Heat transfer model to characterize the focal cooling necessary to suppress spontaneous epileptiform activity (Invited Paper)

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Heat transfer model to characterize the focal cooling necessary to suppress spontaneous epileptiform activity

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ABSTRACT

Epilepsy is characterized by paroxysmal transient disturbances of the electrical activity of the brain. Symptoms are manifested as impairment of motor, sensory, or psychic function with or without loss of consciousness or convulsive seizures. This paper presents an initial post-operative heat transfer analysis of surgery performed on a 41 year-old man with medically intractable Epilepsy. The surgery involved tumor removal and the resection of adjacent epileptogenic tissue. Electrocorticography was performed before resection. Cold saline was applied to the resulting interictal spike foci resulting in transient, complete cessation of spiking. A transient one dimensional semi-infinite finite element model of the surface of the brain was developed to simulate the surgery. An approximate temperature distribution of the perfused brain was developed by applying the bioheat equation. The model quantifies the surface heat flux reached in achieving seizure cessation to within an order of magnitude. Rat models have previously shown that the brain surface temperature range to rapidly terminate epileptogenic activity is 20-24°*C*. The developed model predicts that a constant heat flux of approximately -13,000W/m^2, applied at the surface of the human brain, would achieve a surface temperature in this range in approximately 3 seconds. A parametric study was subsequently performed to characterize the effects of brain metabolism and brain blood perfusion as a function of the determined heat flux. The results of these findings can be used as a first approximation in defining the specifications of a cooling device to suppress seizures in human models.

Keywords: Brain Cooling, Focal Cooling, Epilepsy, Bioheat Equation, Implantable Device

NOMENCLATURE

$T \equiv$ Temperature
$\rho \equiv$ Density
$c \equiv$ Specific Heat
$k \equiv$ Thermal Conductivity
$\omega\rho_b \equiv$ Capillary Perfusion Rate
$\dot{q}'''_{met} \equiv$ Metabolic Heat Rate

1. INTRODUCTION

Epilepsy is characterized by paroxysmal transient disturbances of the electrical activity of the brain. Symptoms are manifested as impairment of motor, sensory, or psychic function with or without loss of consciousness or convulsive seizures. Resection, in which the diseased part of the brain is surgically removed, is currently the only viable treatment for people who suffer from intractable epilepsy. It has recently been reported that in-surgery focal cooling of the cerebral cortex reproducibly abolished epileptiform discharges[1] (i.e. voltage spikes as measured through electrocorticography). The case report[1] describes a 41 year-old man with medically intractable epilepsy. The man's surgery involved tumor removal and the resection of adjacent epileptogenic tissue located in the right posterior-superior

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frontal lobe of the cerebral cortex. Immediately preceding resection, cortical mapping through electrocorticography (ECoG) was performed in order to identify the functionality of the tissue to be removed. Epileptogenic discharges are common during the cortical mapping process. Frequent (~12/*min*) high amplitude epileptiform discharges were recorded from the precentral gyrus via ECoG. Cold saline was applied to the resulting interictal spike foci resulting in transient, complete cessation of epileptogenic discharges.

This report describes a transient finite element heat transfer model of the brain developed to simulate this suppression of epileptogenic discharges. The results of the simulation represent the first steps toward the development of an implantable cerebral device to conjointly detect and suppress epileptiform activity.

2. METHODLOGY

A temperature distribution of the perfused brain was developed by applying the bioheat equation[2] to the surface of the brain:

$$\rho_B c_B \frac{\partial T}{\partial t} = \nabla(k_B \nabla T) + \omega \rho_b c_b (T_a - T_v) + \dot{q}'''_{met} \qquad \text{(Pennes Equation)}$$

where the subscripts *B,* and *b* stand for brain tissue and blood respectively. The parameters T_a and T_v are the temperatures of the arterial blood and venous blood, respectively. The $\dot{q}'''_{met}$ term, defined above, is an energy generation term associated with the production of heat due to cellular metabolism. The source/sink term, $\omega \rho_b c_b (T_a - T_v)$, is included to account for the heat transferred from blood perfusion[3]. It is typical to assume that the arterial temperature enters the tissue control volume at the deep body temperature and the venous temperature exits the control volume at the tissue temperature, *T*. These assumptions lead to the following modified version of the Pennes Equation:

$$\rho_B c_B \frac{\partial T}{\partial t} = \nabla(k_B \nabla T) + \omega \rho_b c_b (T_{DB} - T) + \dot{q}'''_{met} \qquad (1)$$

where T_{DB} represents the deep body temperature.

The Q_{10} law of thermal physiology, or the Van't Hoff rule, states that for every 10°*C* reduction in tissue temperature, the metabolic heat rate is correspondingly reduced by a factor of Q_{10}. This law can be applied to both cooling and heating applications. Mathematically, the law is stated as:

$$Q_{10} = \frac{\dot{q}'''_{met}}{\dot{q}'''_{met_{DB}}}^{10/T - T_{DB}} \qquad (2)$$

The parameter $\dot{q}'''_{met_{DB}}$ corresponds to the initial metabolic heat rate at the deep body temperature. Typical metabolic heat rates have Q_{10} values in the 2-3 range, i.e. doubling or tripling with every 10°*C* increase in temperature. However, given the relatively small time scale and temperature range of the surgical conditions, in this model all perfused brain thermal parameters, including the metabolic heat rate, were taken as isotropic and constant, Table 1.

Table 1. Perfused brain thermal parameters[4]

$$\rho_B = 1039 \frac{kg}{m^3}$$

$$c_B = 3680 \frac{J}{kg \cdot K}$$

$$k_B = 0.565 \frac{W}{m \cdot K}$$

$$\dot{q}'''_{met} = 525.0 \frac{W}{m^3}$$

$$\omega \rho_b c_b = 8.6 \times 3680 \frac{kg}{m^3 \cdot s}$$

The case report of the surgery[1] describes the continual impingement of 4°*C* saline solution for 30 seconds. This was modeled as a constant surface temperature boundary condition at the surface of the brain in the finite element model. It is hypothesized that the focal point of epileptiform activity on the surface of the human brain is relatively small with respect to the area of impinging saline. It was also anticipated that the depth of penetration to suppress epileptiform activity was on the order of a 2 to 3 millimeters. This motivated the use of a one-dimensional semi-infinite geometry. Under these conditions, Equation (1) simplifies to:

$$\rho_B c_B \frac{\partial T}{\partial t} = k_B \frac{\partial^2 T}{\partial x^2} + \omega \rho_b c_b (T_B - T) + \dot{q}'''_{met} \qquad (3)$$

A finite element model of Equation (3) was subsequently developed. The finite element model was developed utilizing FEMLAB, a MATLAB based finite element modeling package (The COMSUL Group, Stockholm Sweden). The semi-infinite geometry was discretized into 2880 elements consisting of 2881 nodes. The numerical simulations were performed on 1.5GHz personal computer with 523,280 KB RAM. Typical simulations were performed in less than 10 seconds.

3. RESULTS

The developed model was utilized to simulate the aforementioned surgery and to characterize the effects of brain metabolism and blood perfusion.

Surgery Simulation

Figure 1 shows the transient temperature profiles of the brain under the surgical conditions described above. The development of the temperature profiles is shown in 5 second increments. Figure 1 indicates that the effects of the cold saline were primarily confined to a short distance below the surface of the brain. Rat models have previously shown that the surface temperature range to rapidly terminate epileptogenic activity is 20-24°*C*[4]. Figure 1 indicates that the application of 4°*C* saline to the surface of the human brain resulted in a 20°*C* 'penetration' temperature at approximately 1.7 millimeters below the surface of the brain.

The finite element model was subsequently used to quantify the surface heat flux drawn by the cold saline. Figure 2 shows a plot of the variation of the surface heat flux during the application of the cold saline.

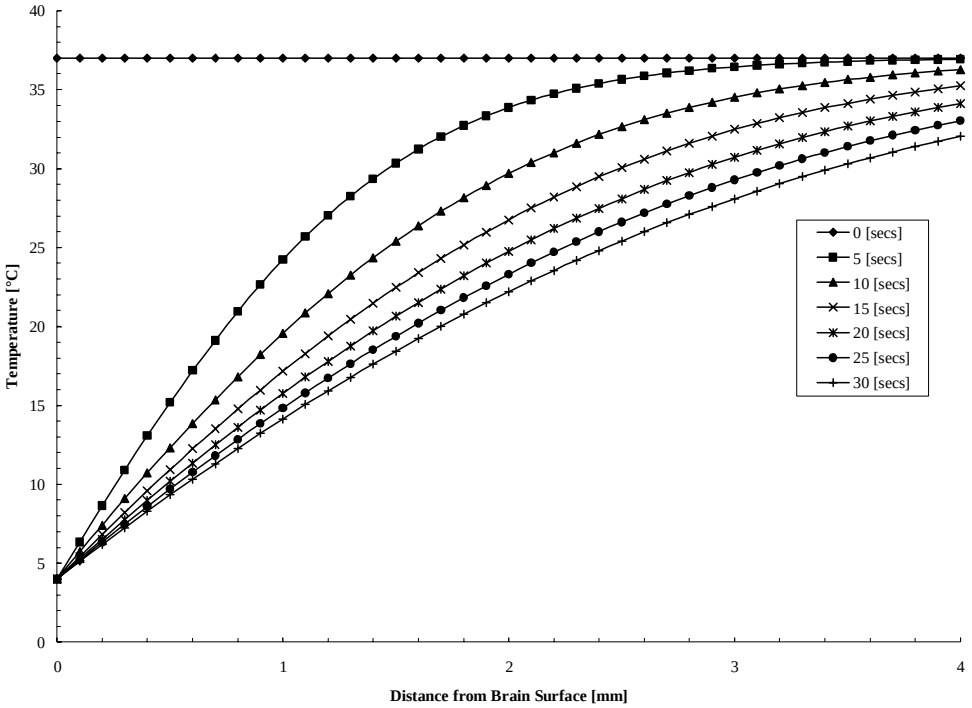

Figure 1: Semi-infinite domain transient temperature profiles of the surgical conditions described in [1]

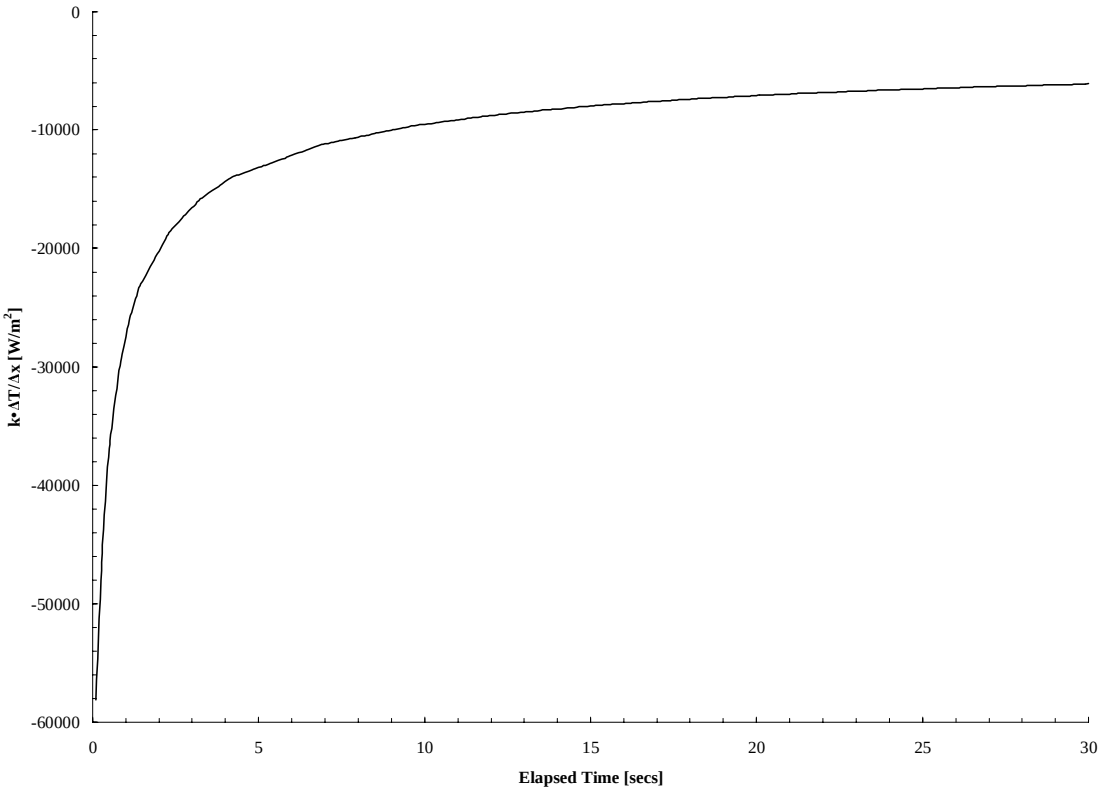

Figure 2: Semi-infinite domain variation in surface heat flux during the cold saline application process

The model suggests a sharp drop in surface heat flux magnitude, as expected, during the first 3-5 seconds of cold saline application. The heat flux gradually begins to "level-off" as the temperatures close to the surface begin to approach the constant temperature boundary condition.

Within an order of magnitude, Figure 2 provides an estimate of the heat flux experienced during the application of the cold saline. Consequently, heat fluxes on this order were applied as boundary conditions to the developed finite element model of Equation (3). Figure 3 shows that a surface temperature of $20°C$ can be reached in 3 seconds through the application of a constant surface flux of $-13{,}000 W/m^2$.

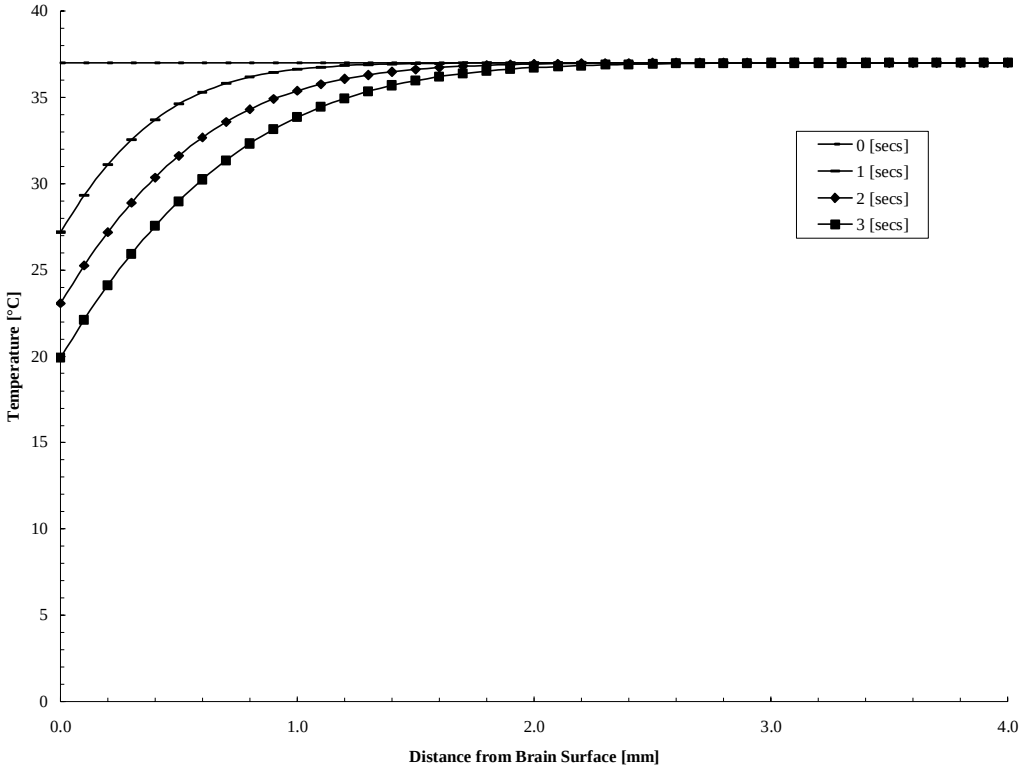

Figure 3: Semi-infinite domain transient temperature profiles resulting from the application of a constant surface heat flux of $-13{,}000 W/m^2$ at the surface of the brain

Effects of Metabolic Heat Rate and Blood Perfusion

The initial sharp drop in surface heat flux shown modeled in Figure 2 indicates that the brain responded swiftly to the application of cold saline. Consequently, it was anticipated that the effects of metabolic heat and blood perfusion were negligible during this cooling process. To evaluate this hypothesis, an additional simulation was performed with these effects eliminated from the finite element model. Therefore, neglecting the metabolism and blood perfusion terms, Equation (3) simplifies to:

$$\rho_B c_B \frac{\partial T}{\partial t} = k_B \frac{\partial^2 T}{\partial x^2} \qquad (3')$$

The finite element model was then modified to solve this simplified equation. A heat flux of -13,000W/m^2 was applied as a boundary condition at the surface of the brain in the semi-infinite model. The heat flux boundary condition was applied for 3 seconds in the semi-infinite model. The difference in solutions with and without the effects of metabolism and blood perfusion is shown in Figure 4.

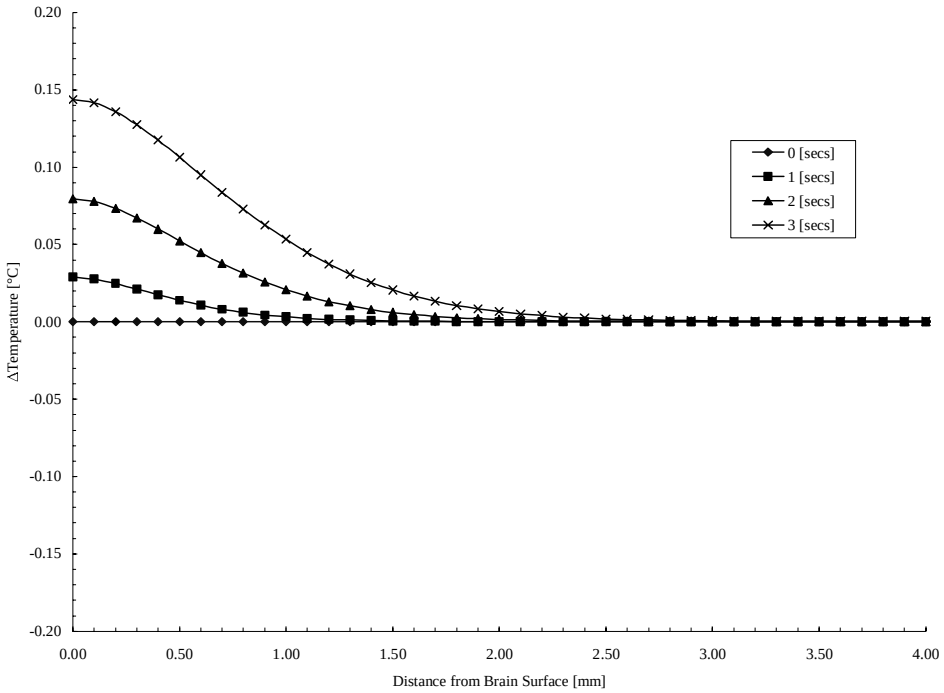

Figure 4: Temperature deviation resulting from neglecting metabolism and blood perfusion in the semi-infinite domain

These results indicate that the maximum error, ΔT, in neglecting metabolism and blood perfusion while reducing the surface temperature to 20°*C* in 3 seconds is less than 0.2°*C*.

4. CONCLUSIONS

It has been demonstrated that focal cooling can abolish spontaneous epileptiform activity in humans while maintaining intact cortical motor function[1]. This, combined with the success of previous animal models, suggests that an implantable focal cooling device could be used to suppress epileptogenic seizures[1,6]. This paper presents attempts to characterize the heat transfer environment necessary to suppress epileptiform activity. The results of this finite element model simulation are taken as the first steps toward the development of an implantable cerebral device to conjointly detect and suppress epileptiform activity.

A finite element model was developed to characterize the focal cooling necessary to suppress epileptiform activity. The modeled transient temperature profiles resulting from the application of cold saline to the surface of the brain of a patient with medically intractable epilepsy are shown in Figure 1. These results indicate that the depth of penetration to suppress epileptiform activity may be less than 2 millimeters below the surface of the human brain. As previously stated, rat models have previously shown that the surface temperature range to rapidly terminate seizures is 20-24°*C*. The developed model indicates that a target surface temperature of 20°*C* can be reached in 3 seconds through the application of a constant surface heat flux of -13,000W/m^2. The model also indicates that, under these conditions, the perfused brain temperature profiles can be approximated while neglecting the effects of metabolism and blood perfusion. Neglecting metabolism and blood perfusion not only simplifies the development of a solution to the Pennes

equation, but also facilitates the selection of a possible 'mock brain' material that may be used to test future devices developed to detect and suppress epileptiform activity.

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