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Research Article

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Thermo-Electrical Field Analysis for the Treatment of Tumors in the Liver Using Low-Frequency Joule Heating

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Abstract

Hepatic tumors occur in liver tissue due to the growth of malignant cells. Low-frequency Joule heating (LFJH) is one of the cancer treatment methods that show tremendous potential to treat hepatic cancer without causing excessive side effects or patient discomfort as other cancer treatments such as chemotherapy. In this localized thermal treatment method, the tumor in liver tissue is heated to a critical temperature range using radiofrequency (RF) energy designed to damage malignant cells. An electrode is introduced over the tumor and electric current is passed through it to induce Joule heating. The volume heat generation due to the Joule heating raises local temperature in tumor cells and causes complete destruction or damage. In this study, a computational simulation model is created based on coupled solution of bio heat equation and electrical field equation and considering a composite region of malignant tumor embedded in liver tissue region. The electrical and thermal fields that can cause damage to the malignant cells without affecting the surrounding tissue are determined and optimized by changing various controlling parameters such as electrode design, frequency, and amplitude of the RF energy

Introduction

In the recent generation, the leading cause of mortality worldwide is malignant tumors. According to recent statistics, "This year, an estimated 35,660 adults (25,510 men and 10,150 women) in the United States will be diagnosed with primary liver cancer. An estimated 24,550 deaths (17,030 men and 7,520 women) from this disease will occur this year" (American Society for Clinical Oncology) [1]. The percentage of survival of a person is measured as one-year survival rate and five-year survival rate. It shows that there is only 17% five-year survival rate after cancer is found in the body. The traditional surgical removal technique is not observed to be effective in most of the cancer treatment cases due to its cost of surgery, medical risks and the location and size of tumor, etc. There are many alternative methods to treat cancer, for example chemotherapy, but since every cell in the body will be reacted with chemo medicine, the side effects for that treatment will be more. The motivation of this study is to find a highly effective treatment that can cure malignant tumors in liver with minimum side effects.

Tungjitkusolmunet et al. developed a 3-D FEM model which consists of a radio frequency (RF) probe and performed temperature-controlled analysis [2]. Lackovic and Magjarevic developed a coupled electro-thermal model using 3-D finite element approach and considered electrode geometry [3]. Zhang et al. discussed about the radio frequency (RF) ablation technique, the principle lying behind it, the developments in this technique and its valuable achievements [4].

Goldberg et al. considered increasing energy deposition, such as reducing excess heat by internal cooling, can have useful results [5]. Garcia et al. aimed in study to find the electrical and thermal damage that will occur within the vicinity of irreversible electroporation using bipolar probe [6]. They also gave a detailed explanation on the number of cancer cells killed due to the electroporation technique [6]. Gazelle et. Al presented some of the early clinical applications with laboratory results obtained with radio-frequency ablation techniques [7].

The primary objective of this study is to test Low Radio Frequency Thermal Ablation (LRFTA) technique for the treatment of hepatic cancers. The treatment involved localized direct heating of the tumor in liver tissue to a critical temperature range using radiofrequency (RF) energy through direct insertion of multiple tiny electrodes to damage the malignant cells completely. The goal is to maintain effective heating and sufficient temperature rise to cause the cancer cell to die with minimum damage to the surrounding tissue. A computational simulation model is developed based on coupled solution of bio heat and electrical field equations and considering a composite region of malignant tumor embedded in liver tissue region. Sensitivity analysis is performed to determine and optimize electrical and thermal fields that can cause damage to the malignant cells without affecting the surrounding tissue by changing various controlling parameters such as electrode design, frequency and amplitude of the RF energy. Damage Integral Simulation (DIS) of the cells and tissues is also performed to correlate with electro-field

solutions to the damage of the cancer cells.

Electro-Thermal Model

Physical Model for Simulation

A basic 3D model is designed to do analysis to determine and optimize electrical and thermal fields that can cause controlled damage to the malignant cells. Figure 1 shows the basic physical model.

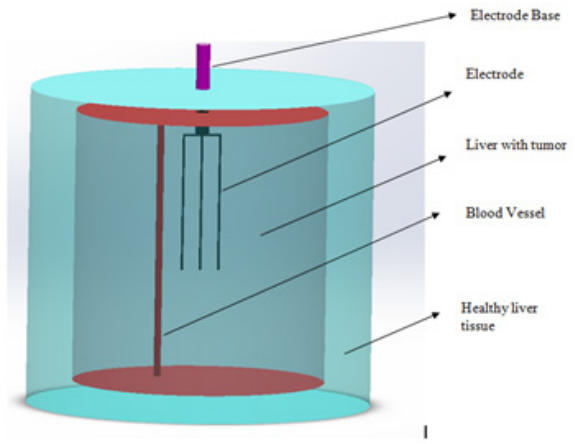

Figure 1: Basic three-dimensional model

The components of this model include i. Liver: The liver is approximated to be in the shape of cylinder to reduce complexity of the model. The inner cylinder is considered as liver which has tumor in it. It is 55mm in diameter and 60mm in length; ii. Blood vessel: A 1mm diameter blood vessel is considered in the model. Even the blood vessel will act as a parameter in tissue heating. Since the temperature of blood is 37°C, it will cool the nearby tissue temperature; iii. Electrode. The electrode consists of three probes which will be inserted into the liver. It is made of Ni-Ti and 22V input potential is given to electrode. Due to the electric potential given to the electrode, heat will be generated because of Joule heating which increases the tissue temperature. The electrode base is insulated and is grounded. It is used to handle the electrode. It is made of polyurethane and is 20mm in length and 3mm in diameter; iv. Healthy liver tissue. The healthy tissue around the tissue having tumor is considered so that the distribution of electric and thermal fields can be noticed and the input parameters can be optimized so that the healthy tissue will not get affected. The dimensions taken are 60mm diameter and 70mm in length.

Simulation Model

The finite element analysis is carried out by coupling electric currents and bioheat transfer modules.

Electric Field

The electric field model shows the electric field generated in the liver tissue because of the applied voltage. The heat generated due to Joule heating in this model is coupled with bioheat transfer model. Governing equation for the electric field:

$$-\nabla.(\sigma\nabla E)=0 \qquad (1)$$

where E is the potential (V) and σ is the electrical conductivity (S/m).

Bioheat Transfer

The bioheat transfer model includes 3-D heat diffusion, blood perfusion and heat generation due to Joule heating caused by the RF energy input and heat generation due to metabolism. The temperature solution from the bioheat model can be integrated into the tissue damage integral model for cell damage analysis.
Governing equation for bioheat transfer:

$$\rho C_p.\frac{\partial T}{\partial t} = \nabla.(k\nabla T) + Q_m + Q_p + JE \qquad (2)$$

and

$$Q_p=\rho_b\, C_b\, \omega_b\, (T_b-T) \qquad (3)$$

Where Q_m is heat due to metabolic reactions; Q_p is heat due to blood perfusion JE is Joule heating; ω_b is the blood perfusion rate; T_b is blood temperature

Thermo-Electrical Analysis

Using the above dimensions, the model is designed in COMSOL and finite element analysis is performed. The model designed looks like Figure 13.

The three-dimensional model consists of liver electrode model. The electrode consists of electrode base 1, electrode base 2 and four electrode probes. Electrode base 1 is insulated so that there will not be any heat transfer from it.

Those two components are assembled while keeping the electrode placed in the center of the liver. Electrode base 2 and electrode probes will be inserted into the liver. The assembly is imported to COMSOL for further analysis and the imported model looks like in Figure 2.

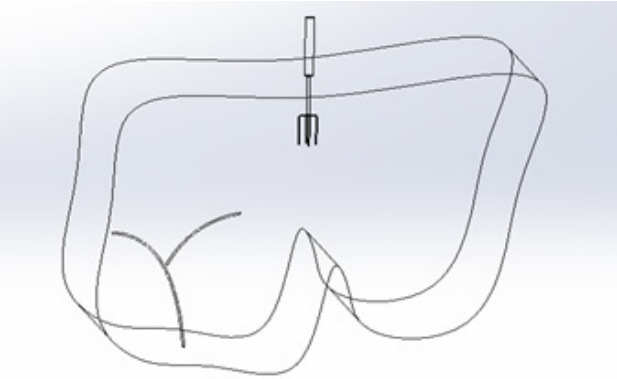

Figure 2: Thermo-electrical model assembly

The distance between the electrode probes is varied reduced while keeping the shape and other dimensions the same. The main effect of this is that we can generate more heat in the region where we are assuming to have malignant tumor. The electrode will be inserted over the malignant tumors of size less than a selected distance and the process is carried out so that the malignant tumor embedded between the electrode probes will be damaged. The electrode design 2 is modeled as shown in Figure 3.

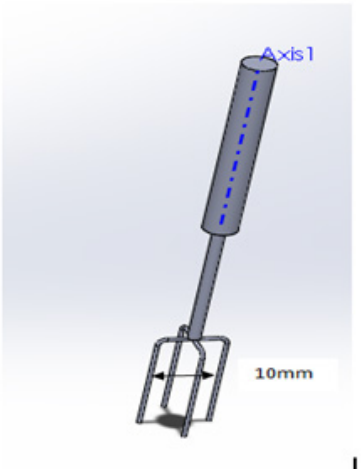

Figure 3: Electrode design -2

Damage Integral

Cutaneous burns occur when the temperature is elevated for a sufficient length of time: 45°C requires more than 3h, above 51°C to temperatures below 70°C requires less than 4min and if it increases beyond 70°C it requires less than 1s to cause thermal damage (Lackovic and Magjarevic, 2009). The thermal injury that occurs to the cells near the electrode can be calculated using ***Arrhenius damage equations.*** Knowing the fraction of cells killed during this treatment plays a crucial role since that calculation can give appropriate and more detailed information about the cancer cells damage.

Arrhenius model equation:

$$\frac{d\alpha}{dt} = \frac{1}{\tau} = A\exp\left(-\frac{dE}{RT}\right) \quad (4)$$

In above equation, the damage accumulation measured by the specific assay in a given time (s-1), t is the time for damage accumulation (s), dα represents the threshold of damage and is assay dependent, τ is the time required to accumulate irreversible damage (s), E is the activation energy (kJ/mol), A is the frequency factor (s -1), T is the absolute temperature (K), and R is the universal gas constant (8.315 J/mol K)" [14].

The fraction of necrotic tissue (θ_d) is expressed as

$$\theta_d = 1-\exp(-\alpha) \quad (5)$$

The above damage integral equation is applied to the thermo-electrical model developed.

Computational Meshing

To perform finite element analysis, the imported model should be meshed to get accurate results. A large number meshes with fine mesh resolutions are generated to perform analysis. Free tetrahedral meshing is applied for the entire component as shown in Figure 4. Depending on the sizes, extra fine mesh is applied for electrode (as shown in figure) and finer mesh is applied for the liver tissue. Figure 4 shows the tetrahedral mesh provided for the component. Figure 4b is the zoom-in view that clearly shows the electrode mesh.

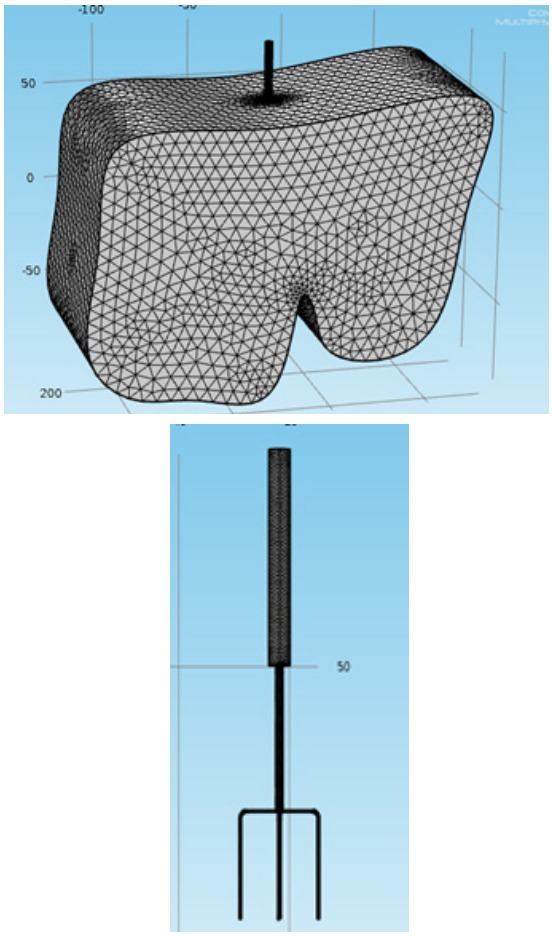

Figure 4: Computational mesh

Results and Discussions

The computational simulation model is used to determine and optimize electrical and thermal fields that can cause effective damage and identify the appropriate electrode design. Further, a damage integral simulation (DIS) of the cells and tissues is also performed to correlate with electro-field solutions to the damage of the cancer cells.

Electric potential distribution in the tissue is shown in Figure 5. A multi-slice 3D-plot is taken in which shows that potential for the electrodes is 22V and as we move away from the electrodes, the electrode potential is reduced uniformly on both the sides of the electrode.

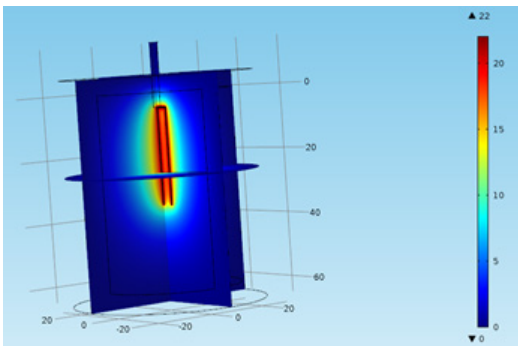

Figure 5: Voltage distribution

Temperature distribution due to the Joule heating in the tissue is shown in Figure 6. From the figure we can observe that the temperature surrounding the electrodes is almost between 75°C and 85°C and on the electrodes it is around 100°C. When we move away from the electrodes the temperature is decreased gradually and reaches normal body temperature.

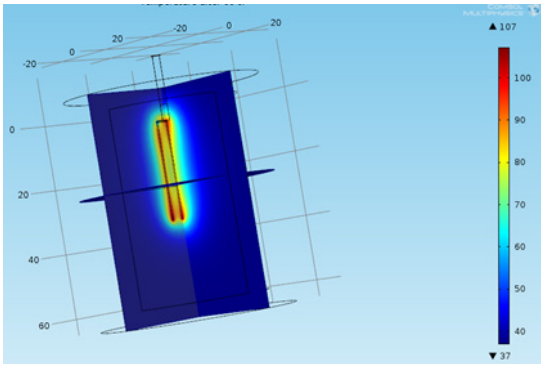

Figure 6: Temperature distribution for the basic model

Iso-surface shows that the area where the temperature band required to damage the cancer cells is achieved.

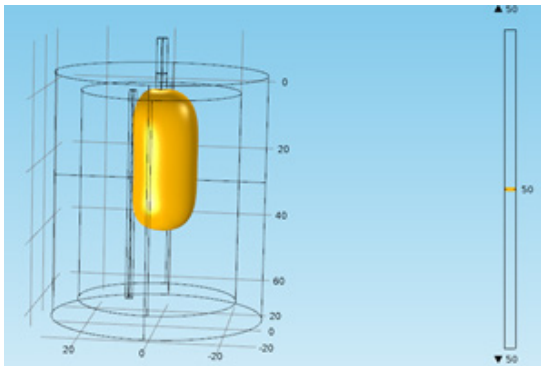

Figure 7: Iso-surface

Electrical potential is measured in x and y directions along a line passing the bottom tip of the electrodes at z = 35mm. Figure 8 shows electrode potential along x-direction and Figure 9 shows electrode potential along y-direction.

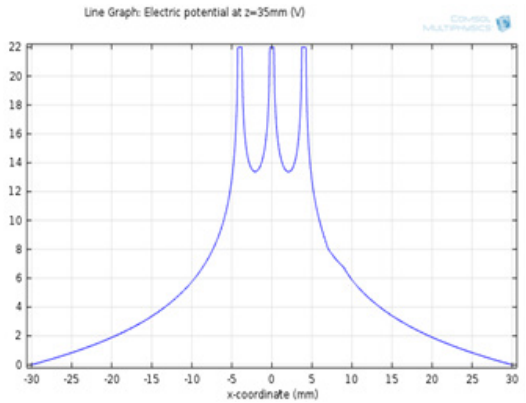

Figure 8: Voltage distribution along x-direction for the model

Figure 8 show that the voltage is reaching 22V for all the electrode probes; in between the electrode probes it is less. And as you move away from the electrodes the voltage distribution is gradually reduced on both the sides and so will not affect the tissue much. Along y-axis voltage is shown and x-axis is along tissue diameter. Figure 9 is the same but in y-direction. Along y-direction only one electrode touches so the temperature reaches 22V near that and is reduced when moved away.

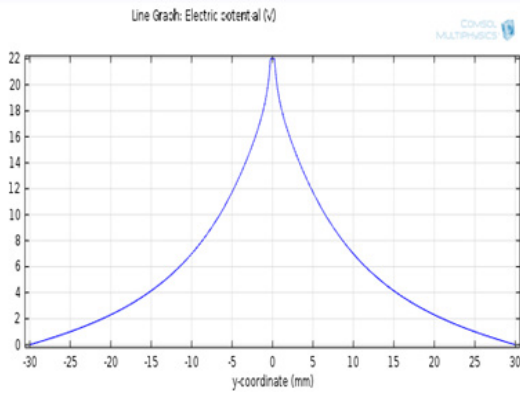

Figure 9: Voltage distribution along y-direction for basic model

Temperature distribution is measured along a line passing through the middle of the electrode in x and y-directions, i.e., at a depth of z = 20mm. Figure 10 shows the temperature distribution along x-direction. The temperature reaches 360K at one of the electrodes and for the other two electrodes it is a little less because of the presence of the blood vessel. The blood vessel will act as a sink and will reduce the surrounding temperature and at the location of blood vessel the temperature drops to 37°C because of the boundary condition we have given. Figure 11 shows the temperature distribution along y-direction and shows a peak temperature reaching 355K at the electrode.

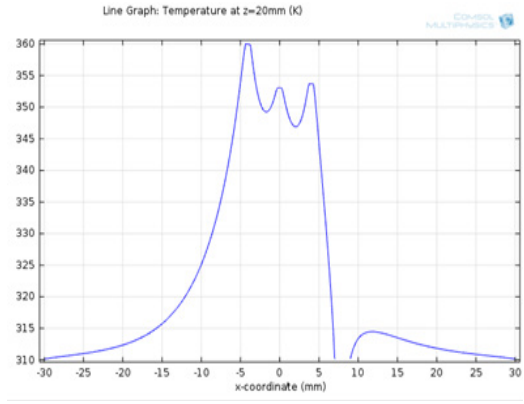

Figure 10: Temperature distribution along x-direction for basic model

Damage Integral Analysis

Figure 11 shows the fraction of tissue damaged during the process. The area around the electrode with dark red color is close to the representative complete cell damage region.

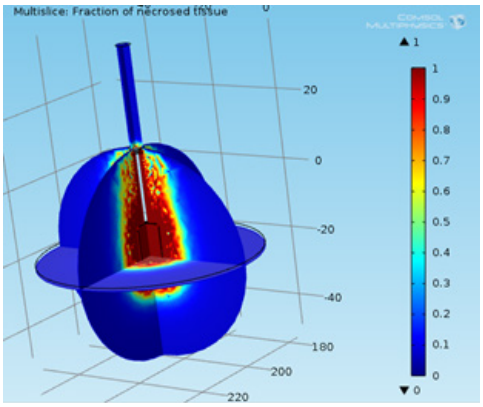

Figure 11: Damage integral plot

We can see that the region between the electrode probes is completely damaged from beginning to the end of the electrode probe. As we move away from the electrode the fraction of tissue damage is only to some extent.

Conclusion

A computational simulation model based on coupled solution of bioheat equation and electrical field equation is developed with malignant tumor region embedded in liver tissue region. Thermal damage to the malignant tumor cells is achieved with the following considerations: a new electrode design, using amplitude of RF energy as 22V and non-periodic heating with the frequency of RF energy as 100s/20s cycle. Localized direct heating of the tumor in the liver tissue to a critical temperature range of 60°C - 65°C is achieved with RF heating and with a frequency of 100/20s. When this temperature range is maintained, the damage to the cancer cells can be observed in a few additional minutes. Damage integral simulation is performed which correlates with electro-field solutions [8-18].

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