electrocardiogram ECG, the pressure in the aorta  $P_{aorta}$ , the impedance change curve REO, as well as the derivative of the bioimpedance curve ICG for a single cardiac cycle. The figure also demonstrates the way of determining the actual impedance change. By way of simple mathematical transformations, dependence (2) is obtained.

$$\Delta Z = \left( \frac{dZ}{dt} \right)_{max} \cdot VET \quad (2)$$

where:  $dZ/dt$  - amplitude of the systolic waveform on the derivative of the bioimpedance curve,  
 $VET$  - ventricular ejection time - duration of the ejection phase.

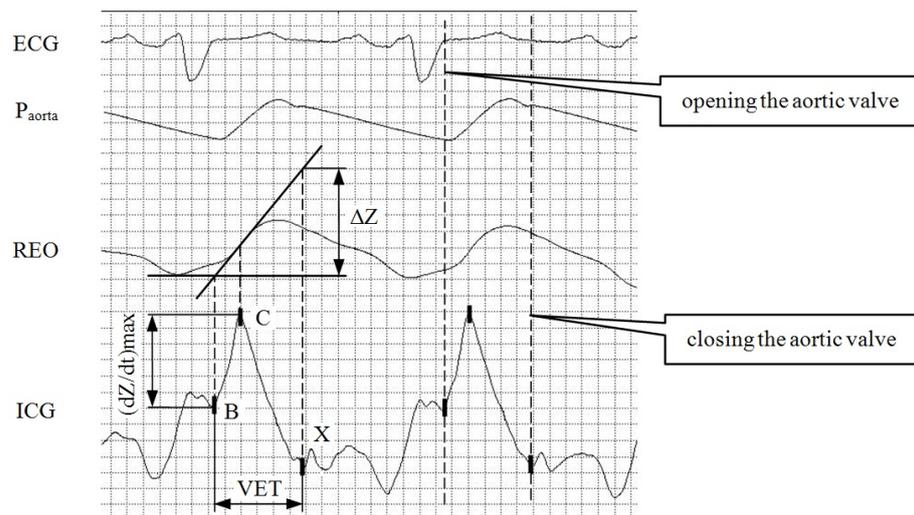


Fig. 2. Physiological signals during a single cardiac cycle and the method of determining the actual impedance change.

By using dependences (1) and (2), we obtain Kubick's formula (3) which provides a basis for determining the stroke volume of the heart with the bioimpedance method.

$$SV = \rho \cdot \left( \frac{L}{Z_0} \right)^2 \cdot \left( \frac{dZ}{dt} \right)_{max} \cdot VET \quad (3)$$

In order to calculate  $dZ/dt$  and  $VET$ , it is necessary to determine characteristic points B, C and X on the derivative of the bioimpedance curve (Fig. 2) which has become a key bioimpedance signal called ICG.

Research later performed by Bernstein and Sramek to improve the precision of determining the volume stroke, led to modification of Kubick's formula [11], [12]. The model of a truncated cone was used for better modelling of the examined area of the thorax. Moreover, individual features were included in the dependences used to determine the stroke volume, such as the patient's height, weight and sex. However, the fundamentals of the ICG signal analysis, i.e. the determination of characteristic points specifying the subperiods of the ejection phase, have remained unchanged.

## 3.2. DETERMING THE STROKE VOLUME OF THE VAD

The described simple models at the basis of impedance cardiography (ICG) do not take account of several factors characteristic of changes in blood impedance in VAD blood chamber. The space with blood has a complex shape which depends on the position of the membrane and changes its volume during operation. Assuming that the measuring electrodes are in a permanent position, only the cross-section of the conductor is subject to change. Impedance increases along with the decrease of blood volume in the chamber. Volumetric conductivity has a dominant impact, however, we ought to also provide for the changing blood resistivity due to the spatial reorientation of erythrocytes during blood inflow and ejection in the chamber. The fact that impedance is measured in a restricted area of the blood chamber and does not include any other elements of the circulatory system, simplifies the analysis of the occurring phenomena. It has been assumed, based on experimental results, that the bypassing of impedance of the chamber through the cardiovascular system, when the natural ejection phases of the heart and chamber do not overlap, affects the bioimpedance signal amplitude only [6].

Figure 3 demonstrates the recordings of pressure P3 and flow FLOW in the outlet cannula of the chamber and bioimpedance signal REO. The comparison of the shapes of the REO signal recorded in VAD, as well as from the patient's thorax and the recordings of pressures in the outlet cannula and in the aorta (Fig. 3 and Fig. 2) depict the discrepancies in the nature of signal changes at the beginning and end of the ejection phase.

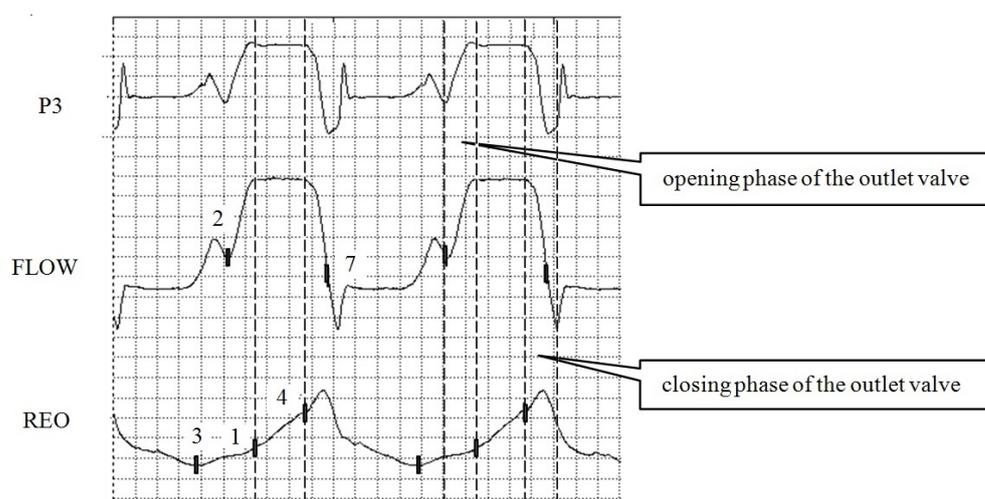


Fig. 3. Signals during VAD's working cycle and position of characteristic points.

In the case of the cardioimpedance signal REO with smooth shapes, the method based on the analysis of the ICG derivative makes it possible to determine with precision the position of characteristic points (Fig. 2): opening of the aortic valve (point B), maximum blood ejection speed (point C) and closing of the valve (point X). The recorded signals are not distorted by change in blood resistivity during opening and closing of the aortic valve.

The case is different for VAD. Owing to dynamic pressure changes during opening and closing of the valves, blood flow is not laminar and local turbulences occur. Changes in the spatial orientation of the erythrocytes during turbulent flow affect blood resistivity. Therefore in the opening and closing subperiods, the bioimpedance signal is affected both by volume changes and by changes in electrical parameters of the blood, caused by changed spatial orientation of the erythrocytes. The bioimpedance signal in these subperiods cannot be used to evaluate VAD volume.

In order to determine the characteristic points of the bioimpedance signal specifying the scope of impedance changes connected with the changing VAD volume, it is necessary to record simultaneously the pressure signals in the blood chamber or in the outlet cannula. Points 1 and 4 on the bioimpedance signal REO (Fig. 3) correspond to extreme plateau points on the pressure curve in the outlet cannula.

They define the scope of blood impedance change related to the moving of the membrane, so to the change of the blood chamber volume. When determining the position of characteristic points 1 and 4, we omit the subperiods of the ejection phase; the subperiods are characterized by significant pressure changes. Point 3 is the value of base impedance  $Z_0$  which depends on the volume of the filled chamber and the frequency of its operation. During the experiments, points 2 and 7 on the FLOW signal (Fig. 3) were used to determine with precision the beginning and end of the ejection phase and to calculate the reference value of VAD stroke volume (using the reference measurement of the FLOW waveform).

What matters is that during the isobaric subperiod of the ejection phase, only blood outflow from the chamber occurs, hence impedance change is a precise reflection of chamber volume change. There is no simultaneous blood inflow and outflow, typical of cardioimpedance measurements from the surface of the patient's body; as a result, the understated change of impedance  $\Delta Z$  requires a correction. Hence, determination of VAD stroke volume can be based directly on the bioimpedance signal.

Dependence (4) shows the formula used to calculate the stroke volume of the blood chamber based on characteristic points marked on the bioimpedance signal REO.

$$SV_{imp} = \alpha \cdot \frac{\overline{\Delta Z}}{Z_0^2} \quad (4)$$

where:  $SV_{imp}$  - VAD stroke volume,

- $\alpha$  - calibration coefficient depending on the parameters of the flow system and HCT,
- $\overline{\Delta Z}$  - the average impedance increase during the blood ejection phase from the blood chamber, defined on the basis of points 1 and 4 on the REO signal,
- $Z_0$  - base impedance, defined by the value of REO signal in point 3.

Stroke volume  $SV_{imp}$  of the chamber for 69 signal recordings gathered during the experiments was calculated by means of the developed algorithm for the analysis of the bioimpedance signal obtained from the blood chamber and by means of formula (4). All recordings were made on an in-vitro flow test stand, for various configurations of the flow system, different HCT and differing VAD stroke volume. The obtained results are shown in Fig. 4.

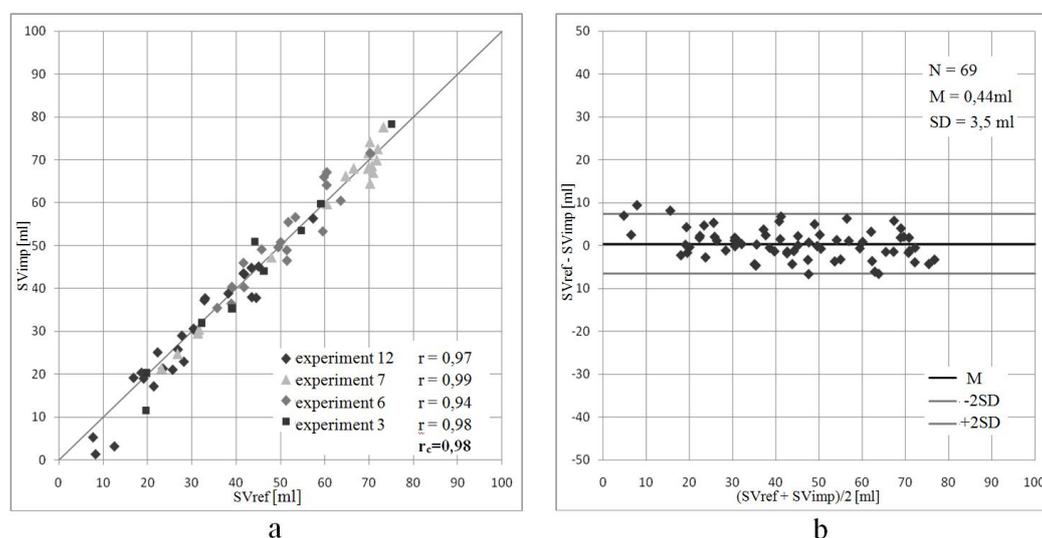


Fig. 4. The plot of  $SV_{imp}$  with reference to  $SV_{ref}$  (a) and a Bland-Altman plot (b).

Fig. 4a shows the plot of stroke volume  $SV_{imp}$  determined by bioimpedance method with reference to volume  $SV_{ref}$  calculated from the FLOW signal from the ultrasonic volume flow meter (Transonic TS206). The correlation coefficients determined for results from specific experiments are different from one another from  $r=0,94$  for results from experiment 6, to  $r=0,99$  for results from experiment 7. A high value of the correlation coefficient  $r=0,98$  has been obtained for all results.

Fig. 4b depicts Bland-Altman plot of the discrepancies in the values of stroke volume determined with the use of the impedance method and reference measurement. The standard deviation from the mean value was  $SD = 3,5$  ml. The biggest measurement errors occur for small stroke volume values. They can be justified by an extremely low amplitude of impedance changes and increased impact of flow turbulences occurring in ejection subperiods characterized by significant pressure changes in the chamber.

#### 4. CONCLUSIONS

The experiments have demonstrated that it is possible to use periodic changes of the bioimpedance signal, caused by VAD volume changes, to determine the stroke volume. High concordance of the results obtained by means of the bioimpedance method in relation to reference measurements should be pointed out. This is a proof that an appropriate algorithm to determine characteristic points on the bioimpedance signal has been developed and that the correct empirical formula has been proposed to calculate stroke volume. Nevertheless, confirmation of the practicality of the method requires experiments on live organisms, as well as the development of an effective and acceptable in clinical conditions method of determining calibration coefficients necessary for VAD stroke volume measurements.

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