Measurement of ejection fraction with standard thermodilution catheters

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Abstract

Right ventricle ejection fraction (RVEF) is clinically used to evaluate right ventricular function. The thermodilution method can be modified to estimate the RVEF. However, this method requires a thermistor with a fast time response in order to yield correct estimates. Digital signal processing techniques that were developed in previous works, allow the use of industry-standard slow time response thermistors for the measurement EF. However, these algorithms were not automated, and the works did not present a complete evaluation of the method’s performance. This article presents a modified automated version of these algorithms, and uses numerical and in vitro simulations to test their performance. In the simulations, the measured ejection fraction was compared to the true ejection fraction. RVEFs ranging from 0.20 to 0.80 were tested for heart rates ranging from 30 to 120 heart beats per min. Statistical analysis of data showed that the new method presents an improved performance. © 2002 IPEM. Published by Elsevier Science Ltd. All rights reserved.

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1. Introduction

An important parameter of the human circulatory system is the right ventricle ejection fraction (RVEF). RVEF used together with the cardiac output (CO) and cardiac rate permit one to evaluate the right ventricular function. Many methods have been used to measure RVEF. Among those methods, the thermodilution technique has been reported to be the more advantageous one. Nevertheless, in order to evaluate RVEF, the thermodilution technique requires thermistors with small time constants (named fast thermistors).

Fast thermistors are expensive. Consequently, the clinical examination is also expensive. One way to decrease its cost is to use conventional thermistors. In this paper, a method based on a digital processing technique is proposed and evaluated. This method allows the use of inexpensive conventional thermistors that present large time constants (named slow thermistors) to measure RVEF.

This paper is organized as follows. Section 2 presents a brief bibliographic and historic review of the methods to measure CO and RVEF. Section 3 discusses the thermodilution technique used to measure CO and RVEF. A mechanical model and a numeric simulation are also presented to clarify the thermodilution technique. An algorithm to recover thermodilution signals from thermistors with high thermal inertia is presented in section 4. Section 5 presents and analyses numerical and in vitro simulations. Finally, section 6 states the main findings and future work.

2. Bibliographic review

The first method used to measure cardiac output was described by Adolph Fick [1]. However, Fick’s method presents some limitations. The most important limitations are: frequent measurements are not possible; car-
Diastolic output must remain constant during measurements; and the method is more accurate for normal or less than normal CO.

Stewart [2] introduced a method in which a substance is injected into the circulatory system in order to measure blood flux. Many substances were used for this purpose, mainly saline and dye solutions. A significant limitation of this technique is the accumulation of the substance in the blood. As a result, the number of measurements that can be taken is limited.

In the 1950s, Fegler [3] proposed a method in which the indicator is the temperature of a fluid injected in the right atrium. Consequently, the indicator (heat) is not accumulated in the circulatory system.

Swan and Ganz introduced a catheter with a thermistor inside of it in the 1970s [4]. Since then, thermodilution has become common in hospitals for evaluating CO [5].

If a fast thermistor is used inside of the catheter, RVEF can also be evaluated. This parameter is defined as the ratio between the ejected volume during the systole and the maximum volume in the diastole. Clinically, the ejection fraction is used to evaluate the ventricle pumping ability.

Maruschak et al. [6] studied the frequency response of fast thermistors mounted in thermodilution catheters. They performed in vitro experiments to compare the measurements taken with fast thermistor with measurements that were taken with slow thermistors. They concluded that a thermistor inside of catheters distorts the measured signal. Based on their findings, they suggested that one could use deconvolution operations to recover the original signal from the distorted signal.

Hori et al. [7] proposed an algorithm based on a system called natural observation system using slow thermistors. The method achieved good results but it is difficult to apply it in hospitals because of risks of contamination.

Da Rocha et al. [8] developed a time invariant linear model that describes the behavior of a thermistor in a convective medium. This opened the possibility for using the deconvolution operation to improve the thermistor impulse response in order to evaluate RVEF in thermodilution catheters.

Da Rocha [9] developed a method based on qualitative and quantitative knowledge of the catheter and of the thermodilution curve to improve the signal measured by slow thermistors. The method presented promising preliminary results but it still requires further evaluation. Furthermore, this technique is computationally time consuming and the algorithm is not automatic.

The method proposed and implemented in this paper is an improvement of the Da Rocha method. This work has three objectives. First, to develop an automatic algorithm in order to eliminate or to reduce the human intervention that is an important source of error. The second objective is to reduce the computational processing time required for the Da Rocha method. Finally, the last one is to evaluate the posed method.

3. The thermodilution technique

The objective of this section is to discuss the thermodilution technique for measuring CO and RVEF. Section 3.1 presents the method basis. Section 3.2 presents the thermodilution mathematical model. Simulations of RVEF measurements are presented in section 3.3.

3.1. Swan-Ganz catheter and the thermodilution technique

An instrument used to measure CO and ejection fraction in the right ventricle is the Swan-Ganz pulmonary catheter. This catheter measures 110 cm long and has a diameter of 2 mm. The catheter presents many channels. Nevertheless, for the purpose of this work only the temperature sensor and injection channel are mentioned here.

The thermistor is located approximately 4 cm from the catheter tip. The thermistor is encapsulated with glass and covered with epoxy to protect the patient from any electrical discharge inside of the heart. However, this insulation also increases the thermistor time constant. The injection channel is used by the physician to inject cold solution into the right atrium or right ventricle.

The catheter is used as follows. It is inserted through the vena cava, right atrium, tricuspid valve and right ventricle. Finally, it is placed into the pulmonary valve. Fig. 1 illustrates the position of the catheter inside the heart. The physician, then, injects a cold solution into the atrium or ventricle and the temperature is measured by the thermistor downstream from the blood flux inside

![Fig. 1. A catheter inserted in the right heart.](image-url)
the pulmonary artery. The temperature variation can then be related to the CO and RVEF as explained in section 3.2.

3.2. Thermodilution model

To measure RVEF, the catheter is inserted in the right heart because its access is less traumatic than that of the left heart access. Thus, this subsection presents a mechanical model of the right heart.

The right heart can be modeled as a pump with two phases. Fig. 2 is this model illustration. The first and the second phases are respectively the filling and the emptying of the right ventricle. The model is explained as follows. After the last pumping action (emptying of the ventricle), the blood flows from the atrium to the ventricle through the tricuspid valve (filling of the ventricle). When the blood fills the ventricle, the pump is set in action reducing the ventricle volume. As a result, part of the blood in the ventricle is rapidly ejected through the pulmonary valve. Following this ventricle emptying action, the filling phase begins again. One important characteristic of this pumping action should be noted. Just a fraction of the volume in the ventricle (typically 55%) is ejected at each emptying phase.

When a cold fluid is injected into the ventricle, it reduces the temperature of the blood inside the ventricle. Each time the blood at body temperature replaces part of the blood inside the ventricle, the temperature in its interior tends to return to the body temperature. This phenomenon is used to evaluate RVEF.

In order to develop equations that describe a thermodilution system, the following set of hypotheses are stated.

1. All the indicator (temperature of the isotonic solution) introduced into the heart passes eventually through the pulmonary artery. In other words, there is no heat transfer between the solution and the endocardium. It is assumed that this is because the contact area between the solution and endocardium as well as the time interval are relatively small.
2. The indicator does not recirculate. Thermal equilibrium is quickly reached between the blood vessels and the isotonic solution. This happens because before the blood recirculates it has to pass through the capillary bed that has a large superficial area in contact with blood [10]. As a result the blood is restored to its normal body temperature after it returns to the heart.
3. There is a perfect mix between blood and indicator [11].
4. The flux is constant during the measurement. This occurs because the observation period is small (5–10 s).
5. The volume and the temperature of the indicator, and the temperature of the blood are known.
6. All the temperatures are referred to the baseline blood temperature, i.e., the blood temperature before the injection is assumed to be 0 °C.
7. The blood and the injected fluid have the same density and specific heat, because the in vitro experiment uses water.

It is also assumed that the heart beats at a period $\Delta T$ and that the volume ejected at each period is $V_e$. The maximum volume, $V_{\text{max}}$, occurs at the end of the filling phase. The minimum volume (at the end of the emptying phase) is $V_{\text{min}}$, and $V_i$ is the total indicator volume injected. The injection time interval is small (typically two or three cardiac cycles). Thus, the injection is described by a brief duration function $f(t)$ [9]. It is also assumed that a certain volume of isotonic fluid, $I_n$, is injected at each cardiac cycle at a temperature $T_i$, and the temperature measured in the pulmonary artery at the final of diastole is $T_n$.

Using the above assumptions, one can deduce an equation to calculate the blood flux in the discrete domain (Eq. (1)) [9].

$$\frac{V_{\text{max}} - V_{\text{min}}}{\Delta t} = \sum_{n=0}^{\infty} I_n \frac{T_{n+1} - T_n}{\Delta t}$$

(1)

In the continuous domain, Eq. (1) can be written as Eq. (2) [9].

$$\text{CO} = \frac{\int_{0}^{\infty} f(t)dt}{\int_{0}^{\infty} T(t)dt}$$

(2)

3.3. The RVEF estimation

When a fast thermistor is employed, the thermodilution method can also be used to evaluate RVEF. A
numerical simulation is performed to illustrate the temperature behavior in an ideal thermodilution system. The parameters used are the following.

1. The ventricle maximum volume (at the end of diastole) is 0.15873 l.
2. The ventricle minimum volume (at the end of systole) is 0.08730 l.
3. The ejection fraction is 0.45.
4. The emptying phase period is 0.2 s.
5. The cardiac rate is 70 bpm.
6. The $\rho_{c_{\text{blood}}}$ is $3.83 \times 10^{-3}$ J/K/l.
7. The $\rho_{c_{\text{indicator}}}$ is $3.83 \times 10^{-3}$ J/K/l.
8. The blood temperature is 36 °C.
9. The temperature of the indicator is 0 °C.
10. The total indicator volume injected is 5 ml.

It is also assumed that the injection duration is small but not instantaneous. The injection in the simulations lasts a period of a heartbeat. The blood flow waveform inside the pulmonary artery can be approximated by a sequence of square pulses [9]. Thus, during the injections, the flux is constant.

The result of this simulation is shown in Fig. 3. The graph represents the temperature changing in the pulmonary artery measured by a very fast thermistor (ideal sensor). Fig. 3 also presents two important characteristics. First, the curve presents many plateaus. Second, it decays exponentially. In fact, one can demonstrate that, after the injections cease, the temperature in the pulmonary artery can be described by Eq. (3).

$$T_n = K_1(1-RVEF)^n = K_1\exp(\ln(1-RVEF)n)$$

where $K_1$ is the curve slope when it is plotted in semilog scale.

The exponential behavior can clearly be seen in Fig.

4. Improvement of thermodilution signal

Slow thermistors distort the thermodilution curve as illustrated by the smooth curve in Fig. 5. The idea here is to use deconvolution operation in order to recover the plateau signal from the distorted one. From basic convolution theory, one can determine the input signal from the output signal if one knows the system transfer function. In this case, the input signal is the plateau signal; the output signal is the smooth curve; and the system transfer function is the thermistor impulse response.

The output signal is readily available since it is the thermistor output. Unfortunately, to obtain the catheter transfer function is not a simple task. Because of the fabrication process, each catheter has a different transfer function. This difference would make it necessary to analyze each one in order to evaluate its impulse response. The problem is that the catheter is a sterile instrument and it has to remain sterile after the experimental test. Thus, to examine it would increase the possi-
The method proposed in this paper overcomes this problem. The thermistor transfer function is evaluated based only on qualitative and quantitative characteristics of the thermistor probe and thermodilution signal. In other words, there is no need to test each different thermistor.

4.1. The thermodilution curve

The main objective of this section is to present a deconvolution algorithm that will be used to recover the true thermodilution signal from the distorted signal measured by the thermistor.

To illustrate how the deconvolution algorithm works, it is explained using an example. The thermodilution curves are presented in Fig. 5. The plateau curve is the true signal and the smooth curve is the signal distorted by the thermistor. One can notice that the thermistor attenuates the higher frequencies of the plateau signal. In this example, the ejection fraction and cardiac rate are respectively 0.55 and 60 bpm.

It is assumed that the plateau curve is generated from a continuous curve (envelope curve). Fig. 6 shows the thermodilution curve (named $T_{\text{fast}}(t)$) and its envelope (named $T_{\text{cont}}(t)$). The plateau curve is generated from the sampling and hold mechanism applied to the envelope curve. The sampling frequency is equal to the heart rate, i.e., 1 Hz.

Now, suppose that $T_{\text{cont}}(t)$ is sampled by an impulse tram. The impulses have the period of the heart beat (1 s). The top and bottom diagrams in Fig. 7 show the result of the sampling operation in time and in frequency domains, respectively. Note that $jw$ denotes that the signal is in the frequency domain, and the double bars indicate the magnitude of the complex signal. There are two important characteristics to be noted about $\|T_{\text{sample}}(jw)\|$. First, $\|T_{\text{sample}}(jw)\|$ presents lobules equally spaced at a sampling frequency. Second, the normalized amplitude is 1 at these lobules.

The next step is to execute the convolution between $T_{\text{fast}}(jw)$ and the unitary pulse ($\text{Pulse}(jw)$). Eq. (4) presents the mathematical expressions for the convolution operation in the frequency domain.

$$T_{\text{fast}}(jw) = T_{\text{sample}}(jw)\text{Pulse}(jw)$$

Fig. 8 is the Fourier transform of $T_{\text{fast}}(t)$. The decreasing lobules in this figure are evident.

Until this point, we have dealt only with the thermodilution signal (the plateaux curve). Now we turn our attention to the sensor behavior. The thermistor behaves as a low-pass filter. The temperature measured by the thermistor, $T_{\text{slow}}(t)$, is an attenuated version of $T_{\text{fast}}(t)$. In fact, $T_{\text{slow}}(t)$ is obtained by the convolution of the ther-
The mistor transfer function, \( h(t) \), and \( T_{\text{fast}}(t) \). Eq. (5) is the mathematical expression for the convolution in the frequency domain.

\[
T_{\text{slow}}(j\omega) = H(j\omega)T_{\text{fast}}(j\omega) \tag{5}
\]

Fig. 5 shows \( T_{\text{fast}}(t) \), \( T_{\text{slow}}(t) \) in the time domain. The magnitude of Fourier transforms of the fast thermistor, of the slow thermistors and of the catheter impulse response, \( ||T_{\text{fast}}(j\omega)|| \), \( ||T_{\text{slow}}(j\omega)|| \) and \( ||H(j\omega)|| \), are presented in Fig. 9.

Note that the temperature measured by the slow thermistor is equal to the temperature measured by the fast thermistor multiplied by the impulse response of the slow thermistor; since the temperature measured by the fast thermistor is considered the true temperature. Thus, from Eq. (4) and (5), the slow thermistor output can be obtained using Eq. (6).

\[
T_{\text{slow}}(j\omega) = H(j\omega)T_{\text{sample}}(j\omega) \frac{\text{Pulse}(j\omega)}{||\text{Pulse}(j\omega)||} \tag{6}
\]

Recall that \( H(j\omega) \) is necessary in order to obtain \( T_{\text{fast}}(j\omega) \) from \( T_{\text{slow}}(j\omega) \). To estimate the value of \( H(j\omega) \), Eq. (6) is now manipulated. Dividing both sides of Eq. (6) by \( \text{Pulse}(j\omega) \), Eq. (7) is obtained.

\[
\frac{T_{\text{slow}}(j\omega)}{||\text{Pulse}(j\omega)||} = \frac{H(j\omega)T_{\text{sample}}(j\omega)}{||\text{Pulse}(j\omega)||} = T_{\text{ref}}(j\omega) \tag{7}
\]

Where \( T_{\text{ref}}(j\omega) \) is used as the reference signal to calculate the impulse response of the thermistor. Manipulating Eq. (7), one can find Eq. (8).

\[
\frac{T_{\text{ref}}(j\omega)}{||\text{Pulse}(j\omega)||} = T_{\text{sample}}(j\omega) \tag{8}
\]

A crucial step of the algorithm is described here. The magnitude of \( T_{\text{sample}}(j\omega) \) is equal to one in the frequencies that are multiples of the cardiac rate \( (60 \text{ bpm} \text{ 60 s}^{-1}) = 1 \text{ Hz}) \) as can be seen in the bottom diagram in Fig. 7. This means that, from Eq. (8), \( ||T_{\text{ref}}(j\omega)|| \) and \( ||H(j\omega)|| \) must have the same amplitudes at those frequencies. Recall two observations: (1) \( ||T_{\text{ref}}(j\omega)|| \) can be obtained from the first side of Eq. (7); and (2) the sampling frequency is the heart rate that is readily obtained from the thermodilution curve. Thus, the first step of the algorithm is to divide \( ||T_{\text{slow}}(j\omega)|| \) by \( ||\text{Pulse}(j\omega)|| \) in order to obtain \( ||T_{\text{ref}}(j\omega)|| \). Fig. 10 illustrates this process.

Note that the circles at the bottom of Fig. 10 mark the multiples of cardiac frequency. Therefore, the magnitude of the Fourier transform of the impulse response of the slow sensor, \( ||H(j\omega)|| \) should pass through the circles. As a result, one could use an algorithm to adjust a curve to these points (frequency, amplitude) to determine the
thermistor transfer function. The problem is to evaluate these points since $\|\text{Pulse}(jw)\|$ can be 0 (see top diagram in Fig. 10). In this case, $\|T_{re}(jw)\|$ would be undetermined in a noiseless case. The points with problems are shown as small circles in Fig. 10.

When the signal is contaminated by noise, the problem becomes more difficult. The increase in difficulty occurs because a region, and not only a point, must be eliminated. One way to solve this problem is to eliminate these points and to use interpolation in the remaining points.

One important observation is that the algorithm does not use any phase information. This could make the algorithm inaccurate since it does not account for this information. However, the sensor is a minimum phase system [9]. This means that there is a unique relationship between amplitude and phase [12]. Thus, just the amplitude or phase is necessary to determine the impulse response.

4.2. Estimation of the impulse response of the thermistor

This section shows how to estimate the impulse response of the slow thermistor. The objective of this section is to interpolate a curve through the lobules found in the previous section.

It was shown in a previous work [8] that the catheter impulse response can be approximated by a sum of three exponentials (Eq. (9)).

$$h(t) = [\exp(-at) + B \exp(-bt)]u(t)$$

(9)

where $u(t)$ is the step function.

Eq. (10) is the Fourier transform in the continuous domain of Eq. (9).

$$H(jw) = \frac{1}{jw + a} + \frac{B}{jw + b} + \frac{C}{jw + c}$$

(10)

If Eq. (10) is developed further, one could find Eq. (11).

$$H(jw) = \frac{1 + B + C}{jw + a} + \frac{B + Ca +Cb}{jw + b} + \frac{bc + Bc + C}{jw + c}$$

$$\frac{(b+c)N^2 + (b+c)B + Bc + Ca +Cb}{(b+c)N^2 + (b+c)B + Bc + Ca +Cb}$$

(11)

Eq. (12) presents the absolute square value of Eq. (11).

$$Y = \|H(jw)\|^2 =$$

(12)

where the simplification constants are shown in the system of Eq. (13).

$$k_1 = 1 + B + C$$

$$k_2 = b + c + Ba + Bc + Ca + Cb$$

$$k_3 = bc + Bac + Cab$$

$$k_4 = a + b + c$$

$$k_5 = ab + (a + b)c$$

$$k_6 = abc$$

(13)

eq a_3 + a_2w^2 + a_4w^4$$

$$a_6 + a_4w^2 + a_5w^4 + w^6$$

(14)

where the simplification constants are shown in the system of Eq. (15).

$$a_1 = 1 + 2B + B^2 + 2C + 2BC + C^2$$

$$a_2 = k_2^2 - 2k_1k_3$$

$$a_3 = k_3^2$$

$$a_4 = a^2 + b^2 + c^2$$

$$a_5 = k_3^2 - 2k_1k_6$$

$$a_6 = (abc)^2$$

(15)

Eq. (14) presents a simplified version of Eq. (12).

$$Y = \frac{a_3 + a_2w^2 + a_4w^4}{a_6 + a_4w^2 + a_5w^4 + w^6}$$

(14)

where the simplification constants are shown in the system of Eq. (15).

$$a_1 = 1 + 2B + B^2 + 2C + 2BC + C^2a_2 = k_2^2$$

$$-2k_1k_3a_3 = k_3^2a_4 = a^2 + b^2 + c^2a_5 = k_3^2$$

$$-2k_1k_6a_6 = (abc)^2$$

(15)

Eq. (14) can be rewritten as a recursive polynomial as shown in Eq. (16).

$$Y = \frac{a_3 + a_2w^2 + a_4w^4 + 2B}{a_6 + a_4w^2 + a_5w^4 + C^2}$$

$$-\frac{1}{b}w^2Y - \frac{1}{a}w^2Y - \frac{1}{c^2}w^2Y$$

(16)

Eq. (16) permits the use of an adaptive filter or neural network to find the parameters $a$, $b$, $c$, $B$ and $C$. In other words, these parameters make the $H(jw)$ passes through the principal lobules of a noisy version of Fig. 10.

Fig. 11 shows a neural network used in the identification of systems. This neural network is used in order to minimize the sum of squares of the deviations between its output and the system output.

Fig. 11 shows a neural network used in the identification of systems, the Functional Link Network, developed by Yoh Han Pao [13]. The main characteristic of this neural network is the absence of a hidden layer.
This allows the use of simple delta rules for training the network instead of the more complex generalized delta rule algorithms, what defines shorter training time periods (generally, 10 times shorter than the training time periods of the Multilayer Perceptron). The structure of the Functional Link Network, as shown in Fig. 11, is similar to the Widrow–Hoff transversal filter. The differences are the functional expansion of the input layer and the logistic sigmoid used in the transfer function of the output neuron. In order to offset the loss of the neurons in the hidden layer, a functional expansion has to be applied to the input layer. In this application, the hybrid model expansion was deemed more adequate than the tensorial or the orthonormal functions models alone.

The System of Eq. (17) shows the relationship between the neural network weights and the parameters $a_5$, $b$, $c$, $B$ and $C$.

$$p_8 = \frac{2B}{a_6}, \quad p_5 = \frac{2C}{a_6}, \quad p_6 = -\frac{1}{c^2}, \quad p_7 = -\frac{1}{b^2} p_8 = \frac{1}{a_2} p_{10} = \frac{1}{a_6}$$

Table 2

| Parameter | Value | Table 2: Catheter parameters after convergence |
|-----------|-------|---------------------------------------------|
| $a$       | 0.5706 s$^{-1}$ | $B$  | 2.1819 |
| $b$       | 2.4361 s$^{-1}$ | $C$  | -3.2469 |
| $c$       | 8.0469 s$^{-1}$ | $D$  | 2.3681 |

In order to minimize the computational processing time and decrease the possibility of undesired local minima in the error surface, the initial estimate is based in the typical behaviour of thermodilution catheters (Table 1). The neuron uses a linear transfer function and the Levenberg–Marquardt learning algorithm. The initial learning rate is 0.0001. The convergence was reached in about 2 s in a Pentium 166 MHz running Matlab. Therefore, the algorithm proposed takes much less time than previous algorithms (2 s instead of 40 min) [9,14].

After minimization, the parameters found are given in Table 2. Fig. 12 is the adjusted curve to the estimated points. Note that Fig. 12 is the noisy version of Fig. 10. The estimated transfer function, $H(j\omega)$, is used to recover $T_{fast}(t)$. Fig. 13 shows the true signal and the signal after deconvolution. Fig. 14 shows Fig. 13 in semilog scale. One can note by Fig. 13 that the deconvolution improved the slow thermistor measurement.
5. Numerical and in vitro simulations

This section presents and analyses numerical and in vitro simulation.

In section 5.1, numerical simulations are presented. In section 5.2, in vitro simulations are introduced. In both sections the data are statistically analyzed.

5.1. Numerical simulations

Numerical simulations were executed to evaluate the performance of the proposed algorithm. Simulations of RVEF ranging from 0.2 to 0.8, and of cardiac rate ranging from 30 to 120 bpm were performed. The method used in the simulation consisted in generating the ideal thermodilution curves (plateau curve); adding gaussian noise to the curves (mean: 0.00 °C, standard deviation: 0.14 °C); and finally, convoluting the curve with the slow thermistor impulse response in order to generate the distorted thermodilution curve. The proposed method to recover the plateau curves was, then, applied to these distorted curves. The impulse response of the catheter were approximated by a sum of four exponentials and its estimated impulse response were approximated by a sum of three exponentials.

Linear regression using the minimum square error method was used to evaluate the relationship between the curves generated and estimated. Correlation coefficient, mean error and standard deviation between estimated and generated curves were also calculated. Furthermore, the t-student relationship was used to test the confidence interval.

A total of 68 curves were analyzed. The correlation coefficient and t-student ratio found were respectively 0.9661 and 30.3840. This indicates a significance level inferior to 0.01. This means that evaluated RVEF and the generated RVEF do not differ significantly.

Fig. 15 shows the linear regression between the estimated and generated curves. The curve slope is 0.9913 and intercepts the y-axis at 0.0288. The mean square error between measured and generated EF is 0.0036 and its standard deviation is 0.0062.

Despite the fact that generated and estimated EF are highly correlated, there is an increase for EF above 0.6. This might be occurring because the temperature in the ventricle returns too rapidly to the blood temperature. Thus, the algorithm used to calculate the curve slope according to Eq. (3) presents a diminished performance.

5.2. In vitro simulations

A mechanical model of the human circulatory system was developed with the purpose of simulating thermodilution curves. Furthermore, an acquisition and control system were projected in order to acquire the thermodilution signal and to keep the water at constant temperature. The block diagram of the system is presented in Fig. 16. The components of the mechanical model in Fig. 16 are associated with the circulatory model.

The mechanical model is used as follows. As was pointed out before, the algorithm is applied to the signal measured by a thermistor mounted in a Swan-Ganz catheter (slow thermistor). This catheter is placed close to a fast thermistor in the mechanical model. Therefore, in order to validate the method, one can compare EF estimated by the algorithm applied to the slow thermistor and the EF measured by the fast thermistor. Later, the set of results were statistically analyzed.

In the mechanical model, the water circulates inside a closed system that represents the human circulatory system. The simulator has a water reservoir kept at a constant temperature (38 °C) that simulates the blood. A microcontroller controls a heater that maintains the water at a constant temperature. A water mixer is used...
to keep the water temperature homogeneous in the reservoir. The tube on the left side of the ventricle represents the right atrium and the tube on its right represents the pulmonary artery. The system also presents two passive unidirectional valves that work as the tricuspid and pulmonary valves. The latex membrane performs the right ventricle function. The water inside the chamber, below the membrane, compresses and decompresses the membrane and has no communication with the liquid inside the membrane. A DC motor is connected to an embolus that moves a water column that compresses and decompresses the latex membrane. The motor is limited to 20–55 rpm.

The simulator operation is described in this manner. Initially the membrane is decompressed and contains its maximum volume of water derived from the reservoir. During the first phase, the motor moves the embolus that increases the pressure inside the chamber. The pressure compresses the membrane. As a consequence, the tricuspid valve is closed and the pulmonary valve is opened. Thus, the water flux goes to the pulmonary artery. In the second phase, the motor forces the embolus to return to the initial position. The membrane is decompressed by this action. As result, the tricuspid valve is opened, the pulmonary artery is closed, and the membrane is filled again with water deriving from the reservoir.

The thermodilution catheter (model 131HF7 from Baxter–Edwards) and a fast thermistor (model A6B4-GC16KA143L/31C-C Thermometrics, Inc., time constant equals 12.5 ms) are installed side by side in the tube representing the pulmonary artery. Both sensors are connected to a computer-based acquisition system. The measurements are executed at the same time by the fast and slow thermistors.

The experiment is performed as follows. First, 5 ml of cold liquid at 5 °C is injected directly into the membrane. Second, the temperature transient is measured by the two thermistors (slow and fast) in the tube that represents the pulmonary artery. The results are then recorded by the microcomputer to be processed. Finally, the ejection fractions measured by the fast thermistor and estimated from the slow thermistors are compared in order to validate the proposed method.

The catheter is tested for the hemodynamic ranges given in Table 3. The frequency range tested is limited because of technical difficulties in obtaining a motor with the necessary speed and torque.

The top diagram in Fig. 17 illustrates typical curves obtained in the experiment. The continuous and traced curves represent respectively measurements performed by the fast and the slow thermistor. The dotted line is the algorithm result applied to the slow thermistor. The same curves are shown in a semilog scale in the bottom diagram in Fig. 17.
A total of 32 curves were analyzed. The linear regression curve obtained has an inclination of 0.9469 and it intercepts the y-axis at 0.0182 (Fig. 18). The mean square error between EF measured and estimated is $5.4615 \times 10^{-4}$ and its standard deviation is $7.8694 \times 10^{-4}$. The ejection fractions measured by the fast thermistor and estimated by the method from the slow thermistor present high correlation in the tested interval ($r = 0.9714$). Therefore, one could conclude that the two methods presented equivalent results in the range tested.

The proposed method shows promising clinical application. The method still needs to be tested in vivo, possibly in pigs. Nevertheless, the results show that the method has great potential for clinical application.

6. Conclusions

The objectives of this work were: (1) to develop a new algorithm based on the Da Rocha method [8,9] in order to estimate the impulse response of slow thermistor mounted in thermodilution catheters; (2) to present an algorithm with a reduced computational processing time; (3) to evaluate the proposed method by means of numerical and in vitro simulations.

An automatic algorithm was developed in order to estimate the transfer function of thermistors mounted in thermodilution catheters. The method was based on the qualitative and quantitative characteristics of the thermodilution curve and of the impulse response of thermistor probes. The algorithm requires a reduced computational processing time (about 2 s). This means that the algorithm might be used to monitor patients in intensive care units.

Statistical analyses of the numerical simulations showed that estimated and real ejection fractions presented similar results. The square mean error between real and estimated data was 0.0036. A high correlation between the data was also found in the studied interval ($r = 0.9961$). In other words, the simulations showed that the deconvolution algorithm can accurately recover the true signal from the distorted signal.

The statistical analysis of the in vitro simulations revealed significant results. The algorithm presented a reduced computational processing time. The square mean error between EF measured by the fast thermistor and estimated by the method using the slow thermistor was $7.8694 \times 10^{-4}$. Furthermore, there was a high correlation between the two methods ($r = 0.9714$). Therefore, one could conclude that the two methods presented equivalent results in the range tested.

The proposed method shows promising clinical application. The method still needs to be tested in vivo, possibly in pigs. Nevertheless, the results show that the method has great potential for clinical application.

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