Mathematical Models Based on Transfer Functions to Estimate Tissue Temperature During RF Cardiac Ablation in Real Time

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Abstract: Radiofrequency cardiac ablation (RFCA) has been used to treat certain types of cardiac arrhythmias by producing a thermal lesion. Even though a tissue temperature higher than 50ºC is required to destroy the target, thermal mapping is not currently used during RFCA. Our aim was thus to develop mathematical models capable of estimating tissue temperature from tissue characteristics acquired or estimated at the beginning of the procedure (electrical conductivity, thermal conductivity, specific heat and density) and the applied voltage at any time. Biological tissue was considered as a system with an input (applied voltage) and output (tissue temperature), and so the mathematical models were based on transfer functions relating these variables. We used theoretical models based on finite element method to verify the mathematical models. Firstly, we solved finite element models to identify the transfer functions between the temperature at a depth of 4 mm and a constant applied voltage using a 7Fr and 4 mm electrode. The results showed that the relationships can be expressed as first-order transfer functions. Changes in electrical conductivity only affected the static gain of the system, while specific heat variations produced a change in the dynamic system response. In contrast, variations in thermal conductivity modified both the static gain and the dynamic system response. Finally, to assess the performance of the transfer functions obtained, we conducted a new set of computer simulations using a controlled temperature protocol and considering the temperature dependence of the thermal and electrical conductivities, i.e. conditions closer to those found in clinical use. The results showed that the difference between the values estimated from transfer functions and the temperatures obtained from finite element models was less than 4ºC, which suggests that the proposed method could be used to estimate tissue temperature in real time.

Keywords: Cardiac ablation, closed loop control, finite element method, radiofrequency ablation, temperature controlled ablation, theoretical model.

INTRODUCTION

Radiofrequency cardiac ablation (RFCA) is currently used to treat some types of cardiac arrhythmia. This technique uses radiofrequency (RF) current (≈500 kHz) to produce a thermal lesion and hence tissue necrosis in the target zone responsible for the arrhythmia. Electrical current is delivered to the tissue through a small active electrode placed at the tip of a percutaneous catheter and a large dispersive electrode located on the patient's back. There are two modes of delivering radiofrequency energy: constant voltage and temperature-controlled. The constant voltage mode means that the applied voltage is constant; under this condition high temperatures (approximately 100ºC) can be reached in the tissue around the electrode tip in few seconds and lesion size is limited by the charring of tissue around the electrode. The temperature-controlled mode, which can make a larger lesion than the constant voltage approach [1], is the one most frequently used in clinical practice [1, 2] and consists of modulating the applied voltage to keep the temperature constant at the active electrode. The temperature sensor embedded in the electrode tip measures the approximate temperature at the tissue-electrode interface. Even though a tissue temperature higher than 50ºC is required to destroy the target, thermal mapping is not currently used during RFCA. This is an important issue, since tissue temperatures above 100ºC are associated with charring and can cause a thrombus [3]. Safer ablations could thus be achieved by knowing the temperature in the tissue in order to ensure the creation of the thermal lesion and to avoid overheating. Our aim was thus to develop mathematical models to estimate tissue temperature in real time from the tissue characteristics (electrical conductivity *(σ)*, thermal conductivity *(k)*, specific heat *(c)* and density *(ρ)*) measured or estimated at the beginning of the procedure and the applied voltage at any time.

Previous work has been conducted on estimating lesion progress on-line by studying impedance progress [4-6]. Numerical modeling (e.g. based on the Finite Element Method (FEM)) has also been proposed to estimate tissue temperature during RFCA [7]. This method calculates the temperature distribution by means of solving numerically

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Table 1. Characteristics of the Materials Used in the Model [10, 12]

Material	Region	σ (S/m)	ρ (kg/m^3)	c (J/kgK)	k (W/mK)	Reference
Cardiac Tissue	Myocardial	0.541	1060	3111	0.531	[10]
Pt-Ir	Electrode	4×10^6	21.5×10^3	132	71	[10]
Insulation	Coating	10^{-5}	32	835	0.038	[10]
Glass fiber	Thermistor	10^{-5}	32	835	0.038	[12]
Polyurethane	Catheter body	10^{-5}	70	1045	0.026	[10]

Note: σ: electrical conductivity, ρ: density, c: specific heat, k: thermal conductivity. Tissue characteristics evaluated at 37°C.

chamber produces a cooling effect on the tissue and on the electrode surface, which was modeled by means of two thermal convection coefficients h_{tissue} and h_{elec} which represent the cooling effect at the blood-tissue interface and at the blood-electrode interface respectively (see Fig. **2A**). We considered a medium blood flow rate, with values for h_{elec} of 3636 W/m^{2}K and for h_{tissue} of 708 W/m^{2}K [10] and an initial temperature of 37ºC. Table **1** shows the values of the physical characteristics of the materials [10, 12]. Electrical and thermal conductivity variations with temperature were not considered in these FEM models in order to obtain a relatively simple mathematical model which could be used as a first step towards a more complex (non-linear model).

We used COMSOL Multiphysics software (COMSOL Inc., Burlington, MA, USA) to implement the numerical solution based on the FEM. In order to avoid boundary effects, the model dimensions R, Z and L (see Fig. **2A**) were estimated by means of convergence tests in which the value of the maximum temperature reached in the tissue (T_{max}) after 120 s of RF heating was used as a control parameter. Parameter values were increased by 1 mm in each simulation. If there was a difference of less than 0.5% between T_{max} and the same parameter in the previous simulation, the former values were considered as appropriate. The mesh was initially heterogeneous and a finer mesh was used around the electrode-tissue interface, where the highest gradient was expected. The mesh was then refined to determine adequate spatial resolution and the time-step was reduced to determine adequate temporal resolution.

Identification of the Transfer Function

In the context of our study, the biological tissue was considered to be a dynamic system with applied voltage (V) as input signal and the temperature obtained at a depth of 4 mm (T_4) as an output signal (see Fig. **2B**). It is assumed that the dynamic evolution of the system output (T_4) with respect to the system input (U) can be expressed mathematically in terms of a differential equation. If the differential equation is linear, the mathematical input/output relationship can be expressed as a transfer function.

The first step was to obtain an accurate identification of the system response of the modeled tissue, which involves obtaining the transfer function $G(s)$. This was carried out firstly by applying a constant voltage of 15 V for 300 s. The The model is assumed to be $U(t)=V^2(t)$ in which V was the applied voltage. We checked that the active electrode tip temperature stabilized around 55°C. We then obtained the evolution of T_4, and MATLAB was then used to estimate the model response.

A first-order transfer function was obtained from the simulated evolution. The estimated transfer functions $G(s)$ in Laplace-transform quantities had the form:

$$G(s) = \frac{\Delta T_4(s)}{U(s)} = \frac{K_V}{1+\tau s} \tag{2}$$

where ΔT_4 is the temperature increase (above a base temperature of 37º), $U(s)$ is the square of the voltage applied to the electrode, K_V is the steady state gain of the system expressed in $^oC/V^2$, and τ is the time constant. A first order transfer function was used since it is the simplest transfer function that leads to results reasonably similar to those obtained from finite element simulations.

From a practical point of view and using the above parameters for the first model obtained, the ablation final temperature could be calculated as follows:

$$T_{4final} = \Delta T_{4final} + T_{initial} \tag{3}$$

where $\Delta T_{4final} = V^2 K_V$, being V the applied voltage and $T_{initial}$ = 37°C.

Description of the Analyzed Cases

In order to study the influence of the tissue characteristics on the mathematical behavior of the ablation process we carried out several computer simulations with varying values of σ, k and c. We considered a variation from −75% to 100%, in steps of 25%, beginning with the value shown in Table **1**. We show an example:

$$k_{-25\%} = k - 0.25k \tag{4}$$

where k=0.531 W/mK and $k_{-25\%}$= 0.398 W/mK is the thermal conductivity variation. A first-order transfer function (2) was identified for each case, with corresponding values of K_V and τ. This group of transfer functions was obtained in order to study the relationship between the transfer function gain (K_V) and time constant (τ) with the variations in tissue specific heat and electrical and thermal conductivity. From the series of the K_V and τ values, a general mathematical relationship for the variation of K_V and τ for different values of σ, k and c was obtained.

Building the Mathematical Model

We divided the study into two parts: firstly, we assessed the influence of the values of σ, k and c independently, i.e. for each variable separately in order to study the relationship between gain and time constant in each tissue characteristic. From these relationships we were able to obtain a mathematical model.

Fig. (5). Temperature evolution from FEM based models (solid line) and temperature estimated from mathematical model (dashed line). Ten cases were considered with changes in the values of tissue characteristics (see Table **2**).

Fig. (6). Error evolution in ºC. The error was obtained from the difference between the estimated tissue temperature (computed from the mathematical model) and the real temperature (obtained by the theoretical model using COMSOL Multiphysics). Ten cases were considered with changing in the values of tissue characteristics (see Table **2**).

mathematical models proved to be reasonably similar to those obtained from numerical models, since they always kept lower than 5ºC, which is around the range of lethal isotherm found in experiments using cardiac tissue [15]. The maximum error of 4ºC was obtained from the maximum difference between the tissue temperature estimated by the mathematical model and tissue temperature obtained from COMSOL Multiphysics. In all the cases the temperature was underestimated. The temperature dependence of the thermal and electric conductivity was not initially considered in the model and may be the likely reason for the consistent underestimation of tissue temperature.

In order to obtain the input parameters for the mathematical models the initial values of the tissue characteristics (σ, k and c) must be known and can be obtained from experimental measurements, as described in previous studies. For example, techniques based on automatic swept-frequency network and impedance analysers have been proposed to measure electrical conductivity [16], and the empirical relation between the power delivered to a heated thermistor by a heating pulse and the temperature rise recorded by the sensing thermistor placed at a distance from the sample could be used to measure thermal conductivity [14]. Further studies will be undertaken in order to obtain a mathematical model that takes into account temperature-dependent parameters and new methods of estimating initial tissue characteristics.

Clearly, tissue temperature estimation is currently a challenge. Although previous studies estimated temperature by means of impedance measurements [4-6] and numerical modeling [7], here we present a new method based on simple mathematical models. Our findings suggest that if the applied voltage ($U=V^2$) and the initial value of the tissue characteristics (σ, k and c) are known, mathematical models based on transfer functions could be used to estimate tissue temperature at specific points with reasonable accuracy. This study could lead to the further development of more detailed mathematical models by considering additional factors, such as insertion depth and circulation blood flow.

CONCLUSIONS

The results suggest that it is possible to estimate temperature at a specific point (at a depth of 4 mm in this case) from the evolution of the applied voltage when the initial value of the tissue characteristics is known. The proposed mathematical model agreed reasonably accurately (around 4ºC) with the results given by FEM.

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