ABSTRACT

The large blood vessels would act as a heat sink and hence plays a significant role during photo-thermal therapy. Gold nanoshell was considered as an high heat absorbing agent in photo-thermal heating to reduce the cooling effect of large blood vessels. In this paper, the thermal history of tissue embedded with large blood vessels during photo-thermal heating were calculated using finite element based simulation technique. A volumetric laser source term based on modified Beer-Lambert law was introduced to take care of laser heating. The results obtained conclude that tissue with different orientation of blood vessels results in different thermal response at the tissue surface. In the later part of the study, gold nanoshells were introduced into the laser irradiated tissue to overcome the cooling effect of large blood vessels during photo-thermal therapy and also the effect of size and concentration of nanoparticles on tissue heating were analysed.

Keywords: photo-thermal therapy, large blood vessels, gold nanoshells.

NOMENCLATURE

T Temperature, K
h heat transfer coefficient, W/m².K
ω blood perfusion, s⁻¹
α absorption coefficient, m⁻¹
β scattering coefficient, m⁻¹
σ Gaussian distribution of laser beam
I intensity of laser, W/m²
r,z space coordinate, m
η volumetric concentration of nanoparticles
R radius of nanoparticles, m
n number of particles per unit volume, m⁻³
Q₀ laser heat generation, W/m³
Coe coefficient, m⁻¹
LBV Large Blood Vessels

Subscripts
b blood
t tissue
a artery
0 tissue surface
e ambient
np nanoparticle
mix mixture

INTRODUCTION

Photo-thermal therapy uses electromagnetic radiation to kill the malignant cell and also able to use longer wavelength light,
which is less energetic and therefore less hurtful to the surrounding healthy cells. Most of the researchers [1–3] have reported that the protein denaturation takes place in the temperature range of 40 − 45°C and cells die in the temperature range of 50 − 70°C for a few seconds of laser heating. It is also important to achieve a uniform temperature distribution in the treated tissue for the complete destruction of diseased tissue. In clinical situation, non-uniformity in temperature can be observed due to the inhomogeneity of blood perfusion and for the presence of large blood vessels (LBV) in the tissue. These blood vessels are generally present in the form artery, vein etc. The convective effect of these blood vessels can carry away a significant amount of the deposited energy which in turn results in incomplete tissue necrosis.

The blood and its surrounding tissues are in thermal non-equilibrium when the diameter of the blood vessel is larger than 500µm [4]. Heat transfer in individual blood vessels as well as in counterflow blood vessels has been explained by Chato [5] and summerized that for a single vessel Graetz number is the controlling parameter. The minimal temperature could be obtained due to the presence of large blood vessels entering the tumor region and maintaining a systematic blood temperature [6] during hyperthermia. Several three dimensional tissue-vascular network has been analysed and concluded [7] that more flexible, high resolution heating pattern is required to reduce the effects of large blood vessels. None of the above studies are helpful for the analysis of laser irradiated photo-thermal therapy, since the light-tissue interaction has not been considered rather a uniform heat generation is used to calculate the tissue thermal history. Recently Zhou et al., [8] has investigated numerically the laser induced thermo-therapy in presence of large blood vessels.

In this study, the steady thermal response of tissue embedded with LBV under laser irradiation has been predicted using finite element based simulation considering a uniform flow at the entrance. The penetration of light in bio-tissue has been modelled by using a simplest Beer-Lambert law. Three different tissue vascular networks along with a perfused tissue model has been analyzed and surface temperature distributions are predicted with constant laser power and beam size. In the later part of the study, we addressed tissue embedded with nanoparticles to enhance its optical properties and ultimately this leads to an increase in surface temperature of tissue.

MODELS AND SIMULATION

Four different typical geometries used in this study were developed and simulated with dimensions of 200mm × 100mm × 50mm in X, Y and Z directions respectively as shown in Fig.1(a)-(d). The four geometries are (a) a perfused tissue (Fig.1(a)), (b) Single Vessel Transiting Tissue (SVTT) at a depth of 2.5mm from top tissue surface (Fig.1(b)), (c) SVTT, 2.5mm away from mid ZX-plane (Fig.1(c)) and Countercurrent Vessel Transiting

![FIGURE 1. ILLUSTRATION OF THE PHYSICAL MODELS.](image)

Tissue (CVTT), at a depth of 2.5mm from top tissue surface and 2.5mm away from mid ZX-plane in either side (Fig.1(d)). The energy transport for the blood flow and in the tissue domain was modeled by convective transport equation and diffusion [9] equation as follows;

\[
\rho_b c_b (V \cdot \nabla T_b) = \nabla \cdot (k_b \nabla T_b) + Q_{l-b} \quad (1)
\]

\[
\nabla \cdot (k_t \nabla T_t) + \rho_b \omega B c_b (T_t - T_b) + Q_{l-t} = 0 \quad (2)
\]

where, \(\rho, c, k, V, T, \omega, Q_l\) are density, specific heat, thermal conductivity, blood velocity, temperature, blood perfusion and
spatial laser heat generation respectively. Subscripts a, b and t represents artery, blood and tissue respectively.

The magnitude of laser heat generation in bio-tissue depends on the tissue optical properties in the form of absorption coefficient ($\alpha$) and scattering coefficient ($\beta$). Assuming Gaussian distribution of the beam ($\sigma$), the heat generation in the tissue depth, $z$ and radius, $r$ based on Beer-Lambert law [10] could be written as:

$$Q_l = \alpha I_0 \exp\left(-\frac{r^2}{2\sigma^2} (0) \exp(\beta z)\right) \exp\{-\alpha z\} (3)$$

where, $I_0$ is the laser intensity at tissue surface

The LBV were placed along X direction and the length of blood vessel along X-axis was taken as very long such that a fully developed flow condition can be assumed and the diameter of blood vessel was 3mm. For each tissue-vascular model, at the inlet of blood vessel;

$$V = 0.13 m/s \quad (4)$$

$$T_b = 37^\circ C \quad (5)$$
at the outlet of blood vessels;

$$k_b \frac{\partial T_b}{\partial x} = 0 \quad (6)$$

The thermal boundary conditions for the top tissue surface were taken as;

$$k_t \nabla T_t = h (T_e - T_t) \quad (7)$$

where, $T_e$ is the ambient temperature and $h$ is the convective heat transfer coefficient. The surface convective heat loss coefficient to ambient was taken as 10W/m$^2$K [11], which is a typical value for natural convection on planar surfaces with surrounding air temperature of 25$^\circ$C. The other surfaces of the tissue were considered as thermally insulated.

Gold nanoshells, with radius ($R_{np}$) of 123nm and core/shell ratio of 0.857 were used in this calculation. Jain et al., [12] calculated the optical properties of gold nanoshells in the wavelength range of 843nm to 1160nm using Mie theory. The wavelength of laser selected in this study was 1064nm and the corresponding optical properties were interpolated as given in Table 1. Certainly, the addition of nanoparticles would enhance the optical properties of tissue and these are calculated [13] as;

$$Coe_{mix} = \eta Coe_{np} + (1 - \eta) Coe_t \quad (8)$$

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Tissue</th>
<th>Blood</th>
<th>Gold Nanoshells</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k$ [W/m.$^\circ$C]</td>
<td>0.5</td>
<td>0.5</td>
<td>318</td>
</tr>
<tr>
<td>$\rho$ [kg/m$^3$]</td>
<td>1050</td>
<td>1000</td>
<td>18900</td>
</tr>
<tr>
<td>$c$ [J/kg.$^\circ$C]</td>
<td>3700</td>
<td>4200</td>
<td>130</td>
</tr>
<tr>
<td>$\alpha$ [$\mu$m$^{-1}$]</td>
<td>0.00004</td>
<td>0.0002</td>
<td>10.0</td>
</tr>
<tr>
<td>$\beta$ [$\mu$m$^{-1}$]</td>
<td>0.00053</td>
<td>0.00015</td>
<td>22.72</td>
</tr>
<tr>
<td>$\omega_b$ [s$^{-1}$]</td>
<td>0.00123</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

where, $\eta$ is the volumetric concentration of nanoparticles which depends on the number of particles per unit volume ($n$) and particle radius ($R_{np}$).

$$\eta = n \left(\frac{4\pi R_{np}^3}{3}\right) \quad (9)$$

Similarly, the addition of nanoparticles would also change the physical properties of tissue and are calculated as;

$$\rho_{mix} = \eta \rho_{np} + (1 - \eta) \rho_t \quad (10)$$

$$c_{mix} = \eta c_{np} + (1 - \eta) c_t \quad (11)$$

$$\frac{1}{k_{mix}} = \frac{\eta}{k_{np}} + \frac{1 - \eta}{k_t} \quad (12)$$

The laser power was considered as 1W with 5mm beam size of circular cross-section. Three different vascular models were discussed and finally compared with a perfused tissue model as shown in Fig.1. A COMSOL multiphysics (COMSOL4.3, Burlington, MA) software based on finite element method were used to solve the coupled fluid flow and heat transfer with velocity tolerance as well as temperature tolerance of 0.0001. After the 3D model was created, it was meshed with a tetrahedral mesh element. To ascertain the strength of the solution and its non-dependence on mesh elements, a several simulations with identical physical as well as optical parameters but with variable number of mesh elements were performed.
Consequently maximum of 0.06% change in the surface temperature were noted when total element size changes from 732043 to 932055 and finally a total element size of 732043 was selected for all models. Thus the meshed model has been solved transiently by GMRES (Generalized Minimum Residual) iterative method with geometric multigrid preconditioner.

RESULTS AND DISCUSSION

In order to find the cooling effect of LBV on tissue heating during photo-thermal therapy for different tissue-vascular net-
work, the surface temperature maps are presented in Fig.2, where Fig.2(a) represents the case of tissue in absence of blood vessels and Fig.2(b)-(d) indicates the surface isotherms for other three vascular network. It is conclusive that the presence of LBV not only reduces the temperature at the tissue surface but also the shape of isotherms obtained are different for different orientation of LBV. Figure 3 represents the comparison of surface temperature distribution along the line of Y=50mm in X direction. The temperature at both upstream and downstream direction of flow (away from heating spot) has been noticed to be higher in case of SVTT than that of the case of perfused tissue. This is owing to the fact that in case of perfused tissue, surface temperature decreases due to the convective cooling effect at the tissue surface whereas, in case of SVTT, there is heat diffusion from the

![Figure 5](image-url)  
**FIGURE 5.** TEMPERATURE DISTRIBUTION IN XY-PLANE AT Z=1mm IN ABSENCE OF NPs (a) AND WITH NPs (b) FOR CVTT MODEL.

![Figure 6](image-url)  
**FIGURE 6.** COMPARISON OF TEMPERATURE DISTRIBUTION ALONG THE LINE OF X=100mm, Z=1mm FOR SVTT (a) AND CVTT (b) BETWEEN THE CASES WITH AND WITHOUT INTRODUCING NPs.

TABLE 2. PARAMETERS FOR GOLD NANOSHells (FOR CONSTANT CORE/SHELL RATIO OF 0.857) [12]

<table>
<thead>
<tr>
<th>Case</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>R_{np} [nm]</td>
<td>70</td>
<td>105</td>
<td>70</td>
<td>105</td>
</tr>
<tr>
<td>n [m^{-3}]</td>
<td>$1 \times 10^{16}$</td>
<td>$1 \times 10^{16}$</td>
<td>$3 \times 10^{16}$</td>
<td>$3 \times 10^{16}$</td>
</tr>
<tr>
<td>$\alpha$ [\mu m^{-1}]</td>
<td>35.66</td>
<td>11.07</td>
<td>35.66</td>
<td>11.07</td>
</tr>
<tr>
<td>$\beta$ [\mu m^{-1}]</td>
<td>22.73</td>
<td>25.50</td>
<td>22.73</td>
<td>25.50</td>
</tr>
</tbody>
</table>

blood to the tissue and hence tissue surface temperature is more compared to the case of perfused tissue.

The cooling effect of LBV could be reduced by introducing gold nanoparticles and the corresponding temperature distributions are shown in Fig.4-6. Here, Fig.4 and 5 indicates the temperature distribution in tissue at a depth of 1mm from the surface and the number of nanoparticles are taken as $1 \times 10^{16}$ m^{-3}. The isotherms represented in Fig.4(a) and (b) are the comparison for the case of SVTT, without and with introducing gold nanoparticles respectively. Similarly Fig.5(a) and (b) describes the comparison for the case of CVTT, without and with introducing gold nanoshells. Figure 6 depicts the comparison of temperature distribution along the line of X=100mm and Z=1mm between the two cases of without and with introducing gold nanoshells, in which Fig.6(a) represents the model SVTT and Fig.6(b) repre-
sents the model CVTT respectively. Certainly, the temperature of tissue surrounding the LBV (X=100mm, Y=50mm and Z=1mm) is increases by approximately 5°C in case of SVTT (Fig.6(a)) and by approximately 4°C in case of CVTT (Fig.6(b)) due to the addition of nanoparticles. Because, the addition of nanoparticles improves the optical characteristics of tissues surrounding the LBV.

In order to analyze the effect of nanoparticles size and concentration (Table 2) on tissue heating embedded with LBV, different sizes ($R_{np}$) and concentrations (n) are used to predict their influence on tissue heating. The results are presented in Fig.7-9. Figure 7 depicts the isotherms at cross section of Z=1mm for all four cases (Table 2). Figure 8 and 9 represents the temperature distribution along the line of X=100mm, Z=1mm for different $R_{np}$ and different n respectively. It has been observed that a decrease in temperature is obtained with increase in $R_{np}$ since, the relative scattering contribution to the extinction increases rapidly with increase in nanoshell size ($R_{np}$) for fixed value of core/shell

FIGURE 7. TEMPERATURE DISTRIBUTION IN XY-PLANE AT A DEPTH OF 1mm FROM THE SURFACE FOR PARAMETER VALUES FROM TABLE 2 CASE I (a), CASE II (b), CASE III (c) AND CASE IV (d)

FIGURE 8. TEMPERATURE DISTRIBUTION ALONG THE LINE OF X=100mm, Z=1mm FOR DIFFERENT NANOPARTICLE SIZE (in case of SVTT).

FIGURE 9. TEMPERATURE DISTRIBUTION ALONG THE LINE OF X=100mm, Z=1mm FOR DIFFERENT CONCENTRATION OF NANOPARTICLES (in case of SVTT).
ratio [12]. The scattering coefficient ($\beta$) of gold nanoshell increases from 22.73$\mu$m$^{-1}$ to 25.50$\mu$m$^{-1}$, whereas the absorption coefficient ($\alpha$) decreases from 35.66$\mu$m$^{-1}$ to 11.07$\mu$m$^{-1}$ with increase in nanoparticle size ($R_{np}$) from 70nm to 105nm as given in Table 2. The tissue temperature surrounding the LBV increases by 5°C with the increase in concentration of nanoparticles from $1\times10^{16}$ to $3\times10^{16}$ since, the accumulation of more number of nanoparticles per unit tissue volume increases the effective absorbing contribution.

**CONCLUSIONS**

This article presents results for numerically simulated cooling effect of LBV during photo-thermal therapy and the contribution of gold nanoshells on tissue heating embedded with LBV. The simulation results indicate that the existence and different orientation of LBV can cause a significant decrease in tissue temperature surrounding the blood vessels. The cooling effect of LBV on tissue temperature surrounding the blood vessels can be reduced by introducing the gold nanoparticles during photo-thermal therapy. A smaller size and high concentration of nanoparticles with fixed core/shell ratio can be used to reduce the cooling effect of LBV on tissue heating.

**REFERENCES**


