Framework of the Bio-Heat Transfer for Laser/Cancer Treatment

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***Abstract*—Controlled thermal ablation poses a challenge during a laser surgery/cancer treatment. A software tool would help physicians predict, organize the treatment as well as maximize therapeutic effects while minimizing side effects. This would provide a precise idea of the predicted reaction depending on selected doses, tissue geometry, and the laser source prior to the treatment; so new treatment strategies can be proposed and evaluated. In this paper, we propose a new approach for the laser surgery/cancer treatment with physician interaction. The physician would enter a scenario by selecting the tissue and specifying tissue tumor size, laser type, probe size, laser power, and time range. The model would then automatically generate the Power Deposition Model; select the tissue thermal and optical properties; start the simulation; dynamically update thermal and optical properties; and show the physiological responses. This model shows the impact of the heat distribution and thermal damage to the tissue during the simulation and then allows the physician to adjust the scenario according to the treatment objective. A case study of the Laser Interstitial Thermal Therapy (LITT) will demonstrate the feasibility of the framework.**

***Index Terms*—framework, bio-heat equation, laser source, thermal damage, tissue cancer, bio-heat transfer simulation**

I. Introduction

The objective of this paper is to present a general mathematical framework of the bio-heat transfer for the Laser/Cancer treatment. This includes thermal conduction based on modified Fourier's law with constant blood perfusion as a boundary condition. The Heat Transfer Module will be used with a material library model for human tissues [1] and probe solid materials. The selected tissue material with tumors will be defined from a database with their density, conductivity, specific heat, diffusivity, relative permittivity, relative permeability and electrical conductivity values. A new material Laser delivery probe will also be defined as source energy.

Expected results during the heating and temperature distribution are thermal distribution throughout the biological tissue and the estimation of the volume of tissues damaged during the treatment. The challenges are that the damaged tissues volume should be included within the tumor tissue volume and that there is a potential that the healthy tissue would be affected during the heating process.

Furthermore, predicting the result of treatment depending on scenarios discussed between physicians and patients will improve the health care system by providing a personalized and focused treatment. Using the laser energy source, light is emitted from a diffusive tip of an optical fiber probe that is inserted into the center of a tissue tumor. The laser light is very nearly [2] single frequency (single wavelength) and coherent. The output of the laser is also focused into a narrow collimated beam. This collimated, coherent, and single frequency light source can be used as a very precise heat source in a wide range of applications, including cancer treatment.

Most models neglect [2] the changes in the optical and thermal properties of the tissue during the temperature elevation, which makes these models unrealistic. We will introduce a mechanism to include these changes in the tissue properties during the heat transfer process.

Laser Interstitial Thermal Therapy (LITT) is a minimally invasive cytoreductive treatment. A low voltage laser is used to induce hyperthermia and kill tumour cells [3]. A case study of the Laser Interstitial Thermal Therapy (LITT) [4]-[6] will demonstrate the feasibility of the framework. We will select a scenario of brain laser/cancer surgery treatment using solid state diode laser in the Nd:YAG range of 1064nm and 12 Watt. This laser energy is transferred to the target tissue via a CO_2 gas-cooled (Joule-Thomson effect) side-firing (directional) laser of 3.3mm diameter. The heating temperature will be between 43 ℃ and 57 ℃ (the tissular necrosis state). The geometry will include two layered cylinders simulating the two tissues (healthy outside and tumor inside) with the probe located at the center of the tumor tissue. Many options exist [2] to model the laser power source: surface heat source or volumetric heat sources (Ray optics, Bear-Lambert law, Beam envelope method, Full wave). The framework will offer a selection of the source type which will be either a surface heat source or Beam envelope method.

Using the Multiphysics Simulation Tool COMSOL 5.2, we build apps for physicians' use. Our COMSOL Multiphysics model is turned into an application with its own interface using the tools provided with the Application Builder desktop environment. Physicians will run the application remotely to study and choose the best scenario for their patients.

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II. Framework for Laser Bio-Heat Treatment

The objective of this paper is to simulate the laser heating of the human tissue as coupling between an electromagnetic wave propagation model (waves are oscillating rapidly in the direction of propagation) and a bio-heating model. Electromagnetic modeling formulations are based on Maxwell's equations as well as material laws for propagation in various media. Bio-heat modeling formulations are based on Penne's equations (with Fourier conduction, or extended Fourier conduction.

We will then use the Finite Element Method (FEM) simulation tool to solve the mathematical model with the initial and boundary conditions, and provide results in two forms. The first is an interactive result through the physician's direct access to the application via laptop or smart phone, and the second, a long term result sent via email.

Since the Finite Element Method requires a very fine mesh, much smaller than the wavelength, we will use the Beam Envelope Method [7]. So, instead of solving for the incredibly computationally-intensive electric field, we will solve for the slowly varying electric field envelope.

The Fig. 1 below illustrates the difference between the sample density for the electric field and the electric field envelope.

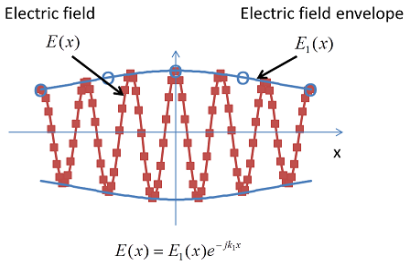

Figure 1. The electric field and the electric field envelope [8].

It is recommended that we have a least five quadratic finite elements per wavelength.

Built into this method is a factorization trick — you separate out the fast-varying portion of the wave as illustrated in Fig. 1: $(x) = E1(X)e^{-jk1x}$. The user provides the wave-vector k1 as an input to the method. To recover the "real" field you just multiply the solution E1(x) with the fast-varying phase factor.

We used the Electromagnetic Waves, Beam Envelopes Interface, which solves a modified version of the full-wave Maxwell's equations, again via the FEM, to solve one frequency-domain wave equations for the electric field envelope(s). The electric field is represented as the product of the solved for electric field envelope and a rapidly varying prescribed phase function. As the electric field envelope has a slower spatial variation than the electric field, a coarse mesh can be used. The Biological Tissue feature adds the bio-heat equation as the mathematical model for heat transfer in biological tissue.

We also did a modules coupling between the Electromagnetic and bio heat modules, so the heating power generated by the electromagnetic power source is transferred to the bio-heat module.

We introduce a Framework of the bio-heat Transfer Using Laser as a power source for Cancer Treatment. The physician will select the following depending on the scenario that he is planning to simulate:

- The tissue type from a human tissue list, the software will then select from a tissues database and assign the optical and thermal properties of the tissue.
- The tissues dimension so that the software will use the information to adjust the simulation by building the geometry of the simulation model. We need to specify the tumor tissue dimension.
- Supposing that the optical and thermal properties will change during the heating process is not a realistic simulation, we will include functions to include the dynamic variability of these parameters.
- For the environmental boundary conditions and the initial conditions, the model will offer to modify the initial temperature.
- The mathematical model will give the option to select the bio-heat transfer equation (Penne's), the modified Fourier or relativist models as conduction methods. The mathematical model includes the convection and the metabolic power. We did not assume that these values are null.
- There are three types of lasers used in cancer treatment; carbon dioxide CO_2 lasers, Argon lasers and neodymium:yttrium-garne (nd:YAG) lasers. The physician will select the laser type (power, duration, spot size) and the software will use the information to adjust the simulation by building the power deposition model. [6]
- Two type of outputs are available; first real-time heat distribution and tissues damages. An email with more detailed graphs will be sent later.

A Framework with steps involved in the mathematical simulation of the surgery/laser treatment (The simulation loop):

A. Dosimetry Plan

The physician defines the dosimetry plan (triggers) with selection of the Tissue from the database, Tumor Tissue size, selection of the laser type (carbon dioxide CO_2 lasers, Argon lasers and neodymium: yttrium-garnet (nd:YAG) lasers), define exposure duration. The temperature starting point of the volume is set to normal body temperature:

- The system will apply the Environmental Boundary conditions and initial conditions.
- The system will form the geometry of the model selected.
- The system will form the mesh of the model selected.
- The system will select the Thermal Properties and Optical Properties of the Tissues from a database.

The system selects and uses the power deposition source.

B. Temperatures Distribution Calculation

The mathematical model will include many options; Fourier or modified-Fourier for conduction, convection, radiation, perfusion and vaporization.

C. Physiological Responses

While time not expired, the system will update thermal and optical properties: variation of the electrical conductivity with temperature, variation of the thermal conductivity and density with temperature. Calculate the variation of the scattering coefficient of the coagulation tissue. Go to Step 2. [Loop]

Step 4. Output the Simulation Results.

Temperature Distribution T(r,t) and Tissue Damage Ω(r,t)

III. Detailed Description of the Framework for Laser Bio-Heat Treatment

A. Dosimetry Plan

The physician will need to define a simulation plan, including laser type, tissue type and dimensions. As soon as the model will provide output, the physicians will analyse them, and adjust the therapy.

B. Environmental Boundary Conditions and Initial Conditions

The model will take a default values for initial conditions but will provide the possibility to update them if needed.

C. Tissue Anatomy

As default dimension the model will have a cross section of a 3D Brain tissue with dimension of 15mm by 15mm, as shown in Fig. 1, the tissue is heated up to 10 seconds by a 5W laser with wavelength of 1064nm. The physician will access via the application to update these dimension.

D. Tissue Thermal Properties

The Model will select the following thermal properties from the database depending on the selected tissue: Density ρ, Heat capacity at constant pressure, Heat capacity *Cp*, Thermal Conductivity K, Density, blood ρ_b, Specific heat, blood *C*b, Blood perfusion rate wb, Arterial blood temperature *T*b, and the Metabolic heat source *Q*met.

E. Tissue Optical Properties

There are a lot of Tissues Optical Properties defined in the literature; Permittivity, Permeability, Electrical Conductivity, Absorption, Scattering, Anisotropy, Real Refractive Index. For our Model we will use the following: Permittivity, Permeability μ and Electrical Conductivity.

The Permittivity is constant because the wavelength is constant in our case. The Permeability is equal to 1 since the tissue is non-magnetic material. Since there is no variation of the frequency we will not use the dispersion models.

F. Power Absorption Tissue Properties

We consider the following Power Absorption properties: Energy Absorption, Specific Absorption Rate (SAR), Frequency Factor and the Activation energy dE.

G. Power Deposition Models

This model will include the simulation of these three laser power sources: CO_2, Argon and Nd:YAG. The Software will then offer the physician to select one of these three.

H. Temperature Distribution and Damage Model

Parabolic heat equation based on Fourier's theory (FHE), and Hyperbolic Heat Equation (HHE), have been used to mathematically model the temperature distribution of biological tissue during thermal ablation. However, both equations have certain theoretical limitations [9]. The FHE assumes an infinite thermal energy propagation speed, whereas the HHE might possibly be in breach of the second law of thermodynamics. The Relativistic Heat Equation (RHE) is a hyperbolic-like equation, whose theoretical model is based on the theory of relativity and which was designed to overcome these theoretical impediments. In this study, the three heat equations for modelling of thermal ablation of biological tissues (FHE, HHE and RHE) were solved analytically and the temperature distributions compared.

Article [9] suggest that temperature values obtained from a model with RHE are always lower than those of the FHE, while HHE values are higher than the FHE, except for the initial heating stage and at points away from the electrode. Both HHE and RHE are mathematically hyperbolic, but temperature profile peaks are only observed with HHE. The three solutions converged for infinite time or infinite distance from the electrode. The percentage differences between the FHE and the other solutions are larger for higher values of thermal relaxation time in HHE or equivalently for low values of the speed of heat propagation in RHE.

We will start with the thermal conduction using Fourier's law for our first step of the simulation (results presented here) then upgrade to the modified Fourier's law and Relativist heat equation. We will then compare the results of these three simulations. The Model will offer the selection of any of these three mathematical models.

1) Parabolic heat equation based on Fourier's theory (FHE)

$$\rho C_p \frac{\partial T}{\partial t} + \rho C_p \, \mathrm{u} \cdot \nabla T + \nabla \, \mathrm{q} = Q + Q_{\mathrm{bio}} \qquad (1)$$

$$q = -k \nabla T \qquad (2)$$

where T is temperature (K), C_p is the heat capacity J/(kg*K)), ρ is the density of the brain tissue (kg/m^3), and k is the thermal conductivity of brain tissue (W/(m*K)), Q is heat source, Q_{bio} is the perfusion and metabolic heat source.

2) Heat equation with modified Fourier for conduction method called Hyperbolic Heat Equation (HHE)

With modern surgery, the medical treatment progressively implies small scale time and high energy. The PHTE are not appropriate. Because the time is too small t ε $[0, \tau]$, with a small value for $\tau > 0$ the thermal equilibrium of a prolonged physical system simply cannot be reached.

A modified Fourier version uses a non-null relaxation time $\tau > 0$, in the dissipation process. This parameter can be interpreted as the finite time required for the flow dissipation to relax to its stable value thermodynamics. The simple generalization for finite speed leads to Cattaneo - Vernotte equation [10], [11]:

$$q(x, t+\tau) = q(x) + \tau \frac{\partial q}{\partial t}(x,t) = -k\nabla T(x,t) \quad (3)$$

The following equation called (HHTE) Hyperbolic Heat Transfer Equation [1]:

$$-\Delta T(x,t) + \frac{\mathbf{1}}{\boldsymbol{\alpha}}\left(\frac{\partial T}{\partial t}(x,t) + \tau \frac{\partial^2}{\partial t^2} T(x,t)\right) = \frac{1}{k}\left(S(x,t) + \tau \frac{\partial S}{\partial t}(x,t)\right) \quad (4)$$

3) Heat equation with Relativist Heat Equation (RHE) for conduction method

Ali and Zhang's Relativistic Heat Equation (RHE) turn out to be [12]:

Equation

$$\frac{\partial T}{\partial t}(x,t) + \frac{\alpha}{C^2}\frac{\partial^2}{\partial t^2}T(\mathrm{x,t}) = \alpha\left(\frac{\partial^2}{\partial x^2}T(\mathrm{x,t}) + \frac{\partial^2}{\partial y^2}T(\mathrm{x,t}) + \frac{\partial^2}{\partial z^2}T(\mathrm{x,t})\right) + \frac{\alpha}{k}\mathrm{S(x,t)} \quad (5)$$

where the constant C is the speed of heat propagation in the tissue.

4) The perfusion equation

$$Q_{bio} = \rho_b C_b \omega_b (T_b - T) + Q_{met} \quad (6)$$

where Q_{bio} is the perfusion and metabolic heat source, ρ_b is the blood Density, C_b is Specific blood heat, Q_{met} is Metabolic heat source, ω_b is Blood perfusion rate, T_b is the blood flow rate, T is time (s), Q_{met} is the metabolic heat source.

TABLE I. SETTINGS OF Q_{BIO} PARAMETERS

Description	Value
Arterial blood temperature	310.15[K]
Specific heat, blood	3650[J/(kg*K)]
Blood perfusion rate	0.866[l/s]
Density, blood	1035 kg/m ^{3}
Metabolic heat source	0

From Table I we consider that the metabolic heat and external heat sources are negligible in respect to the laser inducted heat.

The initial temperature of the brain tissues was considered as T0=293.15 K.

I. Tissue Temperature and Tissue Damage

1) Tissue temperature distribution

The LITT of Brain Tumors was modeled by the bio-heat equation in a 3D geometric study, using electromagnetic module and the bio-heat transfer application mode with time dependent COMSOL 5.2.

2) Thermal damage

We used integrated Thermal damage function on the Heat Transfer Module. Simulation includes damage integral analysis from Energy absorption. The Parameters Frequency factor and Activation factor are defined in Table II. The damage is calculated from the Arrhenius law:

We used the following defined functions used on the COMSOL 5.2, Fraction of necrotic tissue:

$$\theta_d = \min(\max(0, 1 - e^{-\alpha}), 1) \quad (7)$$

where α is a Discontinuous Lagrange (constant) shape function (which describes the degree of tissue injury).

3) Thermal properties dynamic update

Most models neglect the changes in the thermal properties of the tissue during the temperature elevation, which makes these models unrealistic. We will introduce a mechanism to include these changes in the tissue properties during the treatment.

The temperature dependence of the thermal conductivity and density is taken into consideration by the following linear approximations [13]:

$$k(T) = k_{(37C)}(1 + 0.00025(T - 37)) \quad (8)$$

$$\mathrm{p}(T) = p_{(37C)}(1 + 0.00025(T - 37)) \quad (9)$$

For each tissue we will have a different equations defined in the database.

J. Optical Properties Dynamic Update

Most models neglect the changes in the optical properties of the tissue during the temperature elevation, which makes these models unrealistic. We will introduce a mechanism to include these changes in the tissue properties during the treatment.

The variation of the electrical conductivity [14] with temperature is given by:

$$\sigma = 1/(\rho_0(1 + \alpha(T - T_{ref}))) \quad (10)$$

where ρ_0 is the reference resistivity, T_{ref} reference temperature, and α is the resistivity temperature coefficient. The spatially-varying temperature field, T, can either be specified or computed.

K. Model Simulation

A cross section of a 3D Brain tissue with dimension of 15cm by 15cm, as shows in Fig. 2, is heated up to 15 seconds by a 15W laser with wavelength of 1064nm.

The tissue is modeled as a Cylinder of radius rmat and height thickness, 3D, Bio-heat Transfer (ht), Time dependent of range (0,0.1,15) seconds. The initial temperature of the brain tissues is considered 293.15K.

1) Laser procedure

The laser beam [6] is modeled as a heat source in the electromagnetic module.

At the operating wavelength of the laser, it is assumed that absorptivity equals emissivity. The Electric field envelopes (first and second wave) are quadratic, the number of directions is unidirectional, and the type of phase is wave vector.

Equations

$$(\nabla - ik_1)\mu_r^{-1}\left((\nabla - ik_1)E1\right) - k_0^2(\varepsilon_r - \frac{j\sigma}{\omega\varepsilon_0})E1 = 0 \quad (11)$$

$$\lambda = -j\beta - \delta_z \quad (12)$$

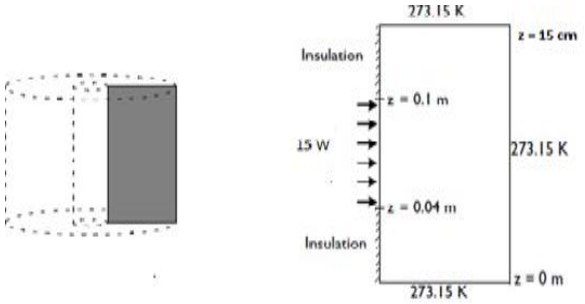

Figure 2. Model geometry and boundary conditions

2) Modeling in COMSOL multiphysics

a) Geometrical description of the model

We will start with the thermal conduction using Fourier's law for our first step of the simulation (results presented here) then upgrade to the modified Fourier's law. We will then compare the results of these two simulations.

b) Heat distribution

The LITT of Brain Tumors was modeled by the bio-heat equation in a 3D geometric study, using the bio-heat transfer application mode with time dependent COMSOL 5.2. Table I and II describe the physical parameters used by our Comsol numerical simulation.

TABLE II. THE PHYSICAL PARAMETERS USED IN OUR COMSOL NUMERICAL SIMULATION. (THERMAL PROPERTIES OF BRAIN FROM [9])

Name	Expression	Value	Description
Plaser	15[W]	15[W]	Laser power
Emissivity	0.8	0.8	surface emissivity of mat1
Temp	293.15[K]	293.15[K]	Initial Temperature
Heat Capacity	3636[J/(kg*K)]	3636[J/(kg*K)]	Brain Heat Capacity
Density	1050[kg/m^3]	1050[kg/m^3]	Brain Density
Thermal conductivity	0.51[W/(m*K)]	0.51[W/(m*K)]	Brain Thermal conductivity
A	7.39e39[1/s]	7.39e39	Frequency factor
dE	2.577e5[J/mol]	2.577e5	Activation energy

Heat Equation

$$\boldsymbol{\rho C_p u \nabla T = \nabla(k \nabla T) + Q + Q_{bio}} \quad (13)$$

$$q = -k\nabla T \quad (14)$$

where T is temperature (K), C_p is the heat capacity J/(kg*K)), ρ is the density of the brain tissue (kg/m^3), and k is the thermal conductivity of brain tissue (W/(m*K)), Q is heat source, Q_{bio} is the perfusion and metabolic heat source.

c) Mesh

The brain tissue is meshed using a triangle swept mesh as shown in Fig. 3.

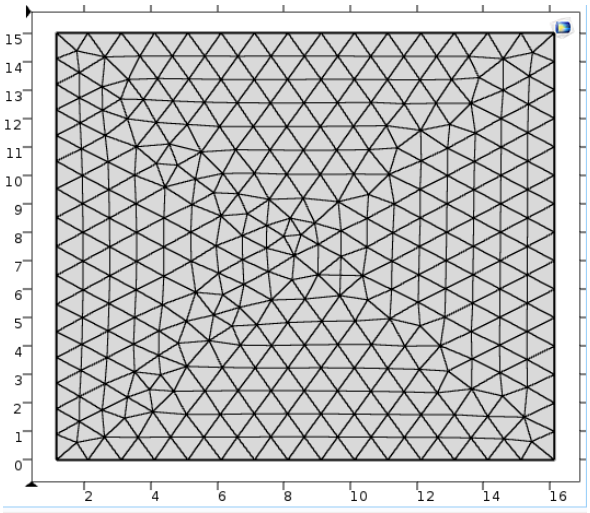

Figure 3. Finite element method (FEM) mesh. Evaluation of each variable at each point of the mesh.

IV. SIMULATION RESULTS

During the simulation, the physician can play with the input values to control the thermal ablation during a laser surgery/cancer treatment.

Fig. 4 to Fig. 6 show the heat distribution and damage during the simulation which will help physicians to predict and organize the treatment. Fig. 4 shows the temperature (℃) at the Surface of the Brain Tissue, Fig. 5. Shows the temperature during 15 seconds at the Surface of the Brain Tissue (Contour: Temperature (℃) Arrow Surface: Total heat flux) and Fig. 6 shows the damage that appears when the value of damage function reaches the threshold of 0.6., this will help preventing the heating side effect. All these graphs are also available as a video stream that shows temperature rise.

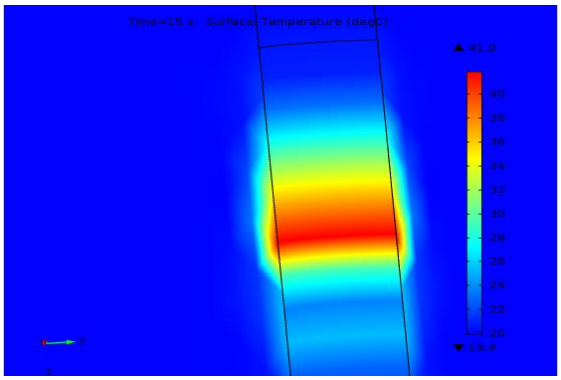

Figure 4. Temperature at the Surface of the Brain Tissue, Temperature (℃).

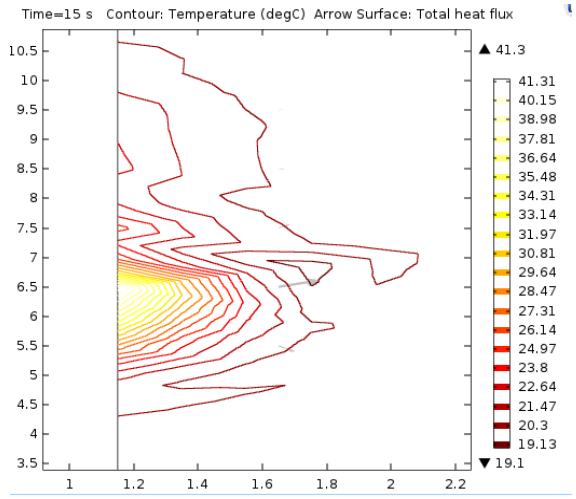

Figure 5. Temperature during 15 seconds at the surface of the brain tissue (Contour: temperature (℃) arrow surface: Total heat flux).

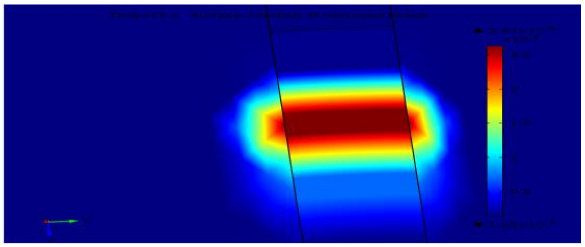

Figure 6. Time=15s surface: Fraction of necrosed tissue. The damage appears when the value of damage function reaches the threshold of 0.6. This is also available as a video stream that shows temperature rise.

V. Apps for Physicians Use

Using Comsol 5.2, we build apps for physicians' use. Our COMSOL Multiphysics model is turned into an application with its own interface using the tools provided with the Application Builder desktop environment. Physicians will use their laptops or smart phones to access and run the application remotely. Fig. 7 shows the input values and the output graphs generated by the application.

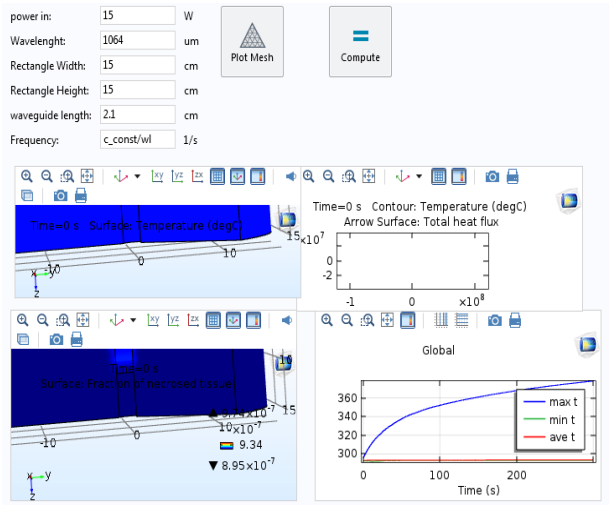

Figure 7. The output of the Apps. The physician enters the parameters and select compute to execute the simulation in real-time.

VI. Conclusion

Controlled thermal ablation presents a significant challenge during a laser surgery/cancer treatment. A tool to help physicians predict and organize the treatment will be helpful.

In this paper, we proposed a framework for the bio-heat transfer of the laser/cancer treatment with physicians' interaction via Comsol Apps. Such model shows the impact of the heat distribution and thermal damage of the tissue during the simulation.

A case study of LITT was proposed to demonstrate the utilization and the feasibility of the framework. The physicians selected a scenario with objective and the Model output the predicted the expected result which are thermal distribution throughout the biological tissues during the heating and the estimation of the volume of tissues damaged during the treatment. The physician may then adjust the scenario depending on the personalized and focused treatment.

Our future work will be the extension of the model to include the management of the dosimetry process. A such software tool will help physicians plan, update and report the dosimetry process of each patient.

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