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2D EVALUATION OF THE RADIATIVE HEAT FLUX IN LIVING TISSUE DURING PHOTO THERMAL TERAPY

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Abstract. *The present paper approaches heat transfer in a class of cancer treatment which uses heat to kill cells affected by the disease. The theme has been chosen based on the great importance of this type of treatment as a tool to fight cancer. This research focuses on Photo Thermal Therapy (PPT), in which the source of heat is a laser beam. Whenever a laser beam is applied to irradiate a diseased region of a tissue, there is no way of avoiding radiation being absorbed by the surrounding healthy region. However, there are ways to partially control the temperature distribution during PTT in order to mitigate the side effects of the treatment and to avoid patient suffering. In this context, heat transfer simulations can be very useful, since they provide knowledge which can lead to procedures for a better control of temperature. In this research a two-dimensional computer code written in FORTRAN90 was devised to find the divergence of the radiative heat flux, which is provided by a Monte Carlo (MC) code. The main objective of this development is to provide a tool which can be used to investigate how the use of nanoparticles can affect the divergence of the radiative heat flux and temperature distribution in living tissues during PTT therapies.*

Keywords: *Photo Thermal Therapy, Numerical method, Nanoparticles, Divergence of the radiative heat flux.*

1. INTRODUCTION

Regarding cancer treatments, hyperthermia is one of the available options, especially for superficial tumors, and the ones too close to vital organs, which end up difficulting the treatment through conventional means. (Espinosa et. al. 2016). According to Pang and Lee (2015) hyperthermia (meaning overheating in greek) is a therapy that heat up living tissue, being broadly used to cause damage to cancer cells through the destruction of its membrane or denaturation of its proteins and DNA. The therapy is also used to make the diseased tissue more sensible to radiation and chemotherapy, allowing to reduce the doses needed in these procedures (Espinosa 2018). The heating process can be accomplished through different heat sources, like laser light, microwaves and ultra-sound (Day et. al., 2006), with all of them having in common the possibility to use nanoparticles to enhance the absorbed heat and mitigate damage to healthy tissues surrounding the tumor, as concluded by Day et al. (2006) and Dombrovsky et. al. (2011). As can be found in the bibliographic works, as those presented by Hou et. Al. (2020) and Day et. al. (2016) the process of heating by a laser is called photothermal therapy (PTT), which is characterized by collimated monochromatic radiation. The near infrared (NIR) radiation is well suited for PPT, because biological tissues are generally semitransparent to NIR wavelengths and absorption by water, hemoglobin or other blood components is low, so avoiding damage of healthy tissue (Tang et al., 2014). The NIR radiation allied with the use of nanoparticles embedded in the diseased region result in an efficient treatment in the sense that heating is concentrated on the tumor mitigating damage to the surrounding healthy tissue (Espinosa et. al., 2016). Calculating the temperature field in PTT is important to gain knowledge about the heat transfer process, which could be very useful to develop now procedures. In addition, the scientific knowledge acquired about computational simulations could be in the future employed on the development of computer programs to predict treatment results, helping to improve patient comfort during the treatment.

Computational analysis is a powerful tool for problem solving when it comes to physics and mathematics. One of the main causes that lead to differences between numerical and experimental results arise from mathematical models implemented in the computer codes to mimic the behavior of real-life phenomena as heat transfer (Patankar, 1980). In order to achieve reliable results, computational analysis leans itself onto two principles, a mathematical equation that describes the phenomenon and a numerical method to solve it, being both accurate enough to generate credible results. The method used in this research to compute radiation heat transfer was the Monte Carlo. This method features the capability of considering diverse complex physical phenomena, which can be tackled in a relatively easy way as compared to others numerical methods. As stated by Modest (2013), the name Monte Carlo is used to any statistical sampling method used to solve a mathematical problem, however, in the present paper it consists in tracking the path that a discrete bundle of energy travels through a participating medium until its absorption. According to Howell (2011), a large number of bundles must be observed to assure that the results are significant. That is a reality to any sampling method, the fewer samples are observed the greater is the possibility to be observing samples that do not represent the behavior of the average population, leading to error in the predictions.

The calculation of the living tissue temperature field in the hyperthermia treatment is done through the bioheat equation proposed by Pennes (1948). This equation considers the heat conduction, heat removal due to blood perfusion and a source term representing body heat generation (Bruno et. al., 2016). In addition, other source terms can be added, including one to take into account the divergence of the radiative heat flux, representing the rate of absorption per unit of volume of the laser radiation by the tissue, which is the focus of this work. As mentioned, the radiative heat transfer solution was obtained with the Monte Carlo method, which was implemented in a FORTRAN90 code.

The results presented in this research are going to be used in future developments in order to properly evaluate the two-dimensional temperature field generated in hyperthermia conditions. For that, this research is a step for the 2d evaluation of heat transfer in living tissue, turning this temperature evaluation an easy process for different configurations for hyperthermia treatment. The evaluation is going to be based off of a FORTRAN90 code to solve the bioheat equation.

2. RADIATION TRANSFER EQUATION SOLUTION

The radiation transfer equation (RTE) acknowledge that some phenomena occur during the process inside the participating media, in the present case living tissue, thus interfering in the radiative intensity in a specific direction. Equation (1) considers the radiation transfer with none of the variables being time dependent (Quasi-steady form).

$$\frac{dI_\lambda}{ds} = \kappa_\lambda I_{b,\lambda} - \beta_\lambda I_\lambda + \frac{\sigma_{sc,\lambda}}{4\pi}\int_{\Omega_i=0}^{4\pi} \Phi_\lambda(\Omega,\Omega_i) I_{\lambda,i}(\Omega_i)d\Omega_i \quad (1)$$

In the above equation, the subscript Lambda (λ) means spectral values, therefore, the terms assigned with it are wavelength dependent. The Right-hand side of the equation represents the variation of the radiative intensity (I_λ) through the $\hat{\mathbf{s}}$ direction. On the left-hand side, the first term accounts for the intensity augmentation by emission, being κ_λ and $I_{b,\lambda}$ respectively the coefficient of absorption of the media and black body spectral intensity. The second term stands for attenuation of the intensity due to scattering away from the $\hat{\mathbf{s}}$ direction and absorption, with β_λ representing the extinction coefficient, which is the sum of the scattering and absorption coefficients. At last, there is the portion that represents scattering from all directions inside $\hat{\mathbf{s}}$. $I_{\lambda,i}$ is the intensity of the radiation coming from the incident solid angle Ω_i around the direction $\hat{\mathbf{s}}_i$ that has part of it scattered into Ω around $\hat{\mathbf{s}}$. How much of it goes under this process is given by the fraction $\Phi_\lambda(\Omega, \Omega_i)d\Omega_i/4\pi$, being Φ_λ the scattering phase function, that gives the probability of having the incident intensity($I_{\lambda,i}$) scattering into Ω. In normal conditions, for each solid angle there is a different value for this function, in a way that the integral is needed to sum up the contribution to the augmentation by scattering coming from all the incident solid angles. Some considerations have been done in order to simplify the equation, first of all the laser emits monochromatic radiation, which means that none of the terms are going to depend on the wavelength. The second consideration is that the scattering is isotropic, leading to $\Phi_\lambda = 1$. The last consideration is that for the temperature of operation in hyperthermia, the medium emission is negligible face to the radiation coming from the laser source. The Equation (2) is the simplified form of RQE.

$$\frac{dI}{ds} = -\beta I + \frac{\sigma_{sc}}{4\pi}\int_{\Omega_i=0}^{4\pi} I_{\lambda,i}(\Omega_i)d\Omega_i \quad (2)$$

According to Modest (2013) when a participating medium is being penetrated by collimated radiation, the intensity inside it has two components, the collimated one originating from the portion that is not absorbed or scattered away from the direction of consideration $\hat{\mathbf{s}}$ and the diffuse one, that originates from the medium emission and intensity scattered away from the collimated rays. Modest (2013) also states that is possible to utilize Eq. (2) to solve problem with collimated radiation utilizing a source term to account for the collimated portion. Equation 3 represents the source term considering $\Phi_\lambda = 1$.

$$S_c = \frac{1}{4\pi}(1-\rho)q_o e^{(-\int_0^s \beta ds')} \quad (3)$$

The final RTE is represented by Eq. 4

$$\frac{dI}{ds} = -\beta I + \frac{\sigma_{sc}}{4\pi}\int_{\Omega_i=0}^{4\pi} I_{\lambda,i}(\Omega_i)d\Omega_i + \frac{1}{4\pi}(1-\rho)q_o e^{(-\int_0^s \beta ds')} \quad (4)$$

The complete RTE for the present case presents some new variable as ρ, q_0 and ds' which represent respectively the reflectivity of the boundary that is being irradiated, the laser power and the length of the path that the collimated radiation travels through the medium.

The boundary condition for the Eq. (4) considering that there is not emission from the medium and its boundaries and that the boundaries are reflecting diffusely is represented by Eq. (5)

$$I_w = \frac{1}{4\pi}(1-\rho)q_o + \frac{\rho}{\pi}\int_{\mathrm{n*s}<0} I_i(\Omega_i)|n.s|d\Omega_i \tag{5}$$

The first term in the right-hand side stands for the radiation that is capable of penetrating the boundary while the second one is due to reflection in the boundary making the intensity in the $\hat{\mathbf{s}}$ direction decrease.

Regarding the Solution of the RTE, it is necessary to find the radiative heat flux that is crossing a specific area inside the medium, this has been done on the research through the use of the Monte Carlo numerical method.

3. MONTE CARLO METHOD

Radiation heat transfer problems most of the time require the use of numerical methods due to its complexity, given that the governing equations are integrals (Modest, 2013). The RTE in its core is a complex equation that depends on many factors such as the importance of the absorption, emission and scattering phenomena and direction and wavelength dependence of the properties. Considering that, depending on the conditions under consideration, a problem involving participating media could be computationally expensive enough to make solving it through conventional methods impractical, turning Monte Carlo into the most viable option for complex cases (Modest, 2013).

As states Modest (2013) Monte Carlo is a name attributed to any statistical sampling method applied to mathematical problems, but for thermal radiation cases the method consists in tracing the path that a group of randomly selected energy bundles travel through a medium until it is absorbed. This random selection is done through a specific formula called cumulative distribution function, assuring the selection is statically meaningful. Before diving into the explanation of the importance of this function, there must be a background construction for better understanding.

Imagine a phenomenon that depends on a specific characteristic, for example, the emission of radiation that depends on the wavelength and direction, and each dependence can be described by a specific function. Assuming that the emission dependence on wavelength is given by the equation f(λ), to Howell (2011) it can be called the frequency function, which gives the emission frequency of occurrence on a specific wavelength according to the real physical process. Dividing this equation by the total area under it, the probability density function is going to be obtained, representing the average distribution of emission in each wavelength. Equation 6 is the representation of this function on the hypothetical case under consideration.

$$P(\lambda) = \frac{f(\lambda)}{\int_0^\lambda f(\lambda)d\lambda} \tag{6}$$

The interval 0 to λ represents the total range of wavelength emitted. To obtain the accurate formula to choose a random number from the Eq. (6) must be integrated over all wavelengths, giving a cumulative distribution function, which can only have values between 0 and 1. Equation 7 denotes this new function

$$R(\lambda) = \int_{-\infty}^{\lambda} P(\lambda)d\lambda \tag{7}$$

Inverting the R(λ) equation to obtain λ(R), it is possible to randomly choose a number between 0 and 1 and having a correspondent λ value. Through that, it is possible to acquire the wavelength of an energy bundle being emitted, and assuring its statistical meaning. Even though wavelength dependence was used as an example, In the present paper, the Monte Carlo method has not been used to find wavelength of emission because the radiation is monochromatic.

4. BIOHEAT EQUATION

The equation created by Pennes (1948) is used to calculate the temperature in biological tissue, and is used more specifically on the ones under hyperthermia treatment. The formulation considers that temperature is space and time dependent, and when thermal conductivity is not variable the configuration is as showed by Eq. (8).

$$\rho c_p \frac{\partial T}{\partial t} = k\nabla^2 T + \rho_b c_b v_b (T_b - T) + \nabla q_{rad} + q_m \tag{8}$$

The left-hand side of the equation stands for variation of energy inside of the control volume, being ρ and c_p respectively the tissue density and specific heat. T is the temperature that's being calculated, t is time, k is thermal conductivity, which may vary with the layer of tissue the conduction is occurring. The second term on the right-side accounts for heat transfer through blood perfusion, being ρ_b, c_b, v_b and T_b respectively blood related density, specific heat, perfusion rate and temperature. The second to last term represents the divergent of the radiative heat flux calculated in this research. At last, there is the term representing the body heat generation.

5. RESULTS

The problem situation solved in this study revolves around calculating the bidimensional divergence of the radiative heat flux inside a cylinder with radius and length of 10 millimeters (mm). The calculations have been performed considering a fat layer tissue with and without embedded nanoparticles (gold nanoshells), to represent the difference that nanoparticles may have on the energy absorption.

The first case considers a plain fat layer receiving radiation from a laser source with a beam radius of 5 mm, incident over the left side and centered with the radius. It has been utilized the same laser power as Dombrovsky et. al. (2011) of 20 kW/m². The medium in consideration is gray and diffuse, that is, the absorption and scattering coefficients do not depend on wavelength or direction. All the characteristics of the fat layer are listed in the Table 1.

Table 1 – Values of fat layer characteristics (Dombrovsky et. al. 2011)

Characteristic	Value
ρ_t (kg/m³)	1000
c_t (J/(kg K)	3674
K_t (W/(m K))	0,185
q_m (W/m³)	368,3
α (1/m)	10
σ_{tr} (1/m)	400

Figure 1 is the divergence of the radiative heat flux 2d graphic.

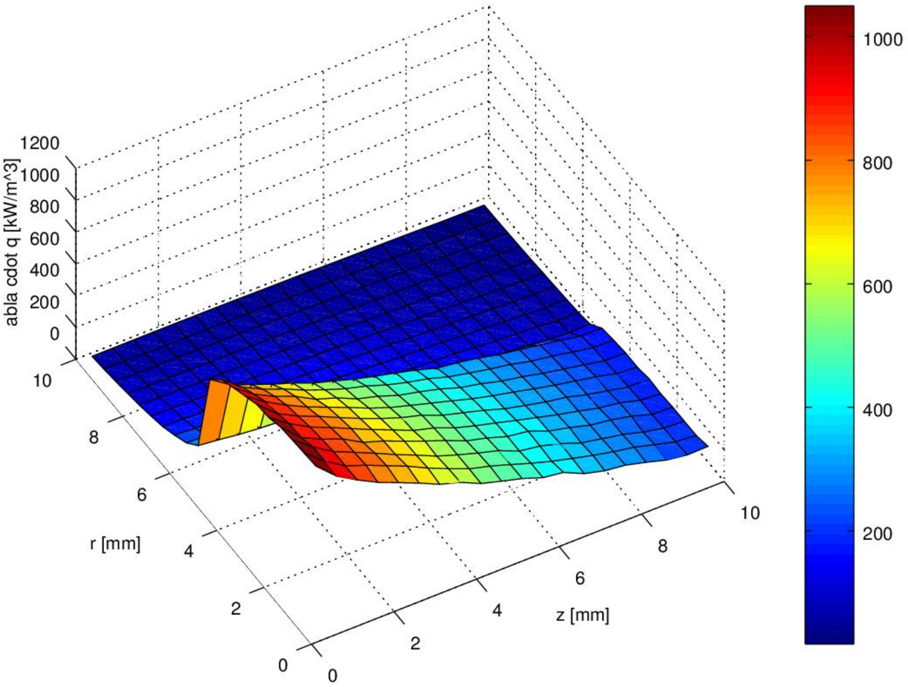

Figure 1. 2D divergence of the radiative heat flux without nanoparticles

Figure 1 denotes a quadratic behavior of the divergence with depth (Z coordinate). This behavior comes from the medium being composed of the same material, thus having absorption and scattering coefficients constant at all locations. According to Modest (2013) the absorption coefficient is proportional to the percentage of the irradiation hitting a surface that is being absorbed, thus, considering that the grid is uniform, the same percentage must be absorbed every step at the grid. If the energy bundles decrease a little every volume it goes through, the percentage absorbed is calculated over a smaller amount, making the absorption decrease with depth (Z coordinate).

As can be noted on Fig. 1, the divergence has a behavior that roughly repeats itself into the r direction (in a specific range of r), varying only with the z direction. With the resources available, it has been possible to generate a unidimensional temperature field. It is possible to conclude that the field is an approximate representation for all z points (0 to 10 mm) and r inside the range of $0 < r < 6$. Figure 2 represents exactly this relation.

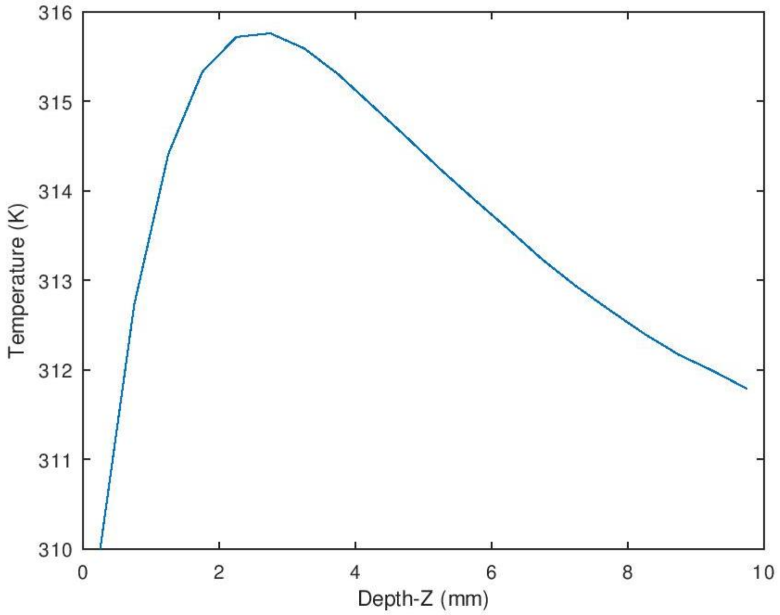

Figure 2. 1D temperature field without nanoparticles

To generate these results seen in Fig. 2, it has been used the same boundary conditions as Bruno et. Al. (2011), which are, fixed temperature of 37 ºC (310 K) on the left boundary and a convective heat transfer on the right one, with a coefficient of h = 50 W/(m²K). Besides that, the initial temperature values have been also set to 37 ºC (310 K). The blood characteristic needed for perfusion are ρ_b = 1060 kg/m³, c_b = 3770 J/(kg K), T_b = 37 ºC (310 K) and v_b = 1 m/s. The evaluation of the temperature is transient, so there must have an entrance data of test duration time, which for this case is 35 s.

Analyzing Fig. 2 it is possible to conclude that without the nanoparticles, the absorption does not seem to be significant, considering the laser power of 20 kW/m³ and the maximum temperature difference slightly under 6°C, leading to a maximum temperature of 315.76 K (42.76 °C). According to Spirou et. al. (2018), the exposition over one hour under this temperature cause hyperthermia damage, but considering that the tissue under analysis is exclusively fat, the high temperature is not an error, because cancerous tissues have a higher absorption coefficient and conduct less heat (Dombrovsky et. al 2011), that is, if a cancerous tissue were included in the analysis the temperature of the fat tissue would not be up to that hyperthermia region. Other thing to notice is how the temperature field does not have an abrupt peak, which would represent a region with far more stored energy.

The second problem revolves around calculating the divergence in the same fat layer, but only now there is nanoparticles (gold nano shells) embedded in the region with coordinates R = 3mm and Z(depth) = 5mm, centered in the radius, initiating in 3mm of depth from the left side. To calculate the characteristics of the nanoparticle embedded part of the tissue there are Eq. 9 and Eq.10, which give the values of the absorption and scattering coefficients respectively.

$$\alpha = \alpha_t + 0.75 f_v \frac{Q_a}{r} \tag{9}$$

$$\sigma_{sc} = \sigma_{sc,t} + 0.75 f_v \frac{Q_s}{r} \tag{10}$$

In the equations, α and σsc are respectively the absorption and scattering coefficients without nanoparticles, while Qa, Qs and f_v stand for dimensionless efficiency factors for absorption and scattering and the volume fraction of nanoparticles in relation to the tissue it is embedded in. Values have been taken from Dombrovsky et. al. (2011), which utilizes nanoparticles with a radius of 20×10^{-9} meters(m), efficiency factors Qa and Qs of respectively 7.9 and 1.053 and $f_v = 10^{-5}$. Utilizing Eq 6. And Eq. 7, it is possible to find that in the nanoparticle embedded tissue, the values of the absorption and scattering coefficients are respectively 2982.5 m^{-1} and 594.875 m^{-1}. With all the information needed it has been possible to calculate the divergence. The results obtained as displayed in Fig. 3.

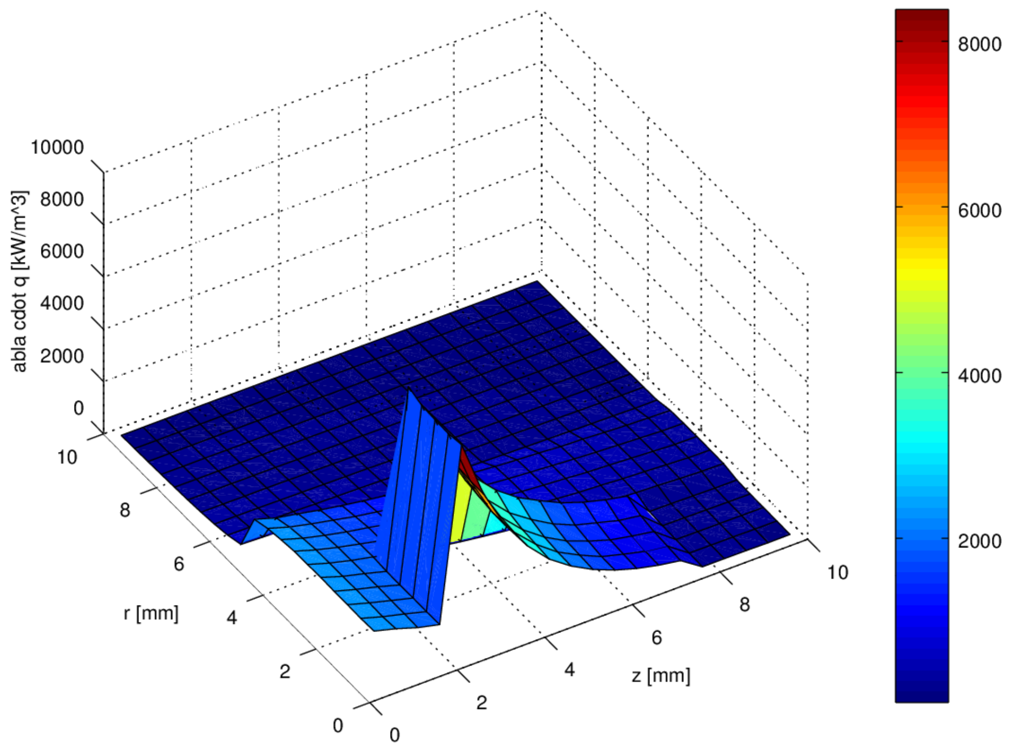

Figure 3. 2D divergence of the radiative heat flux with nanoparticles

In the region where the nanoparticles are embedded it is possible to notice an abrupt peak on the divergence with a linear behavior starting approximately from z = 2 mm and a logarithmic behavior a short distance after. Figure 3 shows the difference that nanoparticles bring to the absorption of the tissues, while without the nanoparticles the peak of stored energy was slightly over 1000 kW/m³, here there is an 8000 kW/m³ peak located in the nanoparticle region.

Once more, there has been generated a unidimensional graphic for the temperature field, considering that the divergence does not change its behavior over the range of $0 < r < 3$ being only z dependent. Besides the changed data due to the presence of nanoparticles, everything else has been reused for this second evaluation.

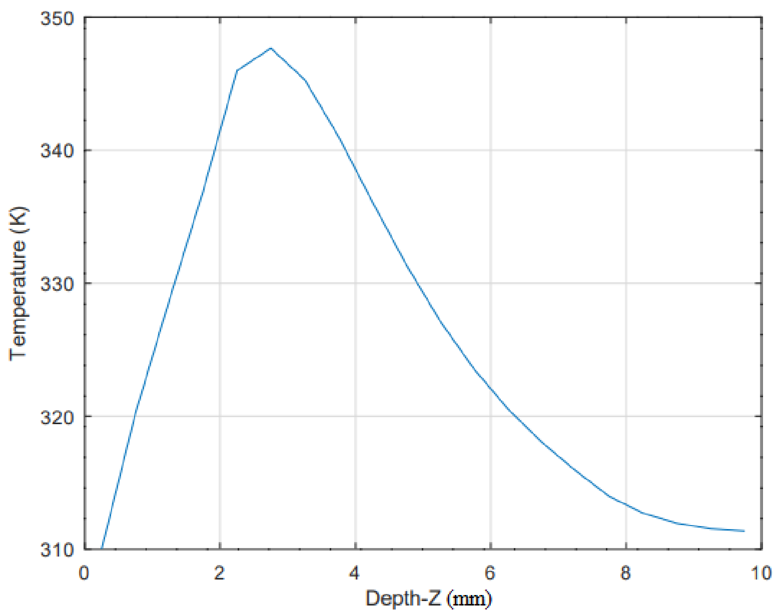

Figure 4. 1D temperature field without nanoparticles

Figure 4 allow to conclude that with the nanoparticles the absorption, in the section where it is located, increases vastly, with a maximum temperature difference that is slightly under 40 °C. Besides that, the temperature field has an abrupt peak where the nanoparticles are located, meaning that the higher temperatures, when compared to the tissue without the particles, on the surroundings of the temperature peak are only due to the inevitable heat conduction. It is important to notice that a peak temperature of 347.66 K (74.66 °C) is not a practical temperature to put diseased tissue under in hyperthermia treatment, so the objective of these temperature fields is to showcase the increase of energy storage on living tissue due to the use of nanoparticles.

6. CONCLUSION

The Monte Carlo method is the ideal path to solve complex cases of radiative heat transfer, just as obtaining the two-dimensional radiative heat flux divergence. This variable is such an important characteristic regarding the hyperthermia treatment, because it shows how much energy is being stored inside the living tissue and considering that temperature control is crucial to avoid healthy tissue damage, the process of obtaining the divergence is crucial to a successful hyperthermia treatment. As observed in the results, the use of nano particles allied to near infrared radiation to enhance absorption is effective enough to make the temperature in the area where the particles are embedded rise, affecting the surrounding areas only by the heat conduction.

In future developments there is going to be used a two-dimensional FORTRAN90 code to compute the divergence of the radiative heat flux and generate the temperature field. These calculations are reached through the solution of the bioheat equation, developing through that an easy solution for temperature assessment in hyperthermia.

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