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# Analysis of actual accuracy in cardiac output measurements by means of thermodilution

M. GAWLIKOWSKI[1] and T. PUSTELNY[2*]

[1] Foundation of Cardiac Surgery Development, 345a Wolnosci St., 41-800 Zabrze, Poland,
[2] Silesian University of Technology, Faculty of Electrical Engineering, 2 Krzywoustego St., 44-100 Gliwice, Poland

**Abstract.** The essential examination in hemodynamic monitoring of the patient is the cardiac output (CO) measurement. Nowadays, in clinical practice the most popular method is indicator dilution, particularly thermodilution. It is realized by applying the Swan-Ganz catheter and observing changes of the indicator concentration. This method is sensitive to many factors and the obtained results should be treated cautiously. The paper presents theoretical and experimental studies of metrological phenomena in CO measurements by means of thermodilution, paying special attention to medical aspects of the measurements. It has been pointed out that the actual unreliability of the mentioned method reaches values from 20% to 45%, which is in opposition to the technical data of patient's monitors (typical accuracy about 5%).

**Key words:** cardiac output, hemodynamics monitoring, thermodilution.

## 1. Introduction

Measurements of the cardiac output (*CO*) are the essential examination in hemodynamic monitoring of the patients hospitalized most often at intensive care wards [1]. In the terms of medicine it is defined as a volume of blood which is pumped by the cardiac muscle during one minute. In terms of physics it should be understood as the average volumetric flow of viscid, non-Newtonian liquid at a constant temperature [2]. *CO* monitoring provides valuable information about the patient's hemodynamic state and allows to decide about the progress of illness and treatment

There are a few methods of *CO* estimation with different invasiveness, unreliability and principles of operation. The most elementary one is Fick's method, based on oxygen consumption by the organ [3]. In many papers Fick's method is considered to be a reference. However, it requires the risky artery puncture and precise measurements of the blood saturation. Due to the reasons mentioned above, nowadays the applications of Fick's method is limited and focused on experimental medicine.

One of the most popular non-invasive *CO* measurement methods is echocardiography. In spite of its low accuracy [4] the estimation of the ejection fraction (and indirectly the *CO*) by means of twodimensional echocardiography (transthoracic or transesophageal) it is quite often applied in clinical practice [5]. This method is readily applied as a screening examination. Rheocardiography seems to be a new trend among non-invasive *CO* measurements [5, 6]. Due to a low number of clinical cases the uncertainty of this method is difficult to estimate. It was pointed out [7] that rheocardiography may be useful in monitoring the patient's hemodynamic longterm tendency but the accuracy of the measurement of an isolated case is low. In spite of non-invasiveness and the easy way of its application this method has not achieved practical popularity.

There are a few other methods of *CO* measurements (e.g. PiCCO, LIDCO, pulse contour [5]) but due to their pure accuracy, sensitivity and specificity they have still been under development and their clinical application is significantly limited.

Nowadays great clinical significance has been attained in *CO* measurements by means of the indicator dilution phenomenon. It is practically realized by the pulmonary artery catheterization technique (*PAC*) which is considered to be a "gold clinical standard" [8] The method itself is relatively easy in its application, safe for the patient and it allows to measure other important hemodynamic parameters, as intracardiac pressures (especially the pulmonary artery wedge pressure) or pulmonary resistance [1, 2, 5]. In the course of clinical studies many investigators have assumed the *PAC* technique as a reference Literature studies and the authors' practical experiences have shown that the accuracy of the thermodilution method depends on many factors (e.g. physical parameters of the indicator, haematological parameters of blood, heart rate, valves diseases [20] and on the way of injecting of the indicator [9, 10]) Manufacturers of the patient's monitor devices quoted, that the unreliability of *CO* measurements by means of thermodilution amounts to about 5% [11, 12]. However this value contradicts clinical observations. This doubt inclined the authors to study the metrological properties of thermodilution.

**Goal:** The goal of this work was to assess the uncertainty of *CO* measurements by means of thermodilution.

*e-mail: tpustelny@polsl.pl

## 2. Principles of the method of indicator dilution

Let us consider the section of a vessel in which the liquid flows with an average volumetric flow $Q$. (cf. Fig. 1). At the point $A$ the mass $m$ of the indicator is injected rapidly into the vessel. The transient concentration of the indicator $C(t)$ (the so-called indicator dilution curve – *IDC*) is measured at the point $B$, remote from the point $A$. Supposing, that there is no leak of the indicator out of the vessel the average volumetric flow of the liquid is defined by (1)

$$Q = \frac{m}{\int_0^\infty C(t)\,dt} \tag{1}$$

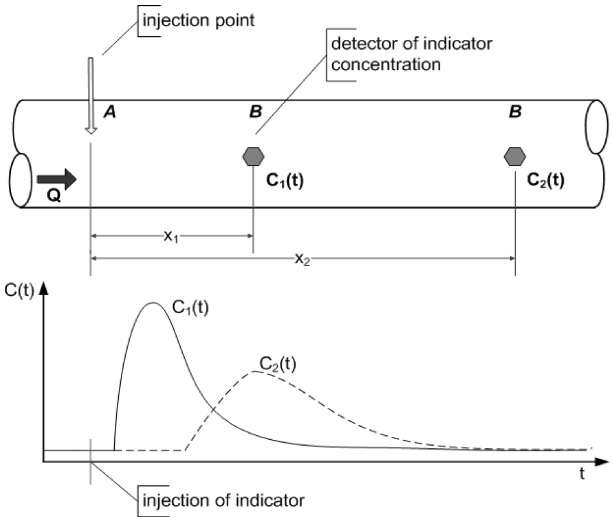


Fig. 1. The idea of flow measurements by means of indicator dilution

Equation (1) is correct for all dilution methods, independently of the type of the indicator and the way of its injection. In practical applications the integration time of *IDC* is limited. In biological objects the shape of *IDC* is more complicated due to the recirculation effect (a certain portion of the indicator returns to the detector through the closed loop of the vessels – cf. Fig. 2).

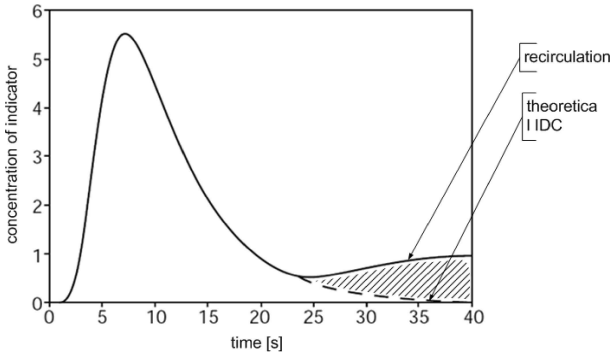


Fig. 2. Indicator dilution curve (IDC) and the recirculation effect

Nowadays, in clinical practice the dominant variation of blood flow measurements by means of indicator dilution is thermodilution. As the indicator the room-temperature ($T_i$ = 21–23°C) or iced ($T_i$ = 1-5°C) 0.9%NaCl is used. The examination runs as follow:

- first the Swan-Ganz catheter (Fig. 3) is inserted into the pulmonary artery (Fig. 4) through the jugular vein, superior caval vein, right atrium and right ventricle (this technique is called pulmonary artery catheterization – *PAC*)
- next the indicator is rapidly injected into the right atrium through the smalldiameter duct inside the catheter,
- the *IDC* is measured by the temperature-sensitive element located at the tip of the catheter,
- *IDC* is registered by the patient's monitor and the *CO* is calculated by means of the Stewart-Hamilton equation **(2)**

$$\Phi = \frac{c_i \rho_i}{c_b \rho_b} \frac{V_i \cdot (T_{b0} - T_i)}{\int_{t_0}^{\infty} T_b(t) dt} \tag{2}$$

where $c_i, c_b$ – specific heat of indicator and blood, $\rho_i$, $\rho_b$ – specific mass of indicator and blood, $V_i$ – volume of indicator, $T_{b0}$ – temperature of blood just before injection of the indicator, $T_i$ – temperature of indicator, *Tb(t)* – indicator dilution curve.

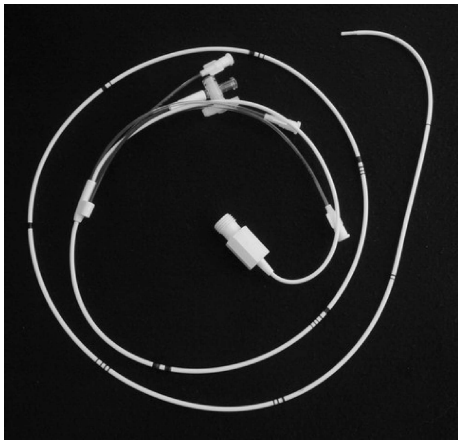

Fig. 3. The Swan-Ganz catheter

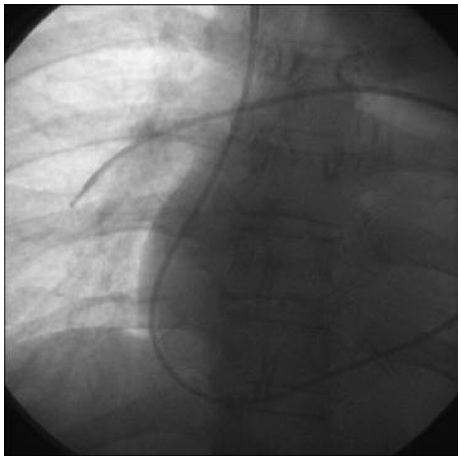

Fig. 4. Location of the Swan-Ganz catheter into the vessels of the pulmonary circulation

The *PAC* technique by means of the Swan-Ganz catheter allows to measure (except *CO*) numerous important hemodynamic parameters, like pulmonary artery pressure (*PAP*), pulmonary artery wedge pressure (*PAWP* - which correspond to the left atrial pressure) and the resistance of pulmonary vessels (*PVR*). Although, the *PAC* examination is invasive, but it provides valuable hemodynamic data. The *PAC* is safe for the patient and does not increase the risk of death [10]. This examination is recommended by the Polish and European Society of Cardiology [8] and is generally applied (a "gold standard") in clinical practice.

## 3. Material and methods

The accuracy of *CO* measurements by means of thermodilution was estimated in two different ways: theoretically and experimentally. The following conditions of experiments were assumed:

- indicator: 0.9%NaCl, iced (1.5...4.5°C) or room temperature (20...23°C), injection volume 10 mL,
- catheter: size 7F, volume of the indicator duct about 0.5 mL,
- thermodynamic parameters of liquids:
- for blood substitute: specific heat = 3528 J/kg·K, mass density = 1065 kg/m$^3$
- indicator: specific heat = 4180 J/kg·K, mass density = 996 kg/m$^3$
- no human or animal blood was used, physical experiments were performed on an adequate model of the pulmonary circulation [13].

**Theoretical estimation of the uncertainty of thermodilution.** Theoretical considerations were carried out by means of the sensitivity analysis method. This method allows to determine the influence of the variations of individual factors on the global value of transmittance $T$ (transfer function of analyzed process) [14]. The $T$ function, depends on $n$ parameters: $T = f(Y1, Y2, \ldots Yn)$. $\delta T = \dfrac{\Delta T}{T}$ denotes the relative increment of the $T$ function and $\delta Y_i = \dfrac{\Delta Y_i}{Y_i}$ denotes the relative increment of the parameter. The relative increment of $T$ caused by variations of $Y_i$ is defined by (3):

$$\delta T = \sum_{i=0}^{n} S_{Y_i}^T \cdot \delta Y_i \tag{3}$$

$S_{Yi}^T$ is a relative sensitivity index of the function $T$ on the parameter $Y_i$. Let us assume, that the relative increments of the parameters $\delta Y_i$ are low ($< 10\%$), then the relative sensitivity index may be defined by (4):

$$S_{Y_i}^T = \frac{Y_i}{T}\frac{\partial T}{\partial Y_i}. \tag{4}$$

The maximum deviation of the function $T$ is given by the equation (5):

$$\delta T_{\max} = \pm \sum_{i=1}^{n} \left| S_{Y_i}^T \cdot \delta Y_i \right|. \tag{5}$$

In this paper the sensitivity analyze of the Stewart-Hamilton thermodilution model Eq.(2) was carried out. The $S_{Yi}^T$ values may be assessed theoretically or experimentally. In the presented work some sensitivity indices were measured and others were estimated theoretically basing on the knowledge of the nature of the occurring phenomena.

**Experimental assessment of the uncertainty of thermodilution.** Due to ethical and practical reasons examinations on animals were abandoned. There are numerous methods of modelling the cardiovascular system [15, 16]. To estimate experimentally the unreliability of thermodilution an adequate physical model of the pulmonary circulation was applied (Fig. 5) [13]. It consisted of the following parts: the right atrium, right ventricle, pulmonary artery valve, tricuspid valve, pulmonary trunk and left and right pulmonary arteries. The spatial arrangement of all the listed structures were similar to those in the cardiac muscle. To simulate the contractibility of the ventricle and atrium flexible membranes made of polyurethane were used.

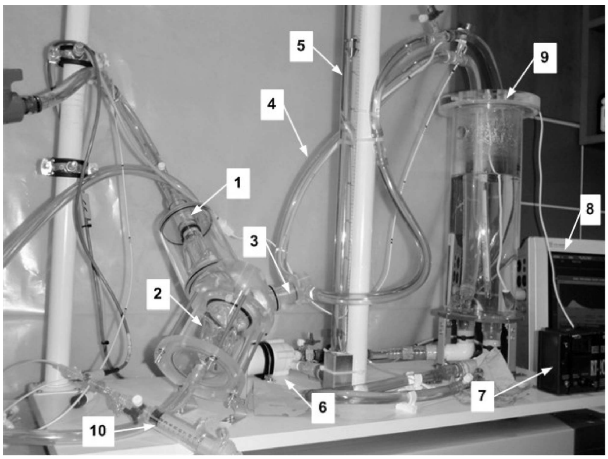


Fig. 5. Pictorial view of the physical model of pulmonary circulation: 1 – atrium, 2 – ventricle, 3 – pulmonary trunk, 4 – pulmonary artery, 5 – rotameter, 6 – centrifugal pump, 7 – temperature regulator, 8 – patient monitor, 9 – equivalence tank, 10 – syringe for injection of the indicator

The membranes are pneumatically supplied by an external pneumatic controller. The model produces a pulsating flow with an adjustable heart rate, ejection time and time dependences between the contraction of the atrium and ventricle. It is possible to simulate valve diseases, arrhythmia, hypothermia and various geometry of pulmonary vessels and pressure load.

The operating liquid was a 30% glycerine and water solution with an antibacterial agent. This mixture is frequently used as a blood substitute and its thermodynamic parameters are similar to those of the blood. The temperature of operation liquid was stabilized by an electronic regulator with an accuracy of $+0.1$°C/$-0.3$°C. Due to the close hydraulic circulation loop the developed model is able to simulate the recirculation of the indicator.

Due to the complexity of the measurements of the pulsating flow in the developed system this kind of flow (generated

by the heart simulator) was transformed into a continuous flow in the hydraulic subsystem consisting of a centrifugal pump and an equalizing vessel (Fig. 6). The continuous flow (which — in steady-state — equals the pulsating flow) was measured by a rotameter with an accuracy of 1.5%.

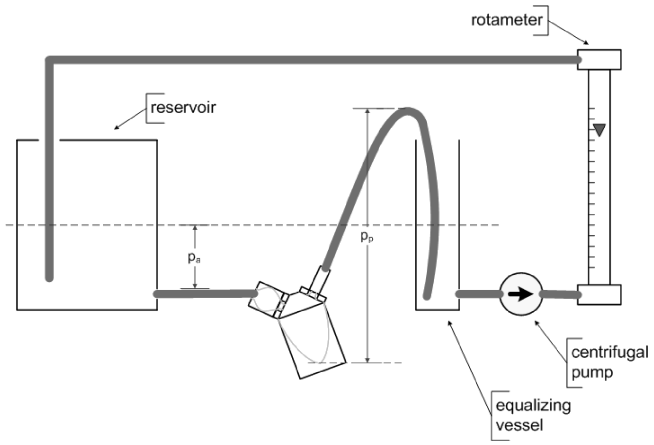


Fig. 6. Pictorial view of the physical model of pulmonary circulation

The functional verification of the developed model was performed by comparing the course of the dilution phenomenon (*IDC* curves) occurring in the physical model and the human circulatory system (13). It was unequivocally proved that the model is able to simulate faithfully *CO* measurements by means of thermodilution.

The uncertainty of *CO* measurements by means of thermodilution was experimentally assessed on two Swan-Ganz catheters (BD2, Becton-Dickinson and 2269, Burron Medical) connected to the patient's monitor (PM9600, Mindray). As indicators iced and room-temperature isotonic salt solutions were applied. The *CO* value measured by means of patient's monitor and reference rotameter were compared. For all values of flow generated by the model $N = 20$ measurements were carried out. The obtained data were statistically analyzed (Student's distribution, $p = 0.05$).

## 4. Results

**Theoretical estimation of the uncertainty of thermodilution.** The relative increments of the parameters were determined in the following way:

- $\boldsymbol{\delta c_i}$, $\boldsymbol{\delta \rho_i}$: due to the stable chemical constitution of the indicator the value of those parameters was equal to zero
- $\boldsymbol{\delta c_b}$, $\boldsymbol{\delta \rho_b}$: the thermodynamic features of the diphase mixture are given by (6):

$$c, \rho_{F12} = (1 - n) \cdot c, \rho_{F1} + n \cdot c, \rho_{F2} \tag{6}$$

Blood consists of cellular components and plasma, the specific heat of which amounts to 3.52 J/mL·K and 4.03 J/mL·K, respectively [17]. Assuming a hematocrit in the range of 25…60% [1, 2], the value of $\delta c_b$ calculated from (6) amounts to 2.5%. The mass density of the plasma and cellular components amounts to 1027 kg/m$^3$ and 1095 kg/m$^3$, respectively [17]. The value of $\delta \rho_b$ calculated from (6) equals 1.3%.

- $\boldsymbol{\delta T_i}$: this parameter depends mainly on the accuracy of $T_i$ measurements. From the technical data of patient's monitors [11, 12] it may be assumed to be 3%.
- $\boldsymbol{\delta T_b}$: this parameter depends on the accuracy of measurement of the blood temperature by means of a thermoelement located at the top of the Swan-Ganz catheter. In order to estimate $\delta T_b$ six catheters connected to a patient's monitor were examined [14] The reference measurements of temperature was carried out by means of a high precision (0.0011°C) thermometer. The temperature was measured within the range of 33…38°C. The average accuracy of blood temperature measurements was 5.3% but the worst was 13.0%
- $\boldsymbol{\delta V_i}$: the value of this parameter is difficult to estimate. The indicator is injected with a medical syringe with a low-precise scale of volume. Moreover, a small portion of the indicator injected previously remains in the catheter canal. In a typical 7F size catheter the volume of the canal amounts to 0.5 mL (5% of typical 10 cm$^3$ volume of indicator).
- $\boldsymbol{\delta S_c}$: the $S_c$ determines the integral of the *IDC* measured by a non-ideal detector (slope of transfer function $k \neq 1$ and offset $T \neq 0$), therefore:

$$\begin{aligned} S_c^* &= \int_0^\infty k \cdot [\Delta T_b(t) + T_0] dt \\ &= k \cdot \left[ \int_0^\infty \Delta T_b(t)\, dt + \int_0^\infty T_0\, dt \right] \\ &= k \cdot (S_c + T_0 \cdot t_{pom})\,. \end{aligned} \tag{7}$$

The $S_c^*$ and $S_c$ represent the integral of *IDC* measured by non-ideal and ideal detectors, respectively. The offset $T$ is zeroing by means of the measurement method realized by the patient's monitor, therefore the $\delta S_c$ depends merely on the $k$-ratio. Taking into account the typical slope of the thermistor transfer function [17], $\delta S_c = 6\%$.

The values of the relative sensitivity indices calculated by means of (4) and the relative increment of the parameters have been presented in Table 1. $S_{Ti}^T$ and $S_{Tb}^T$ depend on the absolute values of $T_b$ and $T_i$ therefore the respective values of those indices have been presented in Table 2.

The unreliability of cardiac output measurements by means of thermodilution, theoretically assessed by the sensitivity analysis of Stewart-Hamilton's equation were calculated from (5) and have been presented in Table 3.

**Experimental assessment of the uncertainty of thermodilution.** Investigations were carried out concerning typical hemodynamic conditions (heart rate: 55-75BPM, ejection time: 40–45%, cardiac output: 1.7–4.1 L/min).

The accuracy of blood temperature measurements by means of the investigated catheters was: $-1.72\%$ (catheter 2269) and 0.27% (catheter BD2). The percentage of relative values of the cardiac output measured by means of thermodilution compared with the reference rotameter has been presented in Fig. 7 and Table 4.

Table 1
Relative values of the sensitivity indices and increment of the parameters

| Parameter | Relative sensitivity index [-] | Relative increment of the parameter [%] |
|---|---|---|
| specific heat of the indicator | 1 | 0 |
| mass density of the indicator | 1 | 0 |
| specific heat of blood | -1 | 2.5 |
| mass density of blood | -1 | 1.3 |
| volume of the indicator | 1 | 5.0 |
| temperature of blood | $\frac{T_b}{T_b - T_i}$ | 5.3 (average)<br>13.0 (max.) |
| temperature of the indicator | $-\frac{T_i}{T_b - T_i}$ | 3.0 (iced)<br>0.5 (room temp.) |
| indicator dilution curve integral | -1 | 6.0 (average)<br>16.0 (max.) |

Table 2
Values of $S^Q_{Ti}$ and $S^Q_{Tb}$ for practical range of $T_i$ and $T_b$

| Indicator | Temperature of blood $T_b$ [°C] | $S^Q_{Ti}$ | $S^Q_{Tb}$ | Remarks |
|---|---|---|---|---|
| iced<br>$T_i = 5$°C | 36.6 | -0.15 | 1.15 | physiology |
| | 30.0 | -0.20 | 1.20 | hypothermia |
| | 38.0 | -0.15 | 1.15 | inflammation |
| room-temperature<br>$T_i = 23$°C | 36.6 | -1.69 | 2.69 | physiology |
| | 30.0 | -3.28 | 4.28 | hypothermia |
| | 38.0 | -1.53 | 2.53 | inflammation |

Table 2
Unreliability of cardiac output measurements estimated by means of the sensitivity analysis of transfer function

| Accuracy | Type of indicator | |
|---|---|---|
| | iced | room-temperature |
| typical | 18.3% | 26.9% |
| the worst case | 34.2% | 54.7% |

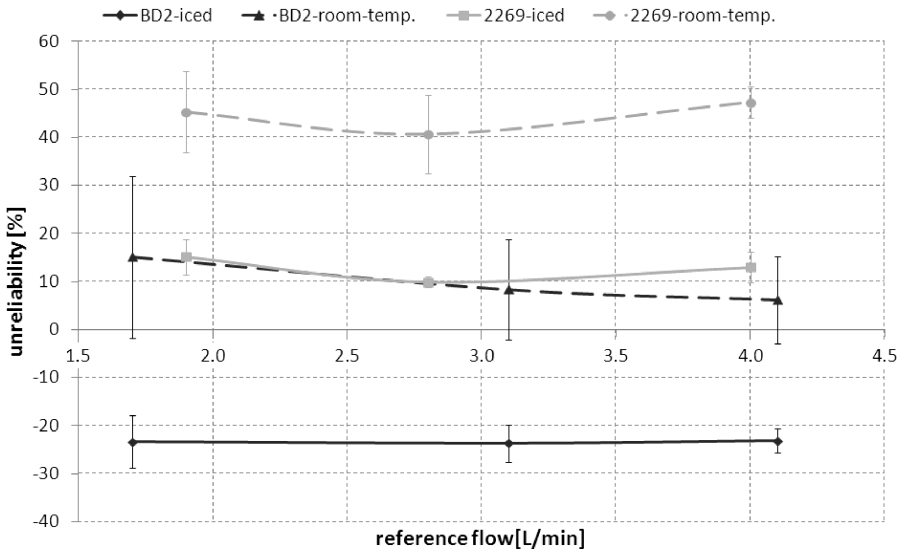


Fig. 7. Comparison of the uncertainty of CO measurements by means of thermodilution concerning various catheters, flows and temperatures of the indicator

Table 4
Unreliability of cardiac output measurements estimated experimentally

| Catheter | Unreliability of co measurement | |
|---|---|---|
| | iced | room-temperature |
| 2269 | 12.7 | 44.4 |
| BD2 | 23.4 | 12.0 |

## 5. Discussion

In clinical applications the room-temperature thermodilution is perceived as less accurate but safer for the patient (a cold indicator quite often causes arrhythmia or tachycardia). In fact, the relative sensitivity indices of the indicator at room-temperature are significantly higher than in the case of an iced one (cf. Table 2). Moreover, the value of indices connected with the temperature of indicator are lower than indices connected with the temperature of the blood. Therefore in order to decrease the unreliability of thermodilution the temperature of blood should be measured more accurately than the temperature of the indicator. It should be noticed that the slope ($k$ratio) of the transmittance of blood temperature detector influences significantly the relative increment of the integral of *IDC*, which makes this measurement critical concerning the accuracy of the thermodilution method.

The effect described above is noticeable in physical experiments. It has been pointed out (cf. Table 4 and Fig. 7) that the iced variant of thermodilution is not always more accurate than at room-temperature. It should be emphasised, that the relative accuracy of measurements of the blood temperature by the catheter BD2 was about six times greater than if the catheter 2269 was used.

Usually the thermoelements applied in Swan-Ganz catheters are made of nickel alloy characterized by non-linear characteristics of resistance *vs.* temperature [18]. In the patient's monitor this function is approximated by linear function near the operating point ($37^oC$). Therefore, measurements of the blood temperature in the case of patients with hypothermia or inflammation will be inaccurate and – in consequence – the results of *CO* measurements by thermodilution will in those patients be not credible [19].

Both: the theoretical and experimental assessments of unreliability of the thermodilution method have shown, that the accuracy of measurements at typical conditions amounts to about 20% (Table 3 and Table 4) but the worst value of accuracy exceeds 45%. The manufacturers of devices designed for *CO* measurement by means of thermodilution claim, that the accuracy of measurement is 5% [11, 12], but they do not inform about the conditions of the experiment (the character of flow, the type of the catheter, the uncertainty of blood temperature measurements, thermodynamic parameters of the medium, the type of the indicator and the reference method of flow measurements). The theoretical analysis presented in this paper allowed to identify factors significant for unreliability of thermodilution and explain the way of their influence on the measurement The results of theoretical considerations were confirmed experimentally.

The clinical meaning of *CO* is significant: it allows to diagnose the illness, to monitor its progress and the effects of the therapy. The 10mL room-temperature indicator is most often applied but – taking into account the presented results (Table 3 and Table 4) – in some cases the accuracy of examination may reach 45%, which makes the result useless. Therefore the medical staff should be conscious of the metrological properties of thermodilution and the outcomes of an incorrectly carried out examination. Due to the fundamental meaning of *CO* in hemodynamic monitoring other methods of its measurement, based on other physical principles should be found.

## 6. Conclusions

1. The accuracy of blood temperature measurements has a fundamental meaning concerning the unreliability of thermodilution. Due to the linear approximation of the transfer function of the thermoelement near the operating point of 37°C, the results of *CO* measurements in patients with hypothermia or inflammation will be inaccurate.
2. The theoretical unreliability of the thermodilution method was confirmed experimentally and amounts to 20% (at typical hemodynamic conditions) but in extreme cases it may reach about 45%. Therefore the examination itself must be carried out with care and the results must be interpreted individually paying special attention to their correctness.

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