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Numerical study of thermal dynamics of gold nanoparticles in laser-induced hyperthermia therapy

Gholamreza Fayaz[1*], **Fahimeh Mosannen Mozafari**[1]

[1] *Physics Department, Tafresh University, Tafresh, Iran*

Abstract

Damage of the normal tissue is a serious concenrn in cancer treatment. Hyperthermia by laser has been considered as a safe cancer treatments methods with lower harmful effects on normal tissues. Using nanoparticles in cancer treatment has improved laser therapy, which is based on a selective cell targeting method to localize cell damages. Metallic nanoparticles such as gold, silver, and copper have been recognized to highly interact with laser beam because of surface plasmon resonance phenomena. However, due to toxicity of silver and copper, gold nanoparticle have received great interest in nanomedicine particularly as a protein denaturizing agent applied to the targeted cells. On the other hand, interaction between laser beam and nanoparticles depends on laser properties and particle characteristics. In this study, we have numerically evaluated the effects of different parameters in the laser beam and particle, to facilitate the accurate controlling of laser-induced hyperthermia process.

Keywords: Laser, Hyperthermia, Cancer, Gold Nanoparticle

Corresponding author: Gholamreza Fayaz Physics Department, Tafresh University, Tafresh, Iran.

P.O.Box: 39518-79611

Tel: +988636227430   Fax: : +988636227814,

E-mail address: rezafz@yahoo.com

Introduction

Hyperthermia is a technique to destroy cancer cells by heating the tissue in the range of 41 to 47 Cᵒ. Laser has been widely used as a versatile tool in medical applications from 1963 (Huang, Prashant, I. El-Sayed & M. El-Sayed, 2008). Specific properties of Nd:YAG and CO_2 lasers makes them the most common medical lasers for applications in deep tumor and skin-deep treatments, respectively. Single frequency and coherency are the two properties that allow lasers to provide a high intensity beam that can accurately penetrate into tumors. However, laser beam usually does not operate in a localized fashion; it can damage the normal cells during killing of cancerous cells. In order to overcome this problem, metallic nanoparticles have been introduced to localize cell damage. By using these substances, free electrons of metals absorb photons of ultrashort pulses via inverse bremsstrahlung and transfer laser energy to the surrounding medium (Huang et al., 2008; letfullin, George, Duree & Bollinger, 2008). To optimize the treatment process and minimize damage of healthy tissues, laser wavelength, pulse width and pulse repetition have to be tuned properly (Pustovalov, 2004). Among metallic nanoparticles, gold has been frequently used in cancer treatment due to its lower toxicity as compared with silver and copper. In this work we have studied the effect of laser properties as well as nanoparticle characteristics to facilitate accurate control of cell damage in cancer treatment process.

Materials and Methods

Modeling
Different models can describe the produced heat in nanoparticles when they are exposed to laser beams. In the interaction between a biological tissue infused by metallic nanoparticles and laser pulses, the temperature of the whole system is increased. Hence, we have to define temperature of conduction electrons (T_e), lattice phonons (T_s), and surrounding medium matrix (T_M) (Palpant, Guillet, Rashidi-Huyeh & Prot, 2004; Bollinger & Letfullin, 2006). Modeling of materials response to the interaction with ultrashort pulses, particularly those in the range of femtosecond and picoseconds, is a challenging task due to comparable time scale of laser pulses and events in lattice and metallic electrons. The process can be described as follows: free electrons absorb energy of the laser pulse and rapidly attain high temperature. Afterwards, they gradually transfer the thermal energy to the lattice. Electron cooling and lattice heating are processes with a time delay of femtoseconds and picoseconds orders, respectively. Since ultrashort pulses end before transfer of the whole thermal energy to the lattice, two temperature term should be included in the model to describe electron and lattice temperatures. In a model with the two temperature terms, the coupled diffusion equations for heat conduction of electrons and lattice are solved. Equations are coupled via electron-phonon coupling constant γ and are described in equation (1):

$$C_e(T_e)\frac{\partial T_e}{\partial t} = -\frac{\partial Q(z)}{\partial z} - \gamma(T_e - T_s) + S$$

$$C_i(T_s)\frac{\partial T_s}{\partial t} =$$

$$-\gamma(T_e - T_s) - \frac{\mu_\infty T_s}{(s+1)r_0^2 \rho_s C_s(T_s)}\left[\left(\frac{T_s}{T_\infty}\right)^{s+1} - 1\right]$$

$$(1)$$

where Q(z) is the heat flux, z is the normal direction to the surface of the target, C_i and C_e are specific heat of subsystem for lattice and electron, and s is a constant depending on thermal properties of the surrounding medium. Here $\mu_s(T_s)$, L, ρ_s, r_0 and μ_∞ denote the heat conductivity, evaporation heat, density, radius of the nanoparticle and heat conductivity of the surrounding medium at normal temperature T_∞, respectively.

Although the two-temperature model is an appropriate approximation for utilizing the uniform heating in femtosecond regime, it has been demonstrated that the one-temperature model can describe laser induction heating even in wider regimes such as picoseconds and nanosecond pulse durations (Letfullin et al., 2008, Letfullin, Iversen & George, 2004). Given that, in the present study, the one-temperature model was adopted in our modeling.

One -temperature model

In the one-temperature model, it is assumed that the heat rapidly transfers from electrons to phonons in subsystem; thereby electrons and lattice phonon temperatures would be equal ($T_e = T_s$). Hence, the temperature can be obtained from equation (2):

$$\frac{dT_s}{dt} = \frac{3k_{abs}If(t)}{4r\rho_s C_s(T_s)} - \frac{\mu_{\infty}T_s}{(s+1)r_0^2\rho_s C_s(T_s)}\left[\left(\frac{T_s}{T_{\infty}}\right)^{s+1} - 1\right] + \frac{3L}{r_0 C_s(T_s)}\frac{dr_0}{dt}$$

(2)

where kabs, I, f(t), and L denote nanoparticles absorption efficiency, laser intensity and evaporation heat, respectively. The first term in the right side of equation (2) describes the produced heat in the nanoparticle and the second term account for the transferred energy to the surrounding medium from the surface of the particle. The last term describes energy loss due to particle evaporation which depends on particle characteristics and pulse duration. This can be realized in five regimes, including free-molecular, convective, diffusive, gas-dynamics, and explosive modes. Under conditions that nanoparticle heating is below the phase transition temperature, the last term can be omitted (Letfullin et al., 2008).

Results and Discussion

Damage of the cells in the explosive mode depends on different properties of nanoparticles, including size, shape, quantity, position, wavelength, intensity, pulse width, and pulse repetition of the laser (Kelly, Coronado, Zhao & Schatz, 2002; Link & El-Sayed, 2000). In this work, we numerically studied the effects of a number of the above-mentioned parameters on control of damage to heatlthy cells during cancer treatment. In our calculations the particle explosion, shock, and acoustic wave production were excluded. We have assumed that the energy is uniformly distributed in the particle volume (Pustovalov, 2004) and water is the surrounding medium.

The effect of particle size

In order to study the effects of particle size on distribution of heat rate, we have considered three spherical particles with radiuses of 10, 20, and 40 nm. In this range of size the, maximum absorption occurs at the wavelength of 520 to 550 nm (Link & El-Sayed, 2000). The laser pulse width and pulse energy were set at 8 ns and 10 mj/cm^2, respectively. By solving equation (2) for the maximum absorption, particle temperatures vs. time can be plotted (Figure 1).
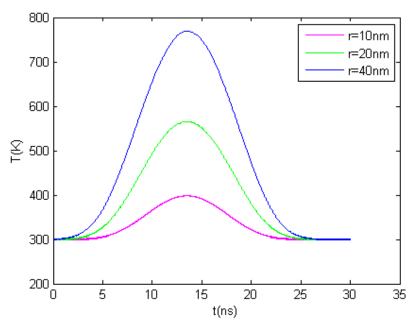

Figure 1: Particle temperature versus time for particles with 10, 20 and 40 nm radius

As shown in the Figure 1, particles are heated even after 8 ns when pulse is over. After 13.5 ns, temperature reaches to its maximum value and then particles start getting cooled which result in the transfer of heat to the surrounding medium. The maximum temperature increases by the increased particle size. Figure 2 shows interpolation of the considered range.
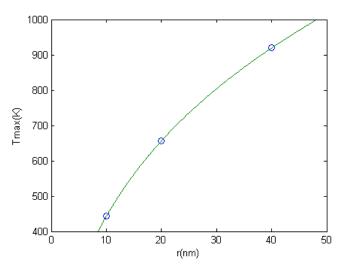

Figure 2: Interpolation of maximum temperature for the range of particle size from 10 nm to 40 nm

The effect of particle shape

We compared behavior of the particle temperature in nanorods and nanospheres. For nanorods, the aspect ratio is defined as the length divided by width. The effective radius is calculated from equation (3) (Huang et al., 2008 ; Letfullin et al., 2004):

$$r_{eff} = \left(\frac{3V}{4\pi}\right)^{1/3}$$

(3)

Nanorods attain the higher maximum temperature due to their higher absorption efficiency compared with the nanospheres.

Figure 3 illustrate the temperature curves for nanorods with effective radiuses of 8.74, 11.43, 17.9 and 21.86 nm with maximum absorption coefficient occurring at wavelength of 788 to 842 nm.

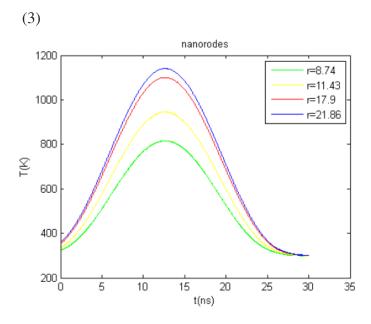We have also compared temperature profiles

Figure 3: Temperature profile versus time for nanorods with different effective radius

of a nanoshpere and a nanorod of nearly same sizes at the maximum absorbance. The maximum temperature of a nanorod with an effective radius of 11.43 nm is nearly two times higher than that of a nanosphere with a radius of 10 nm.
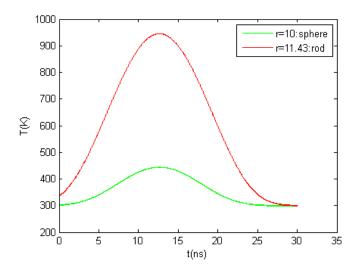

Figure 4: Temperature versus time for a nanorod (r$_{eff}$=11.43 nm) and a nanosphere (r=10 nm)

In the similar experimental conditions including the same biological material and laser intensity, the maximum temperature for nanorods is higher than in nanospheres. On the other hand, since absorption for nanorods occurs in the Near Infra Red (NIR), there is a low chance that healthy tissues are damaged and as well, beam can penetrate deeper into the tissues. These findings suugest nanorods as more interesting than nanospheres in cancer treatment.

The effect of pulse duration
We have also compared effect of different pulse durations on the temperature profile. In Figure 4, temperature versus time is plotted for nanorods with radiuses of 20 and 40 nm when they are exposed to laser pulses with width of 8 and 10 nanoseconds and the same intensity of 10 mj/cm^2.
As shown in the Figure 5, the maximum temperature decreases at the wider pulses.
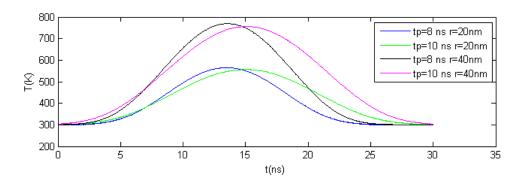

Figure 5: Temperature versus time for nanoparticles with radiuses of 20 and 40 nm at the width pulses of 8 and 10 ns

Conclusion

Our numerical study on the particle and laser properties reveals that by increasing the particle size in the range of 10 to 40 nm, the maximum temperature will increase. It is confirmed that

the maximum temperature for nanorods is higher compared to nanospheres under equal conditions. As a result, nanorods are more preferred where higher temperature is deeded for destroying more resistant cancerous cells. It was also shown that for the wider laser pulses the maximum temperature decreases, though the heating cycle is longer.

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