# Thermal interaction of biological tissue with nanoparticles heated by laser radiation

A. Yu. Krainov, K. M. Moiseeva, A. V. Shapovalov
Tomsk State University,36, Lenina Avenue, Tomsk, 634050, Russia

## ABSTRACT

We explore the problem of thermal interaction of nanoparticles heated by laser radiation with a biological tissue after particle flow entering the cell. The solution of the model equations is obtained numerically under the following assumptions: a single particle is located in a neighborhood exceeding the particle size; the environment surrounding the particle is water with the conventional thermal characteristics. The model equations are deduced from the particle and the environment energy conditions taking into account the heat transfer in the particle and in its environment by conduction. We also assume that at the boundary between the particle and the surrounding water the perfect thermal contact takes place.

The numerical solution of the problem is carried out with the use of an implicit difference scheme and the sweep method. Two cases of the laser pulse action on a particle are considered: a single pulse and a series of pulses. The dynamics of the temperature isoline propagation is obtained at which protein denaturation occurs in the space around the metal nanoparticle in the cases when the particles are heated by a single pulse and a series of pulses. The dependence of the heating rate and the heating depth of the medium on the laser pulse repetition frequency is found.

**Keywords:** laser radiation, nanoparticles, interstitial thermal therapy, dynamic destruction of the cell, numerical simulation, heat exchange

## 1. INTRODUCTION

Thermal interaction of laser light with biological tissue results in denaturation of a volume of tissue that is increasingly widely used to destroy cancerous tumours in laser interstitial thermal therapy (LITT) and in other applications (see a review paper [1] and references therein). Today various wide-band tuning laser sources had been designed which allow to choose optimal frequency for LITT [2,3]. The crucial point in these methods is the control of the size of the coagulation volume. A number of studies have been performed to obtain theoretical estimates of the coagulation zone parameters, e.g. in [4] a perturbation model based on of the diffusion equation has been considered.

In the present paper we consider the problem of thermal interaction of the particles with the medium after failing a stream of particles into the cell. Thermal effects of heated particles on the environment can be either aggregate (an environment point is heated by several particles) or unit. By the unit heating effect we mean that the considered domain of the medium is heated by only a single particle. This effect is possible if the particles are sufficiently far apart. In this case, each particle individually heats a neighborhood around them, and these neighborhoods do not overlap.

With intensive heating, the fluid surrounding a particle can reach the boiling point at a high temperature of the particle. And then the vapor pressure can destroy the cell structure (the vapor creates a bubble that will collapse after cooling of the vapor). Under normal conditions, the water boils at 100 ° C, but in the neighborhood of the particle on the curved surface, the vapor pressure is different from atmospheric pressure. This is due to the fact that at the boundary between liquid and solid body there is an additional pressure determined by the Laplace formula [5]. The extra pressure depends on the particle size, the smaller the particle, the higher the pressure and higher the boiling point.

## 2. PROBLEM STATEMENT AND SOLUTION METHOD

Assumingthat a single particleis in the neighborhood exceedingthe size ofthe particle itself, we consider the problemof heat transfer betweenthe heatedsphericalgold particlesand the environment.Astheenvironmentwe consider water.The mathematical problem statement assumes the heat transfer along the particles and the surrounding water by conduction.At the boundary between the particle and the water is meant "perfect contact", defined by the equality of

International Conference on Atomic and Molecular Pulsed Lasers XII, edited by Victor F. Tarasenko, Andrey M. Kabanov, Proc. of SPIE Vol. 9810, 981020 · © 2015 SPIE
CCC code: 0277-786X/15/$18 · doi: 10.1117/12.2225585

temperature and the heat flux.

Formulation of the problemin dimensional variableshas the form:

The temperature in the particle:

$$c_k \rho_k \frac{\partial T_k}{\partial t} = \lambda_k \frac{1}{r^2} \frac{\partial}{\partial r}\left( r^2 \frac{\partial T_k}{\partial r} \right),\ 0 \le r < R. \tag{1}$$

The temperature in the environment:

$$c_r \rho_r \frac{\partial T_r}{\partial t} = \lambda_r \frac{1}{r^2} \frac{\partial}{\partial r}\left( r^2 \frac{\partial T_r}{\partial r} \right),\ R < r \le R_r. \tag{2}$$

The boundary conditions:

$$r = 0: \quad \frac{\partial T_k(0,t)}{\partial r} = 0. \tag{3}$$

$$r = R: \quad \lambda_k \frac{\partial T_k(R,t)}{\partial r} = \lambda_r \frac{\partial T_r(R,t)}{\partial r}, T_k(R,t) = T_r(R,t). \tag{4}$$

$$r = R_r: \quad \frac{\partial T_r(R_r,t)}{\partial r} = 0. \tag{5}$$

$$t = 0: \quad T_k(r,0) = T_{k,b}, \quad T_r(r,0) = T_{r,b}. \tag{6}$$

Here, $c$is the specific heat capacity, $\rho$is the density, $T$is the temperature,$t$is thedenotes time,$r$ is theradial coordinate,$R$is the particle radius, $R_r$is the surroundings boundary, $\lambda$is the coefficient of thermal conductivity.

The indices are:$k$ – numerates the particle parameters, and $r$ – numeratesthe surroundings parameters (water),and$b$ – relates to the initial values of parameters.

As the initial conditions we assume that the particle is instantly warmed to the temperature $T_{k,b}$.

Problem (1)–(6) was solved numerically using thesweep method [6]. The calculations were obtainedfor four values ofthe particle radius. Thereforethe grid for eachoptionof calculation was chosen soas to providea minimum of 50pointsin theparticle neighborhood.The time step$\Delta t$ was determined by the valueofthe spacestep $\Delta h$andwas setsuch that theCourant numberbe equal to1, $Kur = \frac{\lambda_k}{c_k \rho_k} \frac{\Delta t}{\Delta h^2} = 1$, where$Kur$ is the Courant number.

For the calculation there were chosen the following values of thermal parameters corresponding to water and gold nanoparticles: $\lambda_r = 0.58$ $W/(m \cdot K)$, $\lambda_k = 308$ $W/(m \cdot K)$, $c_r = 4180$ $J/(kg \cdot K)$, $c_k = 130$ $J/(kg \cdot K)$, $\rho_r = 1000$ $kg/m^3$,$\rho_k = 19320$ $kg/m^3$. The initial temperature of the surroundings was considered equal to the normal human body temperature $T_{r,b} = 36.6$ $C$.

## 3. RESULTS

### 3.1. Single-pulse heating up of the environment

The first seriesof calculations wascarried outfor the case ofheatingup the surroundings by a single laser pulse. It was assumed that after laser pulse impact, a single particle was instantaneously heated up to a predetermined temperature.The calculation was performedfor theparticleswith the radiuses $R = 50$ $nm$, 25 $nm$, 10 $nm$, 5 $nm$,the initial temperature ofthe heatedparticleswas variedin the range of$T_{k,b} = 50 \div 300$ $C$. The surroundingslength was setequal to thefive radiuses of the particleand, respectively, was equal to$R_r = 250$ $nm$, 125 $nm$, 50 $nm$, 25 $nm$.The calculation resultsare presented in Figure1.

Figure 1 shows the dependence of the neighborhood of maximum heating of medium on the particles with a predetermined initial temperature Tk,b. The spatial point r where the temperature achieved the value of Tr,44 = 44 C at any moment of time has been chosen in the calculations as the coordinate of heating.

For the coordinate Δr of the maximum heating of the surroundingsit has been taken the most promotion of the isotherm Tr,44from the particle in the medium. The results of the calculations shows that at $T_{k,b}$ = 300 *C* a single particle heats the medium at a distance equal to the radius of the particle itself.After that, the temperature contour line of 44°*C* is returned to the particle and disappears; there is a cooling of the particles to a temperature less than 44°*C*.

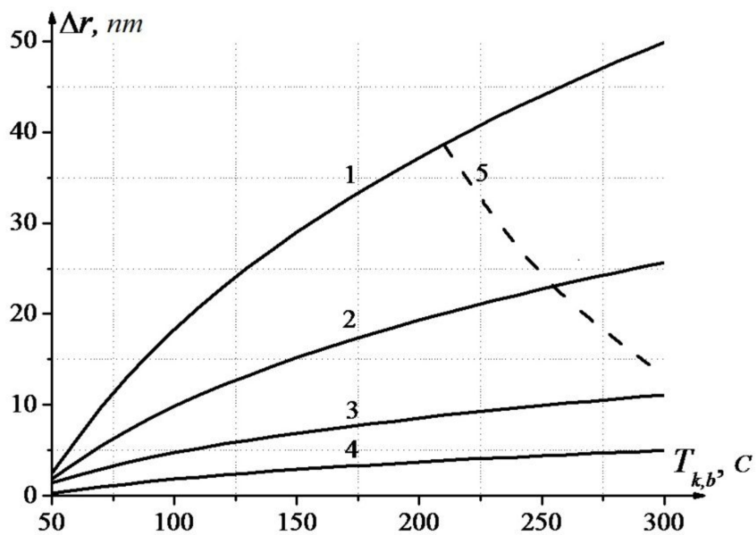


Figure 1.The size of heating of the neighborhood of the surroundings to a temperature of 44°*C*, depending on the initial temperature of the particle.*R* = 1 - 50 *nm*, 2 – 25 *nm*, 3 – 10 *nm*, 4 – 5 *nm*. The dash curve 5 is the boundary according to "capillary effect".

An example of the temperature behavior of the particles and the surroundings is shown in Figure2. It can be seen that the temperature of the particle ($0 \le r \le 50$ *nm*)decreases, and the temperature of the surroundings($r > R$) increases. The behavior of the coordinate *r* for temperature$T_r$ = 44 Ccorresponds to the above description.

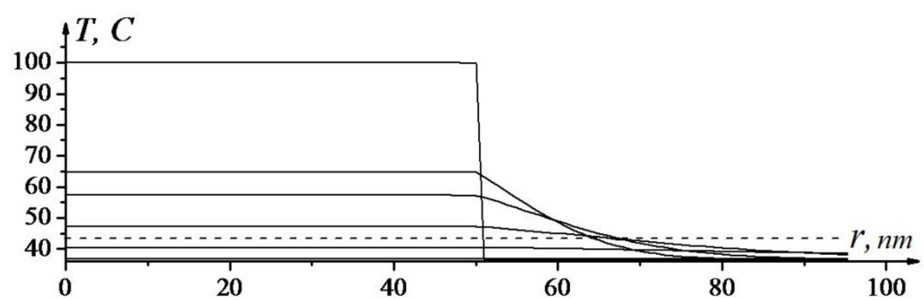


Figure 2 The temperature distribution of the particle and the environment in space at different times.

The value $T = 44$ *C* in Figure. 2 shows a dotted line. The points of intersection of the dashed and the solid lines correspond to the location coordinates of heating at the current time.The pressure of saturated water vapor at theboundarybetween the particle and the liquid is defined as $p = 2\sigma/R$ [5], where σ is the value of the surface tension of the liquid (for the water, depending on the temperature, $\sigma = 75.68\cdot10^{-3} \div 58.85\cdot10^{-3}$ *N/m*). The surface tension decreases with increasing temperature, so the value $\sigma = 50\cdot10^{-3}$ *N*/*m*was takento estimate the overpressure. The corresponding value of the overpressure for *R* = 50 *nm*,25 *nm*, 10 *nm*, 5 *nm* is $p_{iz}$ = 2 *MPa*, 4 *MPa*, 10 *MPa*, 20 *MPa*.The boiling point is $T_b$ = 212 *C*, 250 *C*, 311 *C*, 365 *C*[7].

In Figure 1 the curve5separates the domaincorresponding to the particle temperatureat whichboilingwateris possiblein the neighborhood ofthe particle.This domain alsocorresponds to thepossible destruction ofthe cell.Butthe dynamicmechanism of destructiondue to a sharpincrease in pressureandis not considered here.

### 3.2. Heating the environment by a series of pulses

The heating up of the environment by a single particle may be ineffective in some circumstances. In the cases where the maximally wide domain is needed to be heated at low temperatures, a series of laser pulses can be used to heat nanoparticles periodically.We assume that the particles are heated periodically by a laser through an artificially defined fixed time intervals. With each pulse (assuming instantaneous heating) the particle temperature in the surroundings is increased by a value equal to the initial temperature of the particle.

Depending on the intensity and the temperature of the laser radiation,various behavior of the surroundingstemperature is possible. This may bea rapid temperature increaseup to highvalues, the periodic rise and fallin temperature ora relatively slowheating.To verify how a series of laser pulses, that periodically heat a particle, affects the heating of the medium the calculation of problem (1) – (6) was carried out for the pulses with the period $\Delta\ t_{imp} = 100\ ps$, $50\ ps$, $10\ ps$(picoseconds).

In the calculations, the initial temperature of the particle has been chosenequalto $T_{k,b} = 50\ C$.It was supposed thatafter each of thepulsesthe particletemperatureis increasedby the amount equal $T_{raz}$. The heating temperature was equalto $T_{raz} = T_{k,b} - T_{r,b} = 13.4\ C$ .The calculation was carried out for theparticleradius $R = 50\ nm$, $25\ nm$, $10\ nm$, $5\ nm$.The calculation resultsare presented in Figures3 – 6.The figures show theposition ofthe heating coordinate $\Delta\ r$of the surroundingsto the temperature$T_r = 44\ C$in time.The value$\Delta\ r = 0$ corresponds to the boundarybetween the particleand the surroundingsAccording to Figure 3a for particles of the radius $R = 5\ nm$ at $\Delta t_{imp} = 10\ ps$, a rapid heating of the surroundings takes place, at $\Delta t_{imp} = 50\ ps$the periodic heating and cooling of the surroundings takes place with a gradual increase of the heating domain, at $\Delta t_{imp} = 100\ ps$the period between the heating and cooling of the environment increases. With increasing of the particle radius to $R = 10\ nm$ (Figure 4) the rate of heating medium increases for predetermined periods $\Delta\ t_{imp} = 10\ ps$ (a) and $50\ ps$ (b), and $100\ ps$ (c). When $\Delta\ t_{imp} = 100\ ps$ the surroundingsis heated stepwise with periodic damping and heating up.

With further increase of the particle radius, the heating rate is increased that can lead to overheating of both the environment and the particle.When calculating the heating by the pulse series, the calculation was limited to the boiling point. It was believed that when the boiling point is achieved the laser operation is terminated. From the calculation results it follows that the boiling point of the liquid near the surface of particles is achieved faster for large particles and high intensity of the laser operations.

## 4. SUMMARY

1. A numerical study of warming-up the water in surroundings of a single heated nanoparticle was carried out.

2. It is shown the existence of the limit initial temperature of the nanoparticle at which the dynamic destruction of the cell may occur at the expense of boiling-up the water near the heated nanoparticle.

3.It is shown that the frequency of laser pulses warming-up the nanoparticles effects on the rate and depth of the heating environment.

## ACKNOWLEDGMENTS

This work was partially supported by the Program for Enhancing the Competitiveness of Tomsk State University among the World’s Leading Scientific and Educational Centers.

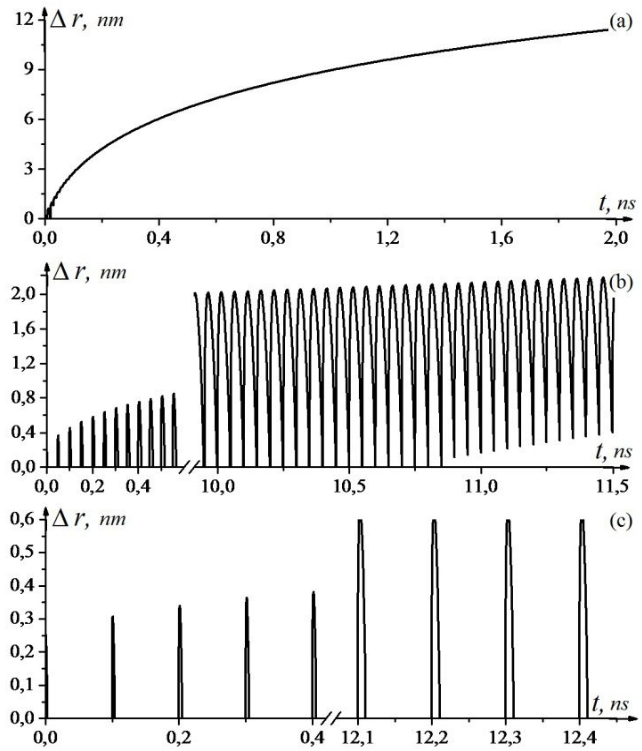


Figure 3. Time dependence of the heating up position to the temperature 44 $^{o}C$. $R$=5 $nm$, $\Delta\, t_{imp}$ = 10 $ps$ (a), 50 $ps$ (b), 100 $ps$ (c).

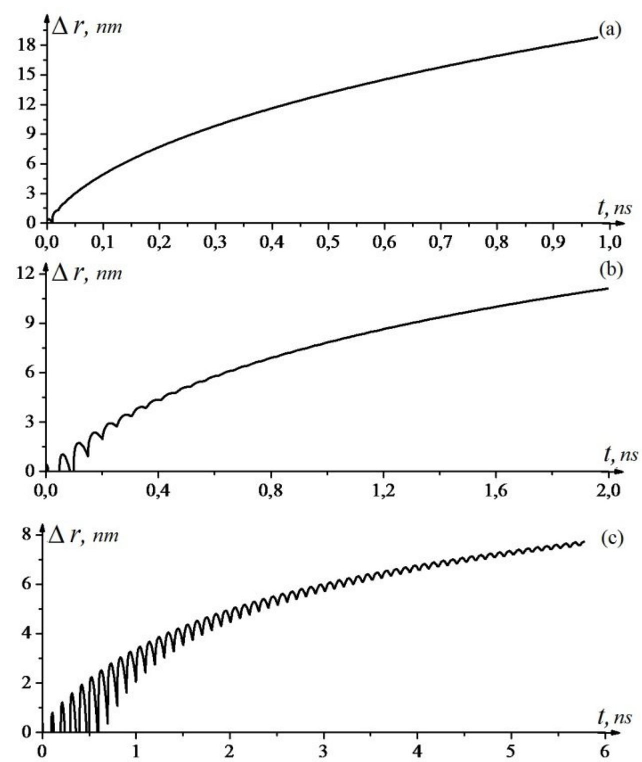


Figure 4. Time dependence of the heating up position to the temperature 44 $^{o}C$. $R$=10 $nm$, $\Delta\, t_{imp}$ = 10 $ps$ (a), 50 $ps$(b), 100 $ps$ (c).

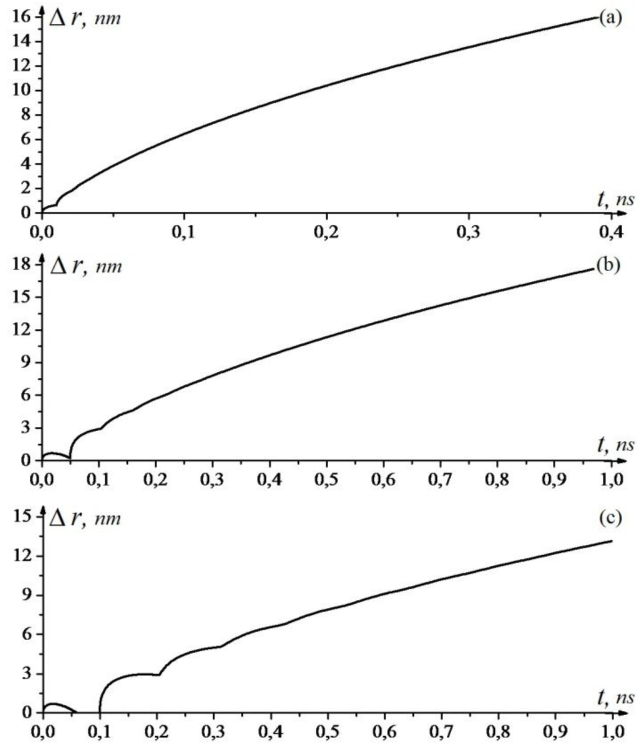


Figure 5. Time dependence of the heating up position to the temperature 44°$C$.$R$=10 *nm*, $\Delta t_{imp}$ = 10 *ps* (a), 50 *ps* (b), 100 *ps* (c).

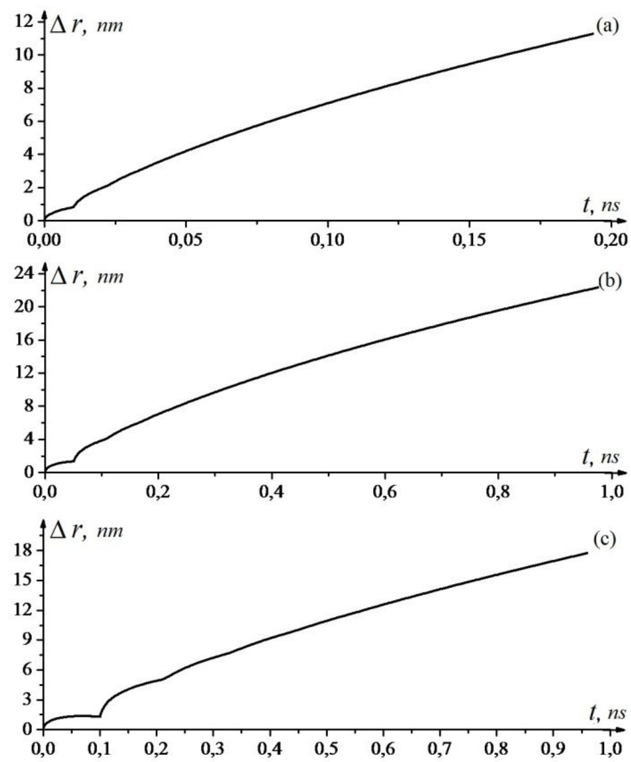


Figure 6. Time dependence of the heating up position to the temperature 44°$C$.$R$=50 *nm*, $\Delta t_{imp}$ = 10 *ps* (a), 50 *ps* (b), 100 *ps* (c).

## REFERENCES

[1] Steven, L. J., “Optical properties of biological tissues: a review”, Phys. Med. Biol. 58, R37–R61 (2013).

[2] Kolker, D. B., Starikova, M. K., Pustovalova, R. V., Karapuzikov, A. I., Kuznetsov, O. M., Karapuzikov, A. A., Kistenev, Yu. V.,“A nanosecond optical parametric oscillator in the mid-ir region with double-pass pump”, Instruments and Experimental Techniques.55, No. 2, 263-267 (2012).

[3] Kolker, D. B., Pustovalova, R. V., Starikova, M. K., Karapuzikov, A. I., Karapuzikov, A. A., Kuznetsov, O. M., Kistenev, Yu. V.,“Optical parametrical oscillator within 2.4-4.3 m pumped by compact nanosecond Nd:YAG laser”, Atmospheric and oceanic optics. 24, No.10, 910-914 (2011).

[4] Chin, L. C. L., Whelan, W. M., Vitkin, I. A., “Perturbative diffusion theory formalism for interpreting temporal light intensity changes during laser interstitial thermal therapy”, Phys. Med. Biol. 52, 1659–1674(2007).

[5] Kikoin, A. K,Kikoin, I. K.,[Molecular Physics],Mir, Moscow, 480 (1978).

[6] Samarsky, A. A., [Introduction to Theory of Difference Schemes], Nauka, Moscow, 650 (1978).

[7] Volkov, A. I.,Zharskiy, I. M.,[Bolshoykhimicheskiyspravochnik],Sovremennayashkola, Minsk, 608 (2005).