Numerical Modeling of Thermal Effects during Irreversible Electroporation Treatments

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Duration of the experiment: 90 min
Max. number of participants: 6
Location: Laboratory of Biocybernetics
Level: Advanced

PREREQUISITES

Basic to advanced knowledge of finite element modeling

THEORETICAL BACKGROUND

Irreversible electroporation (IRE) is a new, safe, and effective minimally invasive ablation modality with the potential to treat many currently unresectable and/or untreatable tumors. The non-thermal mode of cell death in IRE is unique in that it does not rely on thermal changes from Joule heating to kill tumor cells thus allowing for successful treatment even in close proximity to critical structures and without being affected by the heat sink effect. Accurate modeling of the electrical and thermal responses in tissue is important to achieve complete coverage of the tumor and ensure that the thermal changes during a procedure do not generate thermal damage, especially in critical structures (e.g. bile ducts, nerves and sensitive blood vessels).

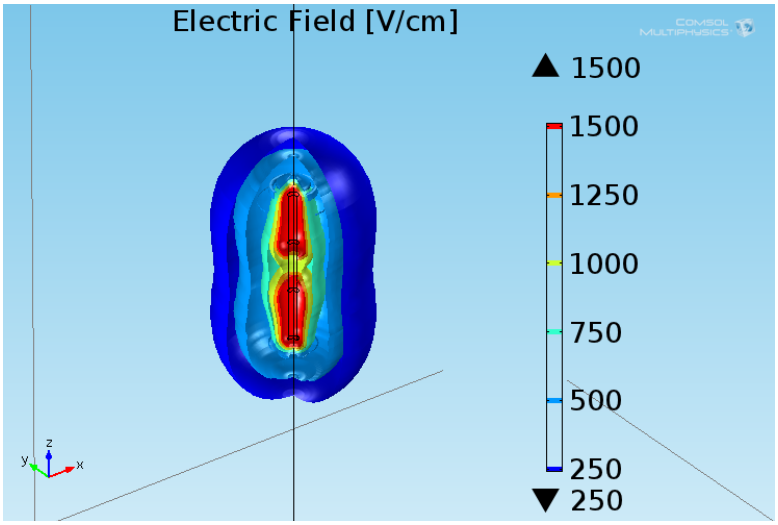

Figure 1: Electric Field distribution resulting from a bipolar electrode with an applied voltage of 1250 V.

The temperature distribution (T) within the tissue will be obtained by transiently solving a modified heat conduction equation with the inclusion of the Joule heating source term $Q = \sigma|\nabla\varphi|^2$

$$\rho C \frac{\partial T}{\partial t} = \nabla \cdot (k\nabla T) + Q \qquad (1)$$

where σ is the electrical conductivity, φ the electric potential, k is the thermal conductivity, C is the specific heat capacity, and ρ is the density of the tissue. At each time step, the current density and electric field distribution are determined and updated in the Joule heating term to capture the electrical conductivity changes in liver tissue from electroporation and temperature.

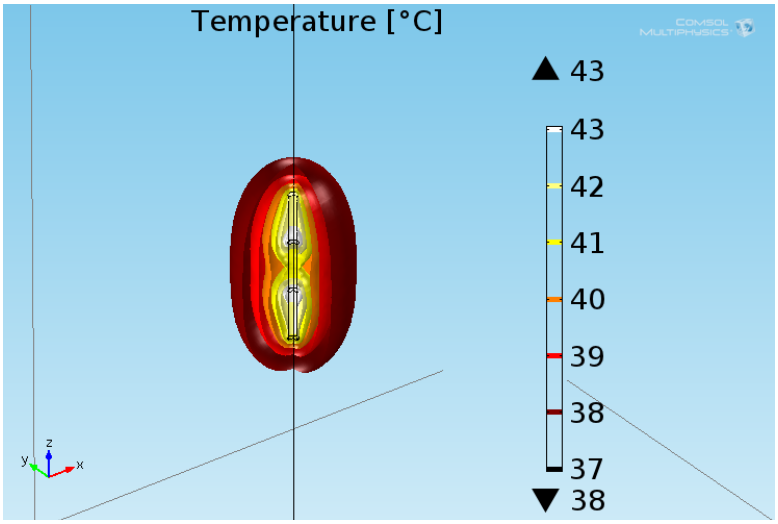

Figure 2: Temperature distribution after a ninety 100-µs pulse IRE treatment in liver tissue at 1 pulse per second.

Thermal damage is a process that depends on temperature and time. If the exposure is long, damage can occur at temperatures as low as 42°C, while 50°C is generally chosen as the target temperature for instantaneous damage. The damage can be calculated based on the temperatures to assess whether a particular set of pulse parameters and electrode configuration will induce thermal damage in superposition with IRE. The thermal damage will be quantified using the Arrhenius rate equation given by:

$$\Omega(t) = \int_{t=0}^{t=\tau} \zeta \cdot e^{\frac{-E_a}{R \cdot T(t)}} dt \qquad (2)$$

where R is the universal gas constant, 8.314 J/(mol·K); ζ is the pre-exponential factor, 7.39×10^{39} s^{-1}, a measure of the effective collision frequency between reacting molecules in bimolecular reactions; E_a the activation energy barrier that molecules overcome to transform from their "native state" to the "damaged state", 2.577×10^5 J/mol for liver tissue. It is important to note that the pre-exponential factor and activation energy are tissue specific parameters that describe different modes of thermal damage such as microvascular blood flow stasis, cell death, and protein coagulation. In terms of finite element modeling of thermal damage, an integral value $\Omega(t) = 1$ corresponds to a 63% probability of cell death and an integral value $\Omega(t) = 4.6$ corresponds to 99% probability of cell death due to thermal effects. In order to convert the damage integral to a probability of cell death, $P(\%)$, we will use:

$$P(\%) = 100 \cdot \left(1 - e^{-\Omega(t)}\right)$$

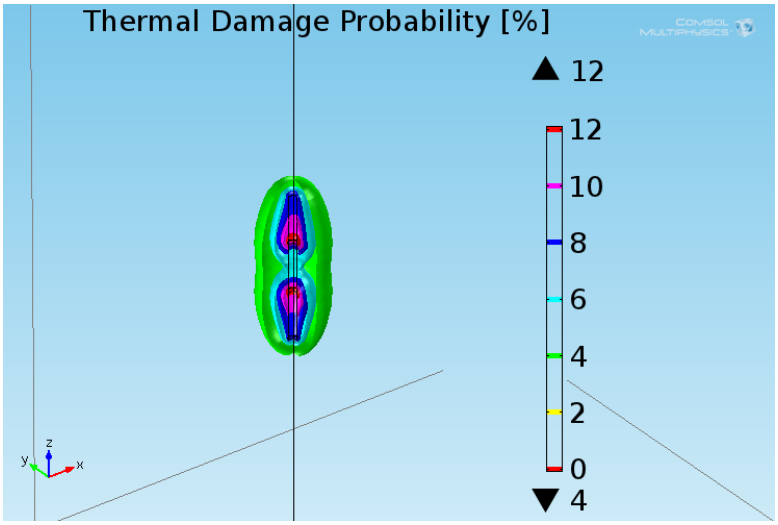

Figure 3: Thermal damage probability of cell death due to excessive thermal effects as a result of Joule heating.

The aim of this laboratory practice is to get familiar with the numerical simulation tools needed for capturing the electrical and thermal responses during a ninety 100-µs pulse IRE. We will accomplish this by coupling the Laplace, Heat Conduction, and Arrhenius equations using COMSOL Multiphysics 5.4 (Comsol AB, Stockholm, Sweden) to determine the IRE zones of ablation and evaluate if the increase in temperature due to Joule heating due to the pulses generates any potential thermal damage.

EXPERIMENT

In this exercise we will compare the effect of a static, σ_0, and dynamic, $\sigma(E)$, electrical conductivity functions in the resulting electrical and thermal effects during an entire IRE protocol in liver tissue. Initially we will determine the volume of tissue affected by IRE from the electric field distributions. We will then evaluate the temperature increase in liver tissue as a result of the Joule heating and determine if there was a probability of cell death due to thermal damage with the given IRE protocols employed. This exercise will provide the participants with accurate predictions of all treatment associated effects which is a necessity toward the development and implementation of optimized treatment protocols.

Specifically:
1) Simulate the electric field distribution using a static conductivity and 1000 V, 1500 V, and 2000 V.
2) Simulate the electric field distribution using a dynamic conductivity and 1000 V and 1500 V.
3) Include the Heat Conduction Equation by coupling with the Laplace Equation via Joule Heating.
4) Explore the resulting temperature distributions as a function of pulse number and frequency.
5) Incorporate the Arrhenius equation to assess potential thermal damage from the Joule Heating.
6) Investigate the effect of pulse frequency (1 Hz, 10 Hz, and 100 Hz) for ninety 100-µs pulses.

FURTHER READING:

Davalos RV, Rubinsky B, Mir LM. Theoretical analysis of the thermal effects during in vivo tissue electroporation. *Bioelectrochemistry* 61(1-2): 99-107, 2003

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Pavšelj N and Miklavčič D, Numerical modeling in electroporation-based biomedical applications. *Radiology and Oncology*, 42(3): 159-168, 2008

Lacković I, Magjarević R, Miklavčič D. Three-dimensional finite-element analysis of joule heating in electrochemotherapy and in vivo gene electrotransfer. *IEEE T. Diel. El. Insul.* 15: 1338-1347, 2009

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