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Sensitivity analysis for radiofrequency induced thermal therapies using the complex finite element method

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ABSTRACT

In radiofrequency induced thermal procedures for cancer treatment, the temperature of the cancerous tissue is raised over therapeutic values while maintaining the temperature of the surrounding tissue at normal levels. In order to control these temperature levels during a thermal therapy, it is important to predict the temperature distribution over the region of interest and analyze how the variations of the different parameters can affect the temperature in the healthy and damaged tissue. This paper proposes a sensitivity analysis of the radiofrequency induced thermal procedures using the complex Taylor series expansion (CTSE) finite element method (ZFEM), which is more accurate and robust compared to the finite difference method. The radiofrequency induced thermal procedure is modeled by the bioheat and the Joule heating equations. Both equations are coupled and solved using complex-variable finite element analysis. As a result, the temperature sensitivity with respect to any material property or boundary condition involved in the process can be calculated using CTSE.

Two thermal therapeutical examples, hyperthermia and ablation induced by radio frequency, are presented to illustrate the capabilities and accuracy of the method. Relative sensitivities of the temperature were computed for a broad range of parameters involved in the radiofrequency induced thermal process using ZFEM. The major feature of the method is that it enables a comprehensive evaluation of the problem sensitivities, including both model parameters and boundary conditions. The accuracy and efficiency of the method was shown to be superior to the finite difference method. The computing time of a complex finite element analysis is about 1.6 times the computing time of real finite element analysis; significantly lower than the 2 times of forward/backward finite differencing or 3 times of central differencing. It was found that the radiofrequency hyperthermia procedure is very sensitive to the electric field and temperature boundary conditions. In the case of the radiofrequency ablation procedure, the cooling temperature of the electrodes has the highest liver/tumor temperature sensitivity. Also, thermal and electrical conductivities of the healthy tissue were the properties with the highest temperature sensitivities. The result of the sensitive analysis can be used to design very robust and safe medical procedures as well as to plan specific patient procedures.

1. Introduction

A radiofrequency induced thermal procedure is a minimally invasive clinical method for the treatment of hepatocellular carcinoma that consists of the heating of biological tissues through the emission of an external electric field. The radiofrequency induced thermal procedure is used when the tumor or other dysfunctional tissues are not surgically resectable due to the location or the potential of significant collateral damage in the surgical process. Radio frequency ablation can be used to treat tumors in the liver as well as those in other organ sites such as lung, kidney, pancreas and bone.

The goal of a radiofrequency induced thermal treatment is to raise the temperature of the tumor to a value in the range from $(42-46)\,°\mathrm{C}$ for hyperthermia therapy, or to a value in the range from $(50-100)\,°\mathrm{C}$ for radiofrequency ablation therapy. The temperature field is applied for certain time so that the tumor tissues are destroyed while keeping the temperature in the healthy tissue region below critical temperature to avoid unwanted damage [1–3]. The success of either hyperthermia and ablation induced by radio frequency depend on: (i) how well the temperature field is controlled and optimized to ensure the temperature is high enough to destroy the cancer cells in the tumor region (ii) how to minimize the damage in the healthy tissues surrounding the

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tumor with reasonable margin prescribed by an oncologist or surgeon.

The thermal modeling of the radiofrequency induced thermal treatment has been studied by several researchers with Pennes [4] the first to introduce a mathematical equation explaining the heat transfer present in a biological tissue. This equation is known as the bioheat transfer equation. Tunç et al. [5] applied the bioheat transfer equation in the analysis of hyperthermia treatments. Chang and Nguyen developed a model to predict the size of the thermal lesions created by the radiofrequency induced thermal procedure using the Arrhenius equation which relates the temperature and the exposure time, using a first order kinetics relationship [6]. Fuentes et al. compared the thermal damage region, recreated in a computer simulation, with the radiofrequency induced thermal procedure in an *in vitro* perfused bovine liver model, finding a good correlation between the two damage regions [1]. In addition, the bioheat transfer in some organs may need a hyperbolic term to account for finite time dispersion of heat energy [7].

Despite significant research efforts, the prediction of the temperature distribution is still an important issue in the reliability and effectiveness of the treatment. Since the human body is a complex blend of tissue with heterogeneous electric and thermal characteristics, it is a difficult task to predict and control the temperature distribution and to determine the optimum heating configuration during therapy. Recent advances in this direction include the development of a patient-specific image-based 3D model for thermal ablation simulation to optimize treatment efficacy [8]. Also, Schumann et al. proposed an access path determination method, for radiofrequency ablation planning, based on image processing and numerical optimization [9]. Therefore, it is important to develop a tool capable of predicting the thermal results given the variation of the material properties and the radiofrequency induced thermal variables. Hence, a thorough sensitivity analysis of each variable involved in the process will allow one to identify those variables with the largest impact on the tumor temperature distribution. The Complex Taylor Series Expansion (CTSE) method was used here to perform this analysis. It was first proposed by [10] and [11]. [12] were the first to obtain a method to approximate derivatives of real functions using complex variables. The CTSE method calculates the first derivative with respect a parameter by perturbing the parameter along the imaginary axes. There is no difference operation involved, and therefore it avoids the cancellation error presented in the Finite Difference Method (FDM). This allows the method to be step size independent, easy to implement and highly accurate. The method has proven to be very attractive in applications where a sensitivity analysis is required, and it has been applied in several fields of engineering as: the computation of sensitivity derivatives of NavierStokes equations [13], shape sensitivity analysis [14], fatigue sensitivity analysis [15], fracture mechanics [16–19], nonlinear problems in plasticity [20] and creep [21], aerodynamics [22,23], structural dynamics [24,25], and nonlinear structural analysis [26], among others. However, the CTSE has not been exploited in bioengineering or medical research.

In this paper, a simplified 2D geometry of the radiofrequency induced thermal process was modelled using the bioheat transfer equation coupled with the Joule heating equation. The sensitivity was calculated using CTSE, and the results were compared with the sensitivity found using the finite difference method in order to demonstrate the superior step size independence of the CTSE method.

2. Radiofrequency induced thermal process

A simplified 2D model of the radiofrequency ablation, adopted and modified from [27], is shown in Fig. 1. The domain Ω is composed of two subdomains, the healthy tissue domain Ω_1, and the tumor domain Ω_2. A point $\boldsymbol{x} = (x, y) \in \Omega$, will have different properties depending on whether it is located in the tumor, $\boldsymbol{x} \in \Omega_2$, or in the healthy tissue, $\boldsymbol{x} \in \Omega_1$. The boundary of the domain $\partial\Omega$ is composed of four parts

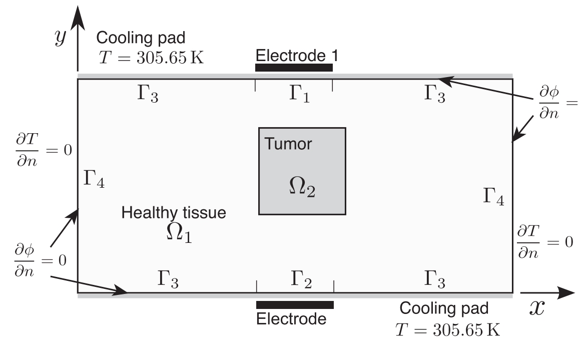

Fig. 1. A simplified 2D model of a radiofrequency induced thermal treatment (hyperthermia) with an embedded tumor.

$\partial\Omega = \Gamma_1 + \Gamma_2 + \Gamma_3 + \Gamma_4$. The electric field is generated from two electrodes located on the top Γ_1 and bottom Γ_2 of the healthy tissue, generating a voltage gradient. The top and bottom of the healthy tissue Γ_3 are covered with a cooling pad that preserves a constant temperature at the surface. The left and right side Γ_4 are assumed insulated surfaces. A detail description of the geometry is presented in Section 4.

The radiofrequency induced thermal treatment can be described as the coupling of two physical phenomena. The first is the heat induced by the electric field generated from the electrodes; the second is the heat transfer in the tissue and considers the metabolic heat, perfusion rate and the heat produced by the electric field. The combination of these two models allows one to predict the temperature field distribution on the domain (organ). A quasi-static electric field approximation was used due to the fact that the wave length of the radiofrequency is much greater compared to the depth of the computational domain, therefore, the free charge continuity equation takes the following form [28],

$$\nabla\cdot\boldsymbol{J}(\boldsymbol{x}) = 0, \tag{1}$$

where the electric current density $\boldsymbol{J} = \boldsymbol{J}(\boldsymbol{x})[\mathrm{A/m^2}]$ is related to the electric field through the Ohm's law

$$\nabla\cdot\sigma(\boldsymbol{x})\boldsymbol{E}(\boldsymbol{x}) = 0. \tag{2}$$

Here, $\sigma = \sigma(\boldsymbol{x})$ [s/m] is the tissue electrical conductivity and $\boldsymbol{E} = \boldsymbol{E}(\boldsymbol{x})$ [V/m] denotes the electric field. The electric field can be defined as the gradient of the electric potential $\phi(\boldsymbol{x})$ [V]

$$\boldsymbol{E}(\boldsymbol{x}) = \nabla\phi(\boldsymbol{x}). \tag{3}$$

Substituting Eq. (3) into Eq. (2) yields the governing electric potential equation,

$$\nabla\cdot\sigma(\boldsymbol{x})\nabla\phi(\boldsymbol{x}) = 0. \tag{4}$$

When the electric conductivity σ is constant over the domain, Eq. (4) is transformed into the Laplace equation $\sigma\nabla^2\phi = 0$. However, this is not the case in the present study as the healthy tissue and tumor tissue have different physical properties. The boundary conditions necessary to solve Eq. (4) are as follows: a Dirichlet boundary condition with the value of the electric potential relative to ground is specified on each electrode Γ_1, Γ_2. A Newman boundary condition equal to zero, $\frac{\partial\phi}{\partial n} = 0$ representing an ideal electrical isolation, is specified on the remaining external boundaries Γ_3, Γ_4, see Fig. 1. The differential in electric potential produces an electric current through the tissue and releases heat. This process is called Joule heating and is also referred to as Ohmic or resistive heating. The amount of heat released is proportional to the square of the current, or in terms of the electric field

$$\begin{aligned} Q_J(\boldsymbol{x}) &= \sigma(\boldsymbol{x})\boldsymbol{E}(\boldsymbol{x})\cdot\boldsymbol{E}(\boldsymbol{x}) \quad \text{or} \\ Q_J(\boldsymbol{x}) &= \sigma(\boldsymbol{x})\|\nabla\phi(\boldsymbol{x})\|^2. \end{aligned} \tag{5}$$

On the other hand, the temperature distribution inside the healthy and the tumor tissue is described by the bioheat transfer equation also known as the Pennes equation [4]. This equation has an added source