Journal of Thermal Biology 61 (2016) 16–28

Contents lists available at ScienceDirect

Journal of Thermal Biology

journal homepage: www.elsevier.com/locate/jtherbio

Numerical investigation of thermal response of laser-irradiated biological tissue phantoms embedded with gold nanoshells

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ARTICLE INFO

Article history:
Received 7 April 2016
Received in revised form
9 August 2016
Accepted 9 August 2016
Available online 12 August 2016

Keywords:
Bio-heat transfer
Radiative transfer equation
Non-Fourier heat conduction
Photo-thermal therapy
Optical inhomogeneity
Gold nanoshells

ABSTRACT

The work presented in this paper focuses on numerically investigating the thermal response of gold nanoshells-embedded biological tissue phantoms with potential applications into photo-thermal therapy wherein the interest is in destroying the cancerous cells with minimum damage to the surrounding healthy cells. The tissue phantom has been irradiated with a pico-second laser. Radiative transfer equation (RTE) has been employed to model the light-tissue interaction using discrete ordinate method (DOM). For determining the temperature distribution inside the tissue phantom, the RTE has been solved in combination with a generalized non-Fourier heat conduction model namely the dual phase lag bio-heat transfer model. The numerical code comprising the coupled RTE-bio-heat transfer equation, developed as a part of the current work, has been benchmarked against the experimental as well as the numerical results available in the literature. It has been demonstrated that the temperature of the optical inhomogeneity inside the biological tissue phantom embedded with gold nanoshells is relatively higher than that of the baseline case (no nanoshells) for the same laser power and operation time. The study clearly underlines the impact of nanoshell concentration and its size on the thermal response of the biological tissue sample. The comparative study concerned with the size and concentration of nanoshells showed that 60 nm nanoshells with concentration of 5×10^{15} mm^{-3} result into the temperature levels that are optimum for the irreversible destruction of cancer infected cells in the context of photo-thermal therapy. To the best of the knowledge of the authors, the present study is one of the first attempts to quantify the influence of gold nanoshells on the temperature distributions inside the biological tissue phantoms upon laser irradiation using the dual phase lag heat conduction model.

1. Introduction

Need of highly efficient methodologies for cancer treatment is inevitable in current times, given its omnipresence and fatal consequences to human health. There has been a lot of interdisciplinary research going into developing such techniques. Photo-thermal therapy is one such technique that is primarily based on the principle that uses photon energy and converts it to thermal energy to destroy the cancerous cells via the mechanisms of hyperthermia, coagulation, and evaporation (Gupta et al., 2007). A high optically absorbing medium is ideal for photo-thermal therapy to ensure maximum conversion of light into heat energy. But most human tissues are highly scattering and less absorbing in nature, causing limitations to the overall performance of photo-thermal therapy (Bayazitoglu et al., 2013). Use of nanoparticles is a promising option to circumvent such limitations. These particles can be tuned to exhibit maximum absorption in the near-infrared region (NIR) (700–1100 nm wavelength of electromagnetic radiation). This region corresponds to the highest physiological transmissivity and laser radiation propagates through tissues with minimum attenuation (Duck, 1990; Cheong et al., 1990). So, when the nano-particles are dispersed in cancer affected tissue subjected to NIR radiation, the tissue domain embedded with gold nano-particles becomes relatively highly absorbing as compared to the medium not having nanoparticles.

Gold nano-particles show very high absorption in the NIR region making them the most suitable option as contrast reagent for photo-thermal therapy as approved by Food and Drug Administration (FDA) (Dreaden et al., 2011). Out of the different shapes and configurations, gold nanoshells are widely used for therapeutic applications and are most effective in laser hyperthermia treatments on account of their easy synthesis and high tunability (Bayazitoglu et al., 2013). Nanoshells assisted photo-thermal therapy has been topic of clinical research interest and a lot of experimental and numerical work has been done to verify and

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http://dx.doi.org/10.1016/j.jtherbio.2016.08.002
0306-4565/

Nomenclature

a	nanoshell outer diameter, nm
c	speed of light in vacuum, 3×10^8 m/s
c_v	specific heat of the tissue
f	repetition rate, Hz
G	incident intensity
I	intensity
I_b	blackbody intensity, $\sigma T^4/\pi$
k	thermal conductivity
L	total length
M	number of discrete directions
N_t	number of nanoshells per unit volume, mm^{-3}
Q_{abs}	absorption efficiency
Q_{sca}	scattering efficiency
q	radiative heat flux
s	distance traveled by beam
$\hat{\mathbf{s}}$	unit direction vector
T	temperature
t	time
t_p	laser pulse width, ps
z	depth

Greek symbols

$\Delta\Omega$	control angle
β	extinction coefficient, $\kappa+\sigma$
ε	emissivity
κ	absorption coefficient
ρ	density of the medium
σ	scattering coefficient or Stefan-Boltzmann constant
τ	relaxation time
Φ	scattering phase function
ω	weight in discrete direction, m

Subscripts

b	blackbody or blood
np	nano-particle
w	wall/boundary
M	metabolic
t	tissue

establish its feasibility. In the pioneering study by Hirsch et al. (2003), irreversible photo-thermal tumor ablation using gold nanoshells has been demonstrated both in-vivo and in-vitro. Lu et al. (2009) successfully carried out in vivo study with hollow nanoshells on live mice infected with malignant cancerous tissues.

In order to understand the thermal response of tissue embedded with gold nanoshells, accurate prediction of temperatures is necessary. In this regard, various mathematical models governing the physical processes and the associated numerical schemes have been already developed in the past as well as in the current times. To estimate the temperatures of the tissue irradiated with laser during photo-thermal therapy, first the intensity distribution inside the biological tissue phantom due to incident laser irradiation needs to be estimated. It can be determined by solving radiative transfer equation (RTE) as given by Eq. (1) (Kumar and Srivastava, 2014; Modest, 2003):

$$\frac{1}{c}\frac{\partial I}{\partial t}+\frac{\partial I}{\partial s}=-\beta I+\frac{\sigma}{4\pi}\int_{4\pi} I\varnothing(\Omega,\Omega')d\Omega' \tag{1}$$

The radiation intensity, I, is expressed as a function of time t, and space coordinate, $s$and the direction Ω. $\varnothing$ is the scattering phase function. Early attempts in numerical studies focused on estimating the one dimensional temperature distribution with gold nanoshells embedded in the tissue. Tjahjono and Bayazitoglu (2008) provided steady state numerical solution for intensity and temperature distribution inside one-dimensional slab embedded with gold nanoshells and heated by a laser while using P1 approximation to determine the diffuse intensity distribution. Vera and Bayazitoglu (2009a, 2009b) also used the P1 approximation and reported intensity variation for different tissues with varying quantities of nanoshell concentration. Dombrovsky et al. (2011) used a two-flux approximation for diffuse intensity and solved a transient, combined thermal model for one-dimensional tissue embedded with gold nanoshells. Sahoo et al. (2014) carried out a numerical study on a cylindrical tissue domain considering the exponential decay of laser radiation coupled with bio heat transfer dual phase lag model. Dombrovsky et al. (2013) used a transport approximation for phase function treatment. Soni et al. (2014) carried out a study on gold nanorods uniformly distributed inside a cylindrical tissue domain. The most recently used method to solve the RTE (Eq. (1)) approximates the integral term as summation quadrature and its discretization can be carried out using various methods. Mishra et al. (2006) provided a comparative study of different discretization methods viz. discrete ordinate method (DOM), discrete transfer method (DTM)and finite volume method (FVM) carried out for a one dimensional optically participating medium. In the most efficient DOM method, the integral in-scattering term in RTE is first replaced by sum of numerical quadrature, that is –

$$\int_{4\pi}\varnothing(\Omega,\Omega')d\Omega' = \sum_{m=1}^{M}\omega^m\varnothing(\Omega,\Omega') \tag{2}$$

where, ω^m is the weight factor associated with each direction Ω. The quadrature is then summed up for all the directions along with their respective weight factors. Singh et al. (2014) carried out a similar numerical investigation using DOM on two-dimensional tissue medium embedded with gold nanoshells.

With this background, the primary objective of the current study is to investigate the impact of gold nanoshells on thermal response of the laser irradiated biological tissue phantom embedded with gold nanoshells. The study involves solving of complete RTE using DOM to determine the transient intensity distribution in a two-dimensional tissue medium. The RTE coupled with bio-heat equation in its most generalized form, known as dual phase lag (DPL) model has been utilized. A short-pulse laser has been employed as a photon energy source. The pulse duration of the laser is of the order of few picoseconds and total duration of therapy is 1 s. The operation parameters are similar to those employed by Kumar and Srivastava (2014). To the best of the knowledge of the authors, the present study is one of the first attempts to understand the impact of embedded nanoshells on the temperature distribution within the body of a laser irradiated biological tissue phantom using DPL based heat conduction model. Simulations have also been performed for studying the influence of size and concentration of gold nanoshells on the levels of temperature achieved inside the optical inhomogeneity that is embedded inside the physical domain.