

Impedance techniques in medical practice

Techniki impedancyjne w praktyce lekarskiej

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Abstract

Hemodynamics monitoring provides important information about the performance of the heart, including preload, afterload, contractility, and pump efficiency. The most popular techniques used to be based on invasive methods, such as the Fick's formula, thermodilution, and invasive intravascular pressure monitoring, and noninvasive ultrasound-based methods such as echocardiography, transesophageal Doppler monitoring of stroke volume, and peripheral arterial tonometry. Impedance methods combined with opportunities provided by telemedicine could bring new quality to the medical practice.

Key words: impedance cardiography, rebreathing, hemodynamics, telemedicine

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Introduction

Conventional, gold standard methods to evaluate haemodynamic parameters including measurements of stroke volume and blood pressures in the vascular bed are associated with risks typical for invasive procedures and are limited to the hospital settings. A search continues for non-invasive methods which could be used in the outpatient settings, with automated analysis of the collected data. A widely available and established method is echocardiography. However, it is characterized by a long learning curve and requires expensive equipment. The ideal method would be reproducible, characterized by a short learning curve, feasible in the outpatient settings, and relatively inexpensive.

Current efforts focus on several areas. One approach is to use techniques based on the evaluation of respiratory gases. These measurements may allow evaluation of the respiratory function and indirect calculation of haemodynamic parameters. Based on multiple studies, methods of estimating cardiac output based on changes in respiratory gas parameters have been introduced to the clinical practice. The technique of estimating stroke volume based on changes in carbon dioxide in breathing air is described by

the Gedeon-Capek equation [1, 2]. It has been introduced to the clinical practice, e.g., in the intensive care unit of the OLVG hospital in Amsterdam [3].

An extension of this technique is the inert gas rebreathing device, the Innoco[®] CO (Cosmed, Italy) [4]. This device is filled with a breathing gas mixture containing oxygen, 0.5% nitrous oxide (N₂O) and 0.1% sulfur hexafluoride (SF₆). Measurement of differences in gas concentrations during breathing allows calculation of the effective blood flow through the pulmonary vascular bed. This stroke volume measurement method was employed, among others, in the Columbia space shuttle. The technique was used to study pulmonary blood flow in patients with lung fibrosis [5]. Comparison with cardiac output measurements by magnetic resonance imaging showed good concordance in both lung disease patients and healthy individuals [6].

Carbon dioxide measurements in breathing air were also used in studies on the effect of posture on haemodynamic parameters [7].

Another approach to evaluate the cardiopulmonary system using breathing air gas measurements is the cardiopulmonary exercise test. Assessment of the composition of the exhaled air during exercise allows calculation of

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numerous body function parameters. The cardiopulmonary exercise test allows evaluation of exercise tolerance and provides information regarding the overall body response, including pulmonary, cardiovascular, and skeletal muscle response to exercise. The obtained metabolic and ventilation parameters correlate with increasing symptoms of exercise intolerance (dyspnoea, acid-base balance abnormalities, and exhaustion) [8–10].

In the 20th century, a method based on measurements of impedance changes, with the chest being considered a volume conductor of an electric current, was used for the first time in studies on the cardiovascular system. During application of a 25–100 kHz current, electrical impedance changes occurring with changes in blood volume during the cardiac cycle are measured. This non-invasive method is called impedance cardiography (ICG) or reocardiography.

Physical basis of ICG

The human body is a biological material. The behaviour of biological objects in the electric field has specific features. Electric current flow through a biological material, a human body, generates resistive and capacitive impedance. The net effect is called mutual impedance. Each tissue has specific characteristics of these impedance components during alternating current application, and the frequency spectrum of these impedance components allows tissue differentiation. These tissues include the circulating blood and air within the chest. The mutual relation between these two components is called chest impedance.

The parameters used in impedance techniques include complex permittivity (describing storage and loss properties of biological materials when placed in an electric field), conductivity, and relative electrical permittivity. Biological materials have variable characteristics depending on electric current frequency, as shown in Figure 1 [11].

Chest impedance includes a component related to changes in the circulating blood volume. Blood volume changes during the cardiac cycle lead to changes in chest electrical impedance. Blood is an inhomogeneous suspension. Electrical properties and orientation of erythrocytes result in changing blood electrical conductivity during circulation phases. During current flow with alpha dispersion in the frequency range of 10–100 kHz, erythrocytes generally do not conduct an electric current. Brownian motion results in their random orientation at rest. An electric current running along the vessel must be conducted around the erythrocytes, which results in low electrical conductivity. Blood flow results in parallel erythrocyte orientation. In these settings, an electrical current runs against a lower erythrocyte surface, with a resulting increase in conductivity [12]. Electrical impedance was found to be related to the haematocrit. Impedance cardiography was used in practice before its theoretical physical basis was established. The theoretical basis

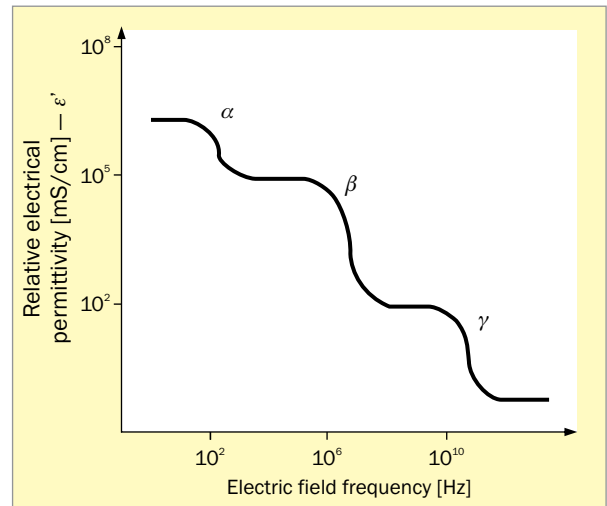


Figure 1. Relative electrical permittivity ϵ' [mS/cm] of a striated muscle in relation to the electric field frequency [Hz] (adapted from [11])

of impedance changes resulting from conductivity changes in a given location was developed by Geselowitz [13] and Lehr [14], and 8 years later expanded by Moratelli [15]. The recording of changes in chest impedance during the cardiac cycle was called impedance cardiography or reocardiography. In classical bioimpedance models, the chest was modeled as a cylinder or a truncated cone.

The difference between the classical measurement algorithm by Kubiček (chest as a cylinder) and the Šramek-Brenstein algorithm (chest as a truncated cone) lies in considering a different geometrical solid as an approximation of the chest shape.

The Kubiček formula (chest as a cylinder) is as follows:

$$SV = \rho \frac{L^2 \times dz/dt \max \times T}{Z_0^2}$$

SV – stroke volume; ρ – blood specific electrical resistance factor/determined individually based on haematocrit; L – distance between electrodes in centimeters; dz/dt max – maximum amplitude of the first derivative of impedance (in [Ω /s]); Z_0 – baseline impedance (in [Ω]); T – left ventricular ejection time (in [s])

The Šramek-Brenstein formula (chest as a truncated cone) is as follows:

$$SV = \rho \frac{L^3 \times dz/dt \max \times T}{4.25 Z_0}$$

SV – stroke volume; ρ – blood specific electrical resistance factor/determined individually based on haematocrit; L – chest length; dz/dt max – maximum amplitude of the first derivative of impedance (in [Ω /s]); Z_0 – baseline impedance (in [Ω]); T – left ventricular ejection time (in [s])

The basic Kubiček formula was modified, yielding the Šramek-Brenstein formula [16].

Practical applications of ICG

The bioimpedance technique was used to monitor cardiac performance and cardiovascular haemodynamics in the astronauts of the Apollo space program [17]. After numerous modifications, ICG is still used for research purposes [18, 19]. It was employed in studies in patients with heart failure, hypertension [20, 21], children with congenital heart disease [22], and individuals with sleep apnea [23, 24], chronic obstructive pulmonary disease (COPD) [25, 26], and pulmonary hypertension [27, 28]. Despite significant limitations of ICG [29], the method has been approved by the US Food and Drug Administration. The clinical uses of ICG covered under the Medicare program (CMS Coverage Issues Manual [50–54], 2005 Federal Register) include:

- monitoring of fluid balance in heart failure;
- management of drug-resistant hypertension;
- adjustment of pacemaker settings;
- evaluation of patients receiving inotropic drugs;
- evaluation of patients after cardiac transplantation or myocardial biopsy;
- differentiating between cardiac and pulmonary causes of acute dyspnoea.

In Poland, ICG was approved by the National Health Fund on Jan 1, 2010 as a useful technique (TISS-28 scoring) for monitoring haemodynamic changes in intensive care units. Measurements of changes on electrical chest impedance were performed during high frequency alternating current application using the four electrode configuration. For example, the Niccomo™ device (Medis,

Germany) used four dual application/sensing electrodes to apply 1.0–4.0 mA current at 25–75 kHz. The receiving electrodes recorded the electrocardiogram and changes in electrical impedance.

In the analyses of the results, the following parameters were used:

- preload – thoracic fluid content (TFC);
- stroke volume (SV);
- cardiac output – $CO = SV \times HR$;
- systolic, diastolic, mean pressure;
- afterload as described by systemic vascular resistance (SVR).

The above parameters were automatically indexed for the body surface area of the studied individual.

Cardiac contractility was described using the following parameters:

- Heather index (the ratio of peak ventricular ejection flow [$dz/dt \max$] to the period of increasing first derivative of impedance with respect to time [electromechanical time interval, or time from the onset of ventricular depolarization to $dz/dt \max$]);
- preejection period (PEP);
- left ventricular ejection time (LVET);
- PEP/LVET ratio (Weissler index).

The results were correlated with echocardiographic and clinical evaluation.

The PhysioFlow Q-Link device used a different electrode configuration (Figure 3 [30]).

Dyspnoea is one of the most common symptoms of heart failure. However, differentiating between various

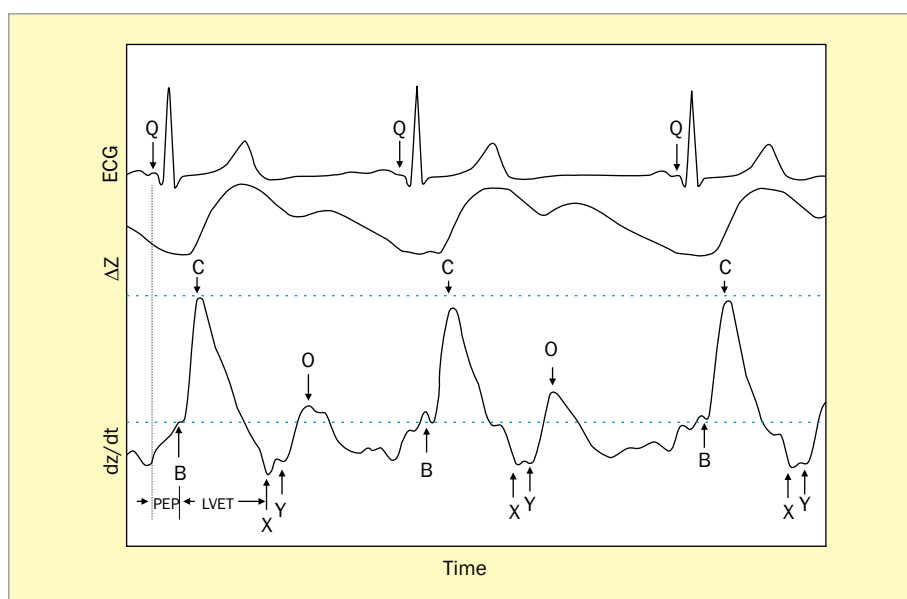


Figure 2. Impedance cardiogram and electrocardiogram. Temporal and amplitude relations; B – aortic and pulmonary valve opening; C ($dz/dt \max$) – peak blood flow through the aortic valve; ECG – electrocardiography; LVET – left ventricular ejection time; O dz/dt – is the effect of limited ventricular ability to accommodate venous inflow during early diastole; PEP – preejection period; Q – onset of ventricular depolarization; X – aortic valve closure; Y – pulmonary valve closure (adapted from [11])

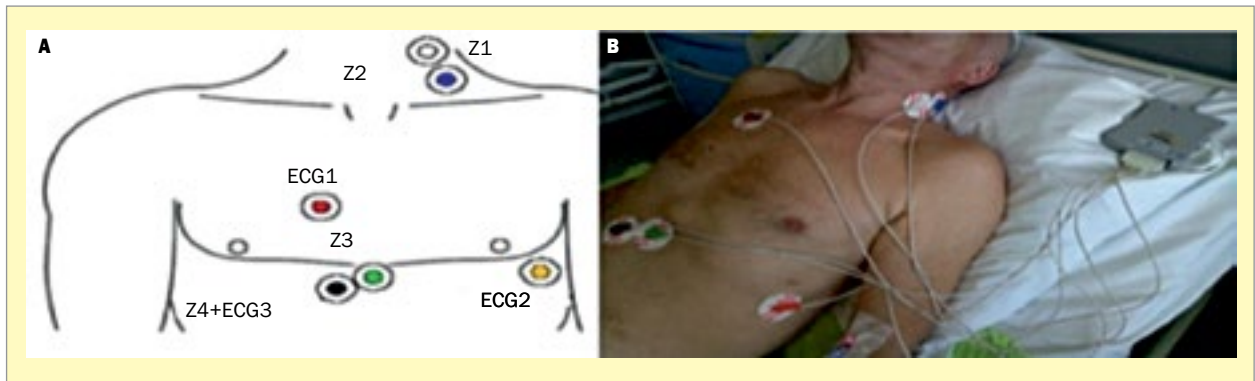


Figure 3A, B. Chest electrode configuration for the measurements of chest impedance changes using the PhysioFlow Q-Link device (Manatec Biomedical, Paris, France). The scheme and photography from the author's own research; Z1, Z4 – current electrodes; Z2, Z3 – voltage electrodes; ECG – electrocardiography (adapted from [30])

causes of dyspnoea continues to be a major challenge in the clinical practice. Dyspnoea is the most common symptom in patients presenting to emergency departments. Early accurate diagnosis may be of a major importance for selecting appropriate treatment. ICG as a non-invasive modality for the evaluation of the cardiovascular system was studied as a tool to support diagnostic and therapeutic decisions.

In the Impact of Impedance Cardiography on Diagnosis and Therapy of Emergent Dyspnea (ED-IMPACT) trial, the utility of ICG for differentiating between various causes of dyspnoea in the emergency department was evaluated [31]. ICG was performed in two academic centres in 89 subjects above 65 years of age who presented with dyspnoea. A complete clinical examination was performed, and haemodynamic parameters obtained from ICG in the emergency department were analyzed. ICG had been performed before laboratory test and chest X-ray results were available. The number of changes in diagnoses and treatment modifications following unblinding of ICG haemodynamic data was evaluated. A comparison of haemodynamic parameters showed significant differences between the group with predominant heart failure and the groups with COPD and other conditions ($p < 0.02$). Thoracic fluid content was highest in the group with heart failure (38.5 ± 12.3 vs. 30.0 ± 6.17 vs. 30.4 ± 5.6 $\text{k}\Omega\text{m}^{-1}$, respectively). SVR was highest in the group with heart failure (1772 ± 565 vs. 1361 ± 407 vs. 1789 ± 638 $\text{dyn} \times \text{sec} \times \text{cm}^{-5}$, respectively).

The cardiac index (CI) was highest in the group with COPD (2.39 ± 0.56 vs. 3.08 ± 0.57 vs. 2.48 ± 0.65 $\text{L}/\text{min}/\text{m}^2$, respectively).

Patients with heart failure had higher SVR, TFC, and lower CI, while patients with COPD had low TFC, SVR, and higher CI. Exacerbated heart failure and COPD were the final diagnoses in 43 (48%) and 20 (22%) patients, respectively. Data from ICG changed the diagnosis in 12 patients [13%;

95% confidence interval (CI) 7% to 22%] and the therapy in 35 patients (39%; 95% CI 29% to 50%). The authors noted that this simple test clearly supported diagnostics and therapeutic decisions.

Another randomized IMPEDANCE-HF trial evaluated whether lung impedance monitoring would reduce hospitalizations in patients with acute exacerbated heart failure. This blinded study was performed in two centres [32]. The study included 256 patients with chronic heart failure and, reduced left ventricular ejection fraction ($\leq 35\%$) and New York Heart Association (NYHA) class II–IV symptoms. All patients were hospitalized due to acute exacerbated heart failure during the previous 12 months. They were randomized to the impedance monitoring group or the usual care group. Telemedical thoracic fluid content monitoring was performed using the electrode configuration shown in Figure 4.

The primary endpoint was hospitalization due to exacerbation of the primary condition. Secondary endpoints were hospitalizations due to other causes and deaths. Significantly fewer patients were readmitted in the monitoring group (67 vs. 158, $p < 0.001$), with lower cardiac and overall mortality. These results suggest that the impedance monitoring is useful in the outpatient setting.

Other authors used a four-electrode configuration to study changes in thoracic fluid content, particularly in lungs. Two electrodes (current and voltage) are placed below the right scapular angle, and two more below the right clavicle in the right parasternal line. Changes in electrical impedance compared to the measurement at the optimal clinical status of the patient indicate an increase or reduction of thoracic fluid content [33]. An increase in thoracic fluid content results in an impedance drop compared to baseline, while a decrease in thoracic fluid content will be reflected by an increase in impedance. In the study, a telemetric system to monitor changes in

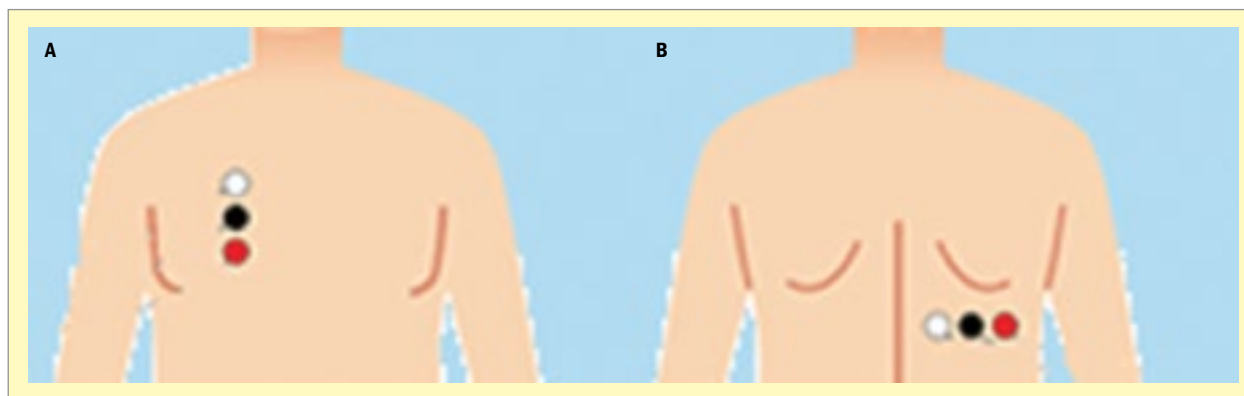


Figure 4A, B. Electrode configuration for measurements of changes in thoracic fluid content based on chest impedance measurements (adapted from [32])

lung fluid content was used. Data obtained during 90-day monitoring in patients discharged after heart failure decompensation were compared to a similar period without monitoring. A reduction in the hospitalization rate by 87% in men and 79% in women was found in the monitoring group. The authors concluded that telemetric lung fluid content monitoring had a significant diagnostic potential to reduce the rate of recurrent admissions for acute decompensated heart failure.

Another group of authors evaluated the utility of telemedical chest impedance measurements to detect fluid accumulation. The recorded data were automatically sent via a cellular phone to the monitoring center. The monitoring was undertaken in 106 patients for 45 days, followed by a follow-up of 75 days. The algorithm used was found to be 87% sensitive and 70% specific. As highlighted by the authors, the study subjects transmitted data on thoracic fluid content changes daily without any significant technical issues [34].

Use of telemetric systems has been a subject of studies undertaken by The National Centre for Research and Development in Poland. ICG was used to monitor cardiac performance in patients with ischaemic stroke in the PBS2/A3/17/2013 project “Internet platform for data integration and cooperation of medical research teams for the purposes of stroke units”. Currently, the STRATEGMED3/305274/8/NCBR/2017 project is underway under the AMULET acronym [35], “A new model of medical care using modern techniques of noninvasive clinical evaluation and telemedicine in patients with heart failure”. Impedance methods were used to monitor therapy in patients with heart failure. In this randomized study, the effect of ICG monitoring on cardiovascular mortality and recurrent hospitalizations due to acute decompensated heart failure compared to usual care is being evaluated in nine centers in Poland. The primary combined endpoint includes cardiovascular deaths and/or hospitalizations due to exacerbation of the primary condition.

Studies on the use of noninvasive techniques to monitor haemodynamic changes during the exercise test were carried out in several centres. A major problem is the selection of the measurement technique for practical studies. For this purpose, four techniques were compared simultaneously:

- conventional Fick technique;
- ICG using the PhysioFlow device;
- pulse contour analysis;
- measurements of changes in breathing gas composition (Innocor – rebreathing).

Values obtained using the Innocor device were lower, and those obtained by ICG were higher compared to other techniques. The authors concluded that the precision of cardiac output measurements depended on the technique used [36]. Other authors simultaneously used ICG and the indocyanine green dye dilution method (CO_{DB}) during the exercise test in patients with COPD. A strong correlation between measurements using these two techniques was noted in 50 patients [37].

Intrathoracic impedance measurement in patients with a cardiac pacemaker

In 2003, encouraging results regarding the use of an ICG device incorporated into a cardiac pacemaker were published by the research group of Patterson and Wang. These authors hypothesized that a device measuring impedance between the pacemaker casing and the pacemaker lead would provide information on the changes in water content in the lung tissue [38]. A computer software automatically calculates a specific impedance curve in an individual patient, providing a measure of water content called the fluid index. Exceedance of the critical level of thoracic water content is signaled by the peripheral device. Studies showed that intrathoracic impedance measurements in patients with heart failure and an implantable cardioverter-defibrillator allowed early detection of acute decompensated

heart failure. The devices to monitor thoracic fluid content incorporated into implantable cardiac devices continue to be modified [39, 40].

Summary

Noninvasive methods, including the impedance techniques, continue to be developed. The impedance techniques

have been introduced in the outpatient settings for the monitoring of haemodynamic changes as the indices of cardiac performance.

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Streszczenie

Monitorowanie hemodynamiczne dostarcza istotnych informacji o wydolności serca – obciążeniu wstępnym, następczym, kurczliwości serca, wydajności „pompy sercowej”. Najbardziej popularne techniki obejmowały pomiary metodami inwazyjnymi – Ficka, termodylucji i pomiary inwazyjnych ciśnień w łóżysku sercowo-naczyniowym oraz metodami nieinwazyjnymi opartymi na technikach ultradźwiękowych – echokardiografii, przezprzełykowym doplerowskim monitorowaniu przepływu przez aortę wstępującą oraz tonometrii aplanacyjnej. Połączenie metod impedancyjnych z możliwością analizy telemedycznej wyników może stworzyć nową wartość w praktyce lekarskiej.

Słowa kluczowe: kardiografia impedancyjna, *rebreathing*, hemodynamika, telemedycyna

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