Analysis of PhotoThermal Ablation

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Introduction

Cancer cells have an increased sensitivity to heat compared to healthy cells such that at 42°C cancer cells are destroyed while normal cells can survive up to 47°C. Thus hyperthermia-based approaches that target specific spatial locations and simultaneously provide controlled thermal exposure represent an important opportunity for future treatment protocols.

Current limitations in available hyperthermia induction methods and tumor accessibility have prevented the widespread implementation of this therapy. However, the development of laser induced hyperthermia, termed Photo Thermal Ablation (PTA), allows tumors sensitized by the presence of gold nanoparticles to be selectively exposed to radiation in the infrared regime. This nanoparticle assisted PTA has shown considerable promise in laboratory controlled, small animal studies, but needs to be further refined for use in human or veterinary clinical practice.

In PTA therapy, interaction of the laser light with the gold nanoparticles produces local heating that causes irreversible damage to the targeted tissue. The PTA thermal profile is directly related to the irradiance distribution of the incident radiation.

To provide a better understanding of PTA, a predictive physics-based computational model of light diffusion in tissue has been developed. The time dependent diffusion of light is solved in COMSOL Multiphysics® using the equation for radiative transfer implemented as a General Form PDE. Results of the implementation have been verified by comparison with predictions of an analytical solution for an infinite homogeneous medium. The model has been extended to predict light diffusion in a layered tissue structure consisting of Epidermis, Dermis, Sub-cutaneous fat and Muscle. Transient temperature distributions through the layered tissue structure are predicted from the balance of heat transfer due to light absorption, heat dissipation due to perfusion in the active tissue layers and losses due to convection from the outer surface.

Keywords

Light diffusion, Weak form solution

Governing Equations

The time-dependent diffusion approximation can be derived from the equation of radiative transfer and is given by:

$$\frac{1}{c}\frac{\partial}{\partial t}\Phi + \nabla\cdot(-\mathrm{D}\nabla\Phi) = -\mu_a\Phi + S \qquad (1)$$

Where:
Φ: photon fluence (number of photons per unit area per unit time),$[1/(m^2\cdot s)]$
$D = 1/[3(\mu_a + \mu_s')]$: optical diffusion coefficient, $[m]$
μ_a: absorption coefficient$[1/m]$
μ_s': reduced scattering coefficient,$[1/m]$
c: speed of light in tissue, $[m/s]$
S: source, other than that due to absorption $[1/(m^3\cdot s)]$

The fluence flux is defined as:

$$\Gamma = -D\nabla\Phi, \qquad [1/(m^2\cdot s)] \qquad (2)$$

Implementation in COMSOL Multiphysics

The **General Form PDE (g)** physics interface was used to solve the light diffusion equation. To maintain consistency in units, the dependent variable and source term units are defined as shown in Figure 1.

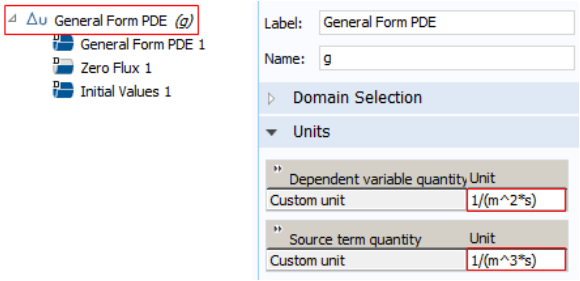

Figure 1. Implementation of units in the General Form PDE

The light diffusion equation (1) is defined under **General Form PDE 1** node as shown in Figure 2.

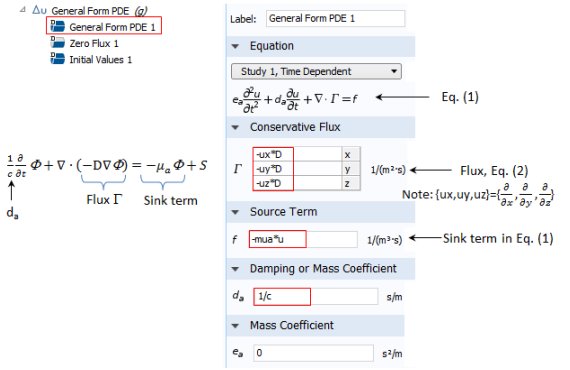

Figure 2. Implementation of light diffusion equation in the General Form PDE

The relevant tissue properties are defined under the **Parameters** node in the model.

Model Validation

To validate the approach used to implement the solution methodology, a comparison was made of the to the results of an existing analytic solution for light pulses in an infinite homogeneous media (1).

For light pulse in an infinite homogeneous media the photon fluence is described by:

$$\Phi = c(4\pi Dct)^{-3/2} exp(-\mu_a ct) exp\left(\frac{-r^2}{4Dct}\right) \quad (3)$$

The light source is given by:

$$S(\boldsymbol{r}, t) = \delta(\boldsymbol{r})\delta(t) \quad (4)$$

Function $\delta(\boldsymbol{r})$ is modeled as sphere of volume *V*, then:

$$\delta(\boldsymbol{r}) = \frac{1}{V} \quad (5)$$

Function $\delta(t)$ is modeled as Gaussian δ- function:

$$\delta(t) = \sqrt{b/\pi} e^{-bt^2}, \text{ where } \beta \rightarrow \infty \quad (6)$$

Results from the COMSOL Multiphysics® model file for the fluence from a point source of light after 2ns exposure in infinite media are given in Figure 3.

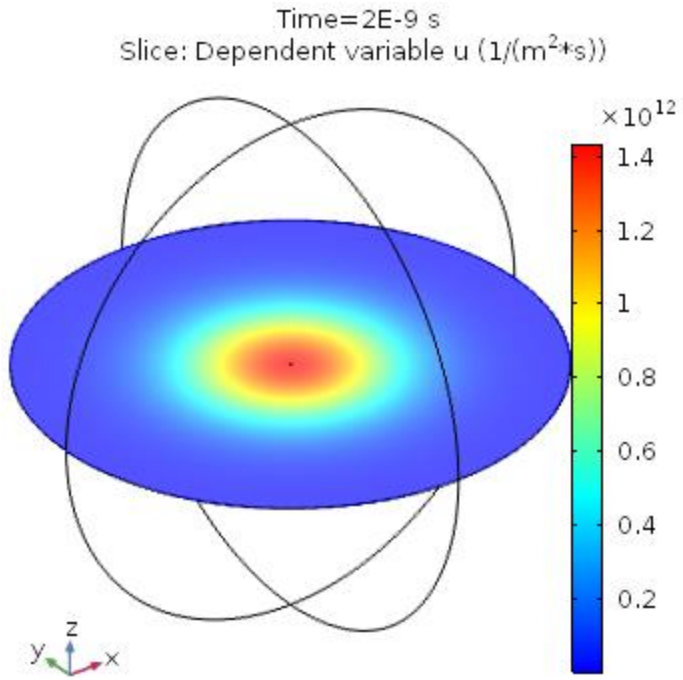

Figure 3. Fluence distribution due to point light source at time t = 2 ns.

A direct comparison with the results of the analytical solution is provided in Figures 4 and 5.

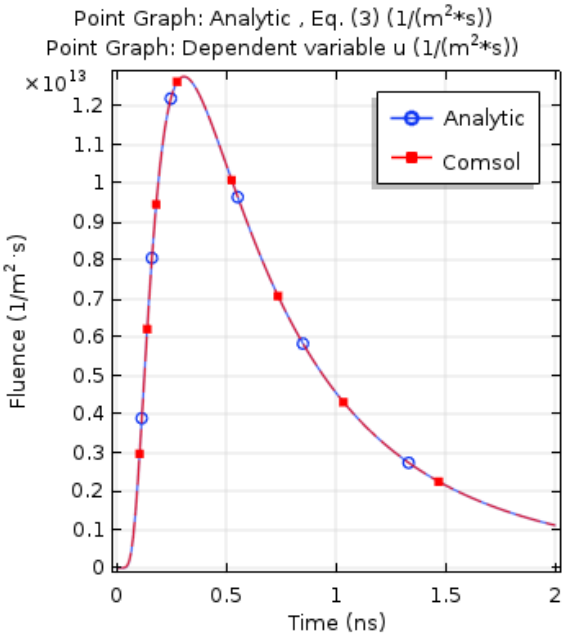

Figure 4. Comparison of predicted fluence as a function of time from the analytical solution and COMSOL Multiphysics®.

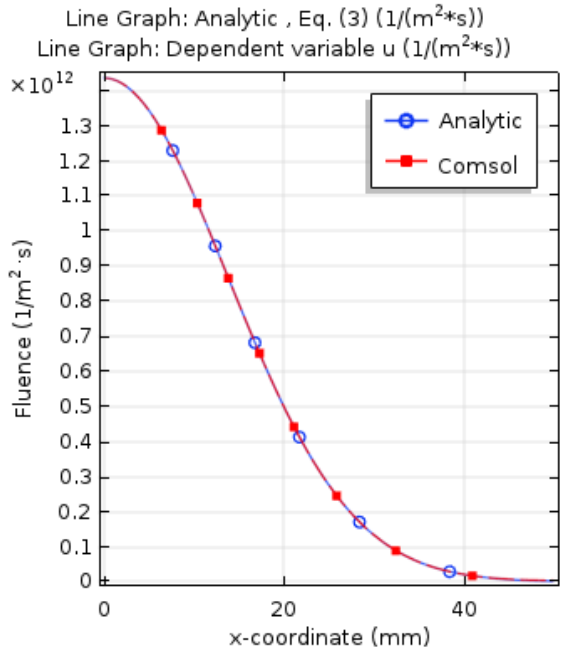

Figure 5. Comparison of predicted fluence as a function of distance from the source using the analytical solution and COMSOL Multiphysics®.

Implementation of light diffusion in tissue

Here the tissue is considered to consist of four major layers:

- Epidermis
- Dermis
- Sub-cutaneous Fat
- Muscle

A quarter symmetric model of the layered tissue is shown in Figure 6.

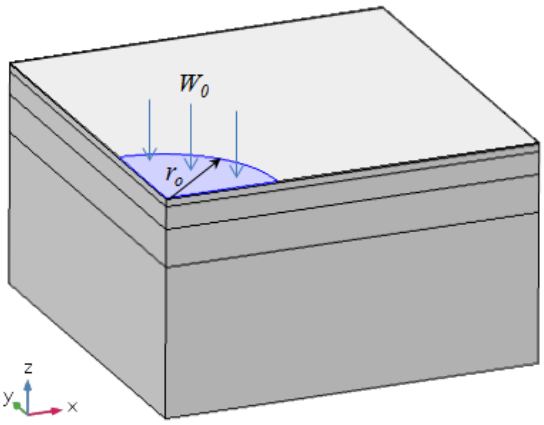

Figure 6. Quarter symmetric model of the tissue layers.

A 5th layer having the same properties as the muscle layer is added to avoid imposing a boundary condition at the bottom. The thickness of this 5th layer is choosen such that all light is absorbed before it reaches the bottom boundary of the layer. Similarly, boundary conditions at the back and right boundaries are not relevant since all light is absorbed before reaching these boundaries. The feft and front boundaries are symmetry planes so that a zero-flux boundary condition (Neumann BC) is imposed. Fluence continuity is automatically imposed at the all interior boundaries.

The laser light source is modeled using the following Dirichlet boundary condition:

$$\Phi|_S = (1-r)\frac{W_0}{\pi r_0^2(1-h\nu)} \qquad (7)$$

where

Φ: photon fluence, $\left[\frac{1}{m^2 s}\right]$
W_0: laser power, $[W]$
r_0: laser beam radius, $[m]$
$h\nu$: photon energy power, $[J]$
r: air/tissue reflection coefficient, [1]

In the current model, the laser power is assumed to be uniform over the source boundary.

Results for light diffusion in tissue

The predicted distribution of photon fluence after 2 ns is shown in Figure 7.

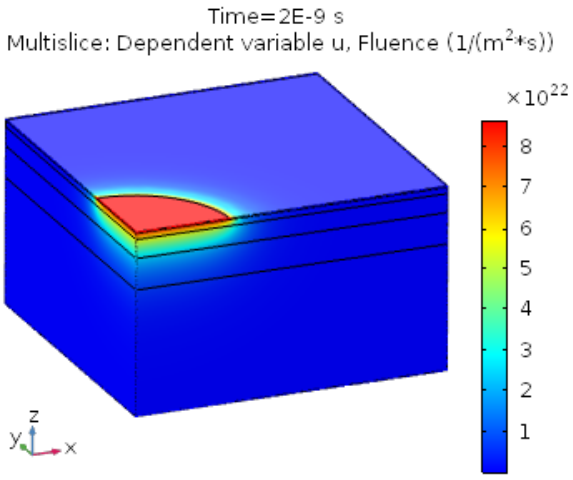

Figure 7. Predicted distribution of photon fluence after 2 ns.

As shown in Figure 8, the fluence distribution reaches steady-state after approximately 0.5 ns, suggesting that from practical perspective the diffusion of light in tissue can be adequately solved as a stationary problem.

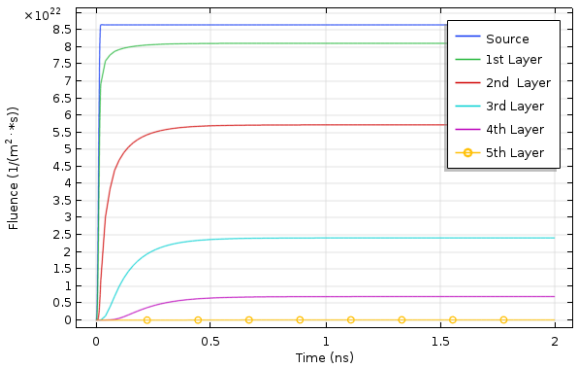

Figure 8. Fluence as a function of time for each layer of tissue.

A comparison of time-dependent and stationary solutions is provided in Figure 9.

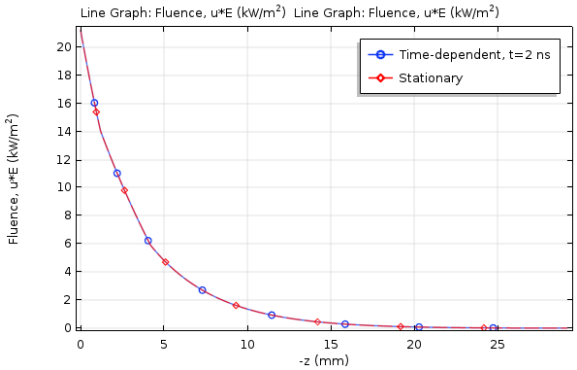

Figure 9. Comparison of the time-dependent and stationary solutions for the fluence distribution through the depth of the tissue.

Generation of heat due to photon absorption in tissue

Changes in tissue temperature due to photon absorption were addressed using the following time-dependent equation for the heat transfer in tissue:

$$\rho C_p \frac{\partial}{\partial t} T + \nabla \cdot (-\mathrm{k}\nabla T) = Q_{light} + Q_{bio} \qquad (8)$$

The heat source, Q_{light} (W/m^3), due to light absorption is calculated from:

$$Q_{light} = \mu_a \Phi \cdot (h\nu) \qquad (9)$$

Where:

Φ: photon fluence (number of photons per unit area per unit time),$[1/(m^2 \cdot s)]$
μ_a: light absorption coefficient$[1/m]$
$h\nu$: photon energy,$[J]$

Heat transfer, Q_{bio} (W/m^3), due to blood perfusion is calculated as:

$$Q_{bio} = \rho_b C_{p,b} \omega_b (T - T_b) \qquad (10)$$

Where:

ρ_b : blood density,$[kg/m^3]$
$C_{p,b}$: blood specific heat $[J/(kg \cdot K)]$
ω_b: blood perfusion rate,$[1/s]$
T_b: arterial blood temperature,$[K]$

For the results presented here, blood perfusion is considered to be active in all the tissue layers and all layers of the tissue have the same initial temperature:

$$T|_{t=0} = T_{init} \qquad (11)$$

Convective cooling is imposed at the top free surface of the tissue:

$$q_{conv} = h_0 (T_{amb} - T) \qquad (12)$$

Where

h_0 : heat transfer coefficient,$[W/(m^2 \cdot K)]$
T_{amb} : ambient temperature $[K]$

A heat transfer boundary condition due to blood flow is imposed at the right hand, back and bottom boundaries as described by:

$$q_b = u_b \rho_b C_{p,b} (T_b - T) \qquad (13)$$

Where:

u_b : blood flow speed in undamaged veins,$[m/s]$

Thermal insulation boundary conditions are imposed at the symmetry planes (left and front boundaries) and at the boundary which is in contact with laser:

$$-\boldsymbol{n} \cdot \boldsymbol{q}|_{\Gamma} = 0 \qquad (14)$$

Where:
$\boldsymbol{n}$: unit normal to the boundary

Results of photon absorption in tissue – tissue heating

The spatial distribution of temperature after application of the laser source for four minutes is shown in Figure 10.

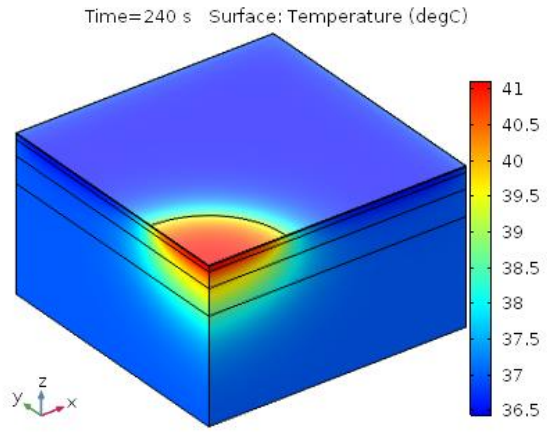

Figure 10. Contour plot of tissue temperature.

The transient temperature history is shown in Figure 11 and the temperature profile through the tissue thickness is given in Figure 12.

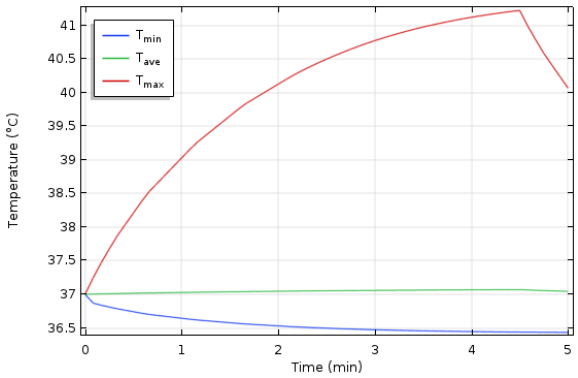

Figure 11. Transient thermal response of layered tissue.

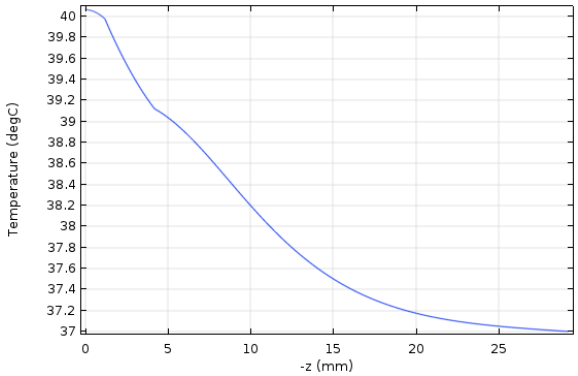

Figure 12. Temperature profile through the thickness of the tissue.

Conclusions

The computational model developed for this work simulates light diffusion by mammalian tissues exposed to laser light having a known power distribution and wavelength, and predicts the light's 3-dimensional irradiance distribution in the tissue.

The initial model was extended to predict increases in tissue temperature due to photon absorption.

References

1. http://www.atomic.physics.lu.se/fileadmin/atomfysik/Education/Mandatory_cources/FAFF35_Medicinsk_Fysik/Exercise_2_2013.pdf