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Thermal dosage investigation for optimal temperature distribution in gold nanoparticle enhanced photothermal therapy

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ABSTRACT

Thermal therapy is a promising alternative treatment to conventional surgery for benign disease and cancer. However, it suffers from surface overheating and undesired damage to health tissues. In the present work, we studied the laser-tissue interaction involved in the process of gold nanoparticle (GNP) enhanced photothermal therapy. Monte Carlo method (MC) and Beer's law were applied to calculate the heat generation of tissue and GNPs irradiated by laser. Afterward, the heat generation was used in Comsol as a source term in the bioheat transfer equation. The influence of period heating, GNPs volume fraction, laser irradiation area, and tumor aspect ratio were investigated. It was found that period heating could be used to prevent the surface overheating problem. Despite that higher GNPs volume fraction can lead to higher light absorption efficiency of tumor, lower volume fraction will be better for the heat source distribution. Furthermore, smaller laser irradiation area can be applied to prevent the overheating of the surrounding tissues when the aspect ratio of tumor is larger than a critical value.

1. Introduction

Thermal therapy is a promising alternative treatment to conventional surgery for the treatment of benign disease and cancer [1–4]. It is either used alone or in conjunction with other treatments, such as radiotherapy and chemotherapy [5,6]. The basic idea is to use heat to destroy cancerous tissues. In thermal therapy, cell death is caused by different reasons, such as apoptosis, necrosis, or autophagy. It is characterized by what leads to the death of cells, which includes the disruption of cell membrane, cell shrinkage, chromosomal DNA fragmentation et al. [7–9] Due to its minimally invasive or even non-invasive nature, it is especially applicable for patients who are not suitable for radiotherapy, chemotherapy or surgical therapy. Despite the fact that thermal therapy has many advantages, there is a chance that nearby healthy tissue can be damaged [10–12]. Overheating of the tissue surface is also a major issue of the application of thermal therapy [13], which needs further investigation.

The heat generation can be caused by ultrasound and electromagnetic wave which includes radiofrequency, microwave, and near-infrared [14–16]. Because of the precise controllability [17,18] and the 'optical window' of tissue [19], infrared and near-infrared laser-induced thermal therapy (LITT) is a very promising method of thermal therapy. To solve the problem of unselective heating of normal and cancerous tissues, the nanoparticles enhanced LITT was widely studied *in vivo* and *in vitro* [2,20]. Due to the superior optical and biological properties, gold nanoparticles (GNPs), such as gold nanosphere, nanorod, nanoshell, nanocage et al., are often employed as the contrast agent for LITT [21–25]. In the 'optical window' region, the tissue has a relative low absorption, which allows the light to propagate for a long distance and also weakens the local heating phenomenon for the healthy tissue. By coating with specific structures and materials, GNPs can be designed to accumulate in a specific organ or tumor [26,27], which can be applied to generate heat to kill the cancerous tissues. The heat generation is caused by the oscillation (see Fig. 1a) of GNPs, also known as surface plasmon resonance [28,29].

For the surface overheating problems, scholars made their efforts basically on two aspects, surface cooling and heating strategy. Singh et al. [13] studied the LITT with a forced convection cooling surface. The impact of convective heat transfer coefficient was fully addressed. Dombrovsky [30] developed a period heating strategy that uses period heating instead of continuous heating to prevent the overheating of tissue surface. Period heating allows the surface to cool down when the laser is shut off. Meanwhile, it barely influences the temperature inside the tissue. However, there still remains some problems required to be investigated thoroughly. The factors that influence the period heating effect are

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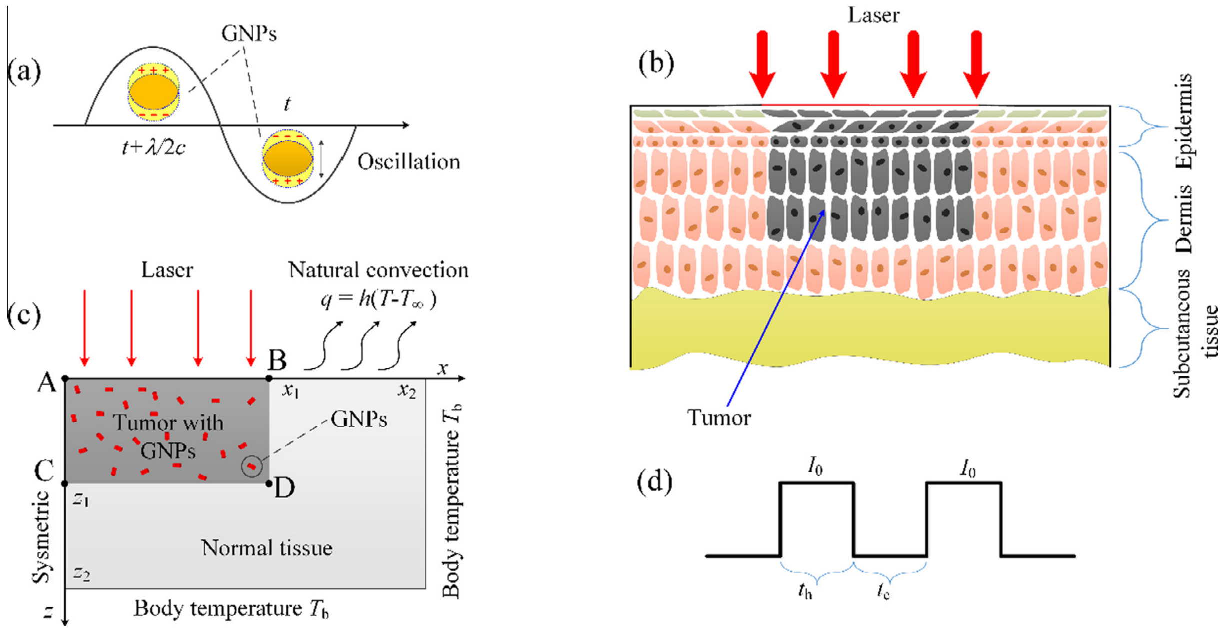

Fig. 1. (a) Schematic of surface Plasmon resonance of gold nanoparticles; (b) 2D structure model of human skin with skin tumor area irradiated by laser; (c) simplified 2D physical model of tumor surrounded by healthy tissue; (d) schematic of incident laser for period heating.

not fully addressed, such as the tumor size, the heating and cooling period duration, and the GNPs volume fraction. Furthermore, the problem of healthy tissue damage still exists even with period heating strategy. Therefore, the influence of these parameters are studied thoroughly in the present work.

With GNPs' assistance, the healthy tissue is barely directly heated by the laser. But the heat conducted from the tumor to the surrounding tissue may still cause permanent damage to the healthy tissue. The forced convection cooling may lead to a relatively complicate instrument and also does not suit for inner tumor treatment. In the present work, we studied the laser-tissue interaction involved in the process of GNP enhanced photothermal therapy. The interaction between light and participating media are well investigated, numerically and experimentally [31–33]. Monte Carlo method (MC) and Beer's law were applied to calculate the heat generation of tissue and GNPs irradiated by laser. Afterward, the heat generation was used in Comsol as a source term in the bioheat transfer equation. The remainder of this work is organized as follows. The optical properties of tissues with embedded nanoparticles are summarized in Section 2.1. The thermal damage model is introduced in Section 2.3. The influence of period heating, GNPs volume fraction, laser irradiation area, and tumor aspect ratio are studied in Section 3. The main conclusions are drawn in Section 4.

2. Theory and methods

The physical model for a typical skin tumor can be simplified into a 2D rectangle geometry (see Fig. 1).

2.1. Optical properties of tissue with embedded nanoparticles

The optical properties of human tissue are essential factors for the propagation of light which has a growing interest in both diagnostic and therapeutic applications [34,35]. There are plenty of researches that try to determine the optical properties of a certain kind of living tissue of human or other animals, *in vivo* and *in vitro* [36,37]. The point of interest of the present study is to investigate the temperature fields under different conditions for a skin tumor irradiated by laser. Therefore, the optical properties of human skin in different researches are listed in Table 1. The basic optical properties for the calculation of radiative transfer are absorption coefficient μ_a, scattering coefficient μ_s, and asymmetry factor g. For material with high scattering albedo, which means $\mu_a/(\mu_a+\mu_s) \geqslant 0.5$, there is no intolerable difference between the results of different g and μ_s but with the same μ_s' $(=\mu_s(1-g))$. The scattering albedo for tissue is normally larger than 0.9 [38]. Furthermore, there is an 'optical window' in the region 600–1300 nm which is frequently used in diagnostic and therapeutic applications [39,40]. In this range, the tissue has relatively small absorption and scattering coefficients so the light can propagate deeper in the skin or other soft tissues. Hence, only μ_a and μ_s' in that range are discussed. It can be seen from Table 1 that μ_a and μ_s' vary in a small range between wavelength 600–1300 nm.

Given that the properties of surrounding tissues and the injected nanoparticles are known, the optical properties of the composite media can be calculated as follows [45]:

$$\mu_a = \mu_{a,m} + \mu_{a,n} \quad (1)$$

$$\mu_s' = \mu_{s,m}' + \mu_{s,n}' \quad (2)$$

where $\mu_{a,m}$ and $\mu_{s,m}'$ are the absorption and reduced scattering coefficients of matrix media, respectively. $\mu_{a,n}$ and $\mu_{s,n}'$ are the absorption and reduced scattering coefficients of nanoparticles respectively, which can be expressed as [30]:

$$\mu_{a,n} = 0.75 f_v \frac{Q_a}{r} \quad (3)$$

$$\mu_{s,n}' = 0.75 f_v \frac{Q_s'}{r} \quad (4)$$

where f_v is the volume fraction of nanoparticles. Q_a and Q_s' stand for the dimensionless efficiency factor of absorption and transport efficiency factor of scattering for single particles, respectively. r is the radius of nanoparticles.