Thermal Ablation of Tumour with Biocompatible Gold Nanorods: A Numerical Study

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Abstract

Cancer is a life-threatening disease in which a lump is formed due to the growth of cells which starts damaging the healthy cells of the body. Removing the lump with hyperthermia is a technique where the lump is heated in the range of 50-60 °C with an electromagnetic wave (EMW). The absorptivity of the lump (tumour) is very low, due to which it cannot absorb the irradiation alone. To absorb the absorptivity of EMW nanoparticles have been added to the tumour, then nanoparticles absorb the irradiation, get heated and transfer the heat to the tumour. In the present study, gold nanorods have been used for absorption purposes, having a diameter of 25 nm and aspect ratios of 1.5, 3.5 and 5.5. The results show that with these aspect ratios broadband spectrum (400-1300 nm) has been covered. The volume fraction of the nanoparticles plays a crucial role in the ablation of the tumour at an optimum volume fraction. The study shows that the absorption coefficient of 40 cm-1 is an optimum value where the maximum temperature of the tumour has been found. Furthermore, the irradiation intensity and irradiation time also play an important role in the ablation of the tumour. In the current manuscript, numerically the effect of irradiation intensity, irradiation time, and volume fraction has been studied.

Keywords: Cardiovascular Fitness Recommendations, personalised recommendations.

1. INTRODUCTION

Cancer is a life-threatening disease in which a lump is formed due to the growth of cells which starts damaging the healthy cells of the body. There are certain techniques (chemotherapy, laser ablation, electroporation, surgery, and radiation therapy) used for the treatment of cancer (Jamil and Ng, 2013). These conventional techniques have limitations for example in cases when the tumour is deep inside the body and out of reach or in many such scenarios these techniques might be very cumbersome (Ashikbayeva *et al.*, 2019). Hyperthermia or thermal ablation technique uses laser or electromagnetic waves to damage the tumour by heating it for a certain period. The electromagnetic waves are incident in the near-infrared region. The ablation temperature in the range of 50-60 °C is sufficient for the complete mutilation of the tumour (Ahmed *et al.*, 2011). The tissue is damaged due to low levels of oxygen, nutrients and pH level. The hyperthermia causes focal hyperthermic injury to the ablated cell, which affects the tumour microenvironment and damages the cell at the membrane and subcellular level. This technique can be applied to the local cell and the whole body. It has been mentioned that the hyperthermia technique alone is not enough to replace one of the established therapy modalities when they have been applied alone, but, the hyperthermia technique is without any doubt enhances the effect of cell killing drug. The

main benefit of hyperthermia is that it is flexible, less expensive and involves less invasiveness as compared to other conventional cancer treatment methods (Carrafiello *et al.*, 2008).

The drawback of this technique is that the absorptivity of the tissue is very less which results in low-temperature rise, thus very low heating takes place. A more promising hyperthermia technique involves the usage of nanoparticles which enhances the optical properties. When the electromagnetic wave (in the range of near-infrared wavelength) is incident on nanoparticles embedded in the tumour, the nanoparticles absorb the irradiation, get heated and help in damaging the breast tumour which is surrounded by healthy tissue as shown in Fig. 1. This method selectively destructs the tumour and the localized hyperthermia provides better-targeted treatment (Manthe *et al.*, 2010).

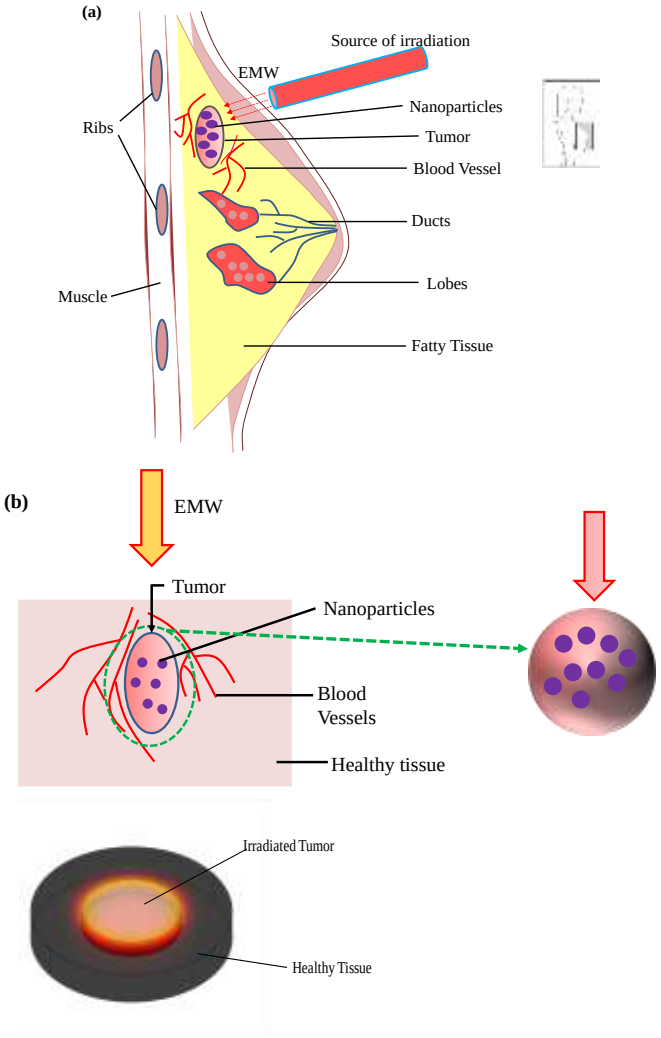

Figure 1 (a) Schematic of the breast tumour irradiated with electromagnetic wave (EMW) and (b) the description of tumour surrounded by blood vessels and healthy tissue.

The nanoparticles used in the hyperthermia treatment mostly are iron oxide, doped iron oxide, superparamagnetic iron oxide, carbon nanotubes and various polymer-based technologies are used (van Landeghem *et al.*, 2009; Lee *et al.*, 2011; Kaur *et al.*, 2016). For the thermal ablation of the tumour, as the optical properties of the nanoparticles play a crucial role, so for the hyperthermia biocompatible gold nanoparticles have been used (Monga *et al.*, 2020). These nanoparticles have been used to achieve the thermal ablation temperature for denaturation of tissue proteins and apoptosis is preferred. The main aim of the present study is to predict the effect of irradiation, irradiation time and volume fraction of the nanoparticles of the ablation of the tumour.

2. NUMERICAL MODELLING OF NANOPARTICLES ASSISTED TUMOUR

2.1 Optical properties of nanoparticles

In the ablation of the tumour, the nanoparticles and their optical properties play an important role. The literature suggests that gold nanorods are more beneficial to use than nanospheres, due to which gold nanorods have been considered in this study. The metallic nanorods show plasmonic peaks at different wavelengths (depending on the diameter and the aspect ratio), due to which the absorption at the plasmonic wavelength happens. These nanorods show two plasmonic peaks, radially and axially (i.e. it has transverse and longitudinal oscillation). In the current study, for the calculation of optical coefficients, Mie scattering has been used. As $\lambda > 10D$, the nanoparticles experience polarization (Ξ) and the induced polarization can be evaluated as

$$\Xi = 4\pi D^2 L\left(\frac{\varepsilon_{gold}-\varepsilon_{tissue}}{3\varsigma_i\left(\varepsilon_{gold}-\varepsilon_{tissue}\right)+3\varepsilon_{tissue}}\right) \tag{1}$$

where D is the diameter of the nanorod, L is the length of the nanorod, $\varepsilon_{\text{gold}}$ is the dielectric constant for gold, $\varepsilon_{\text{tissue}}$ is the dielectric constant of tissue and ς is the geometric factor, where i = 1, 2 and 3.

The geometric factor (ς) is calculated by using equation 2

$$\varsigma = \frac{1-f2}{f2}\left[\frac{1}{2f}\ln\left(\frac{1+f}{1-f}\right)-1\right]$$
$$\text{where } f=\left(1-\frac{D}{L}\right)^{0.5}, \varsigma_2=\varsigma_3=\frac{1-\varsigma_1}{2} \tag{2}$$

Further, the absorption and scattering coefficients are calculated by using equation 3

$$\alpha_{abs} = \frac{2\pi\varphi}{3\lambda V_{np}} img\left(\Xi_1+\Xi_2+\Xi_3\right)$$
$$s_{scat} = \frac{16\pi^3\phi}{18\lambda 4V_{np}}\left(\left|\Xi_1\right|^2+\left|\Xi_2\right|^2+\left|\Xi_3\right|^2\right) \tag{3}$$

where ϕ is the volume fraction, V_{np} is the volume of nanorods, λ incident wavelength.

2.2 Spatial temperature distribution in the tumour

As we know that the bare tumour is unable to absorb the irradiation due to less absorptivity. For a bare tissue the absorption and scattering values are 0.062 mm^{-1} @ 725-325 nm and 0.95 mm^{-1} @ 925 nm respectively (Soni *et al.*, 2015). Further, the scattering and absorption values for the nanorod are around 10 mm^{-1} and 0.375 mm^{-1} respectively. These results show that with the gold nanorods, absorption is more dominant than the scattering. So, in the absorption dominating media, the attenuation of the irradiation is found by the Beer Lambert's law, which states that the extinction of the irradiation happens exponentially in the absorption dominated media and mathematically it is given by equation 4

$$I = I_o \exp\left(-K_{e\lambda}.Z\right) \tag{4}$$

where I_o is the incident radiation, $K_{e\lambda}$ is the spectral extinction coefficient and Z is the depth of the tumour. The absorption of irradiation by the nanorods generates the temperature rise and thus damages the tissue. The initial temperature of the tumour is 35 °C and the outer boundary of the healthy tissue has been considered isothermal. The spatial temperature rise in the tissue has been evaluated by Penne's equation, which is represented by equation 5.

$$\rho_t C_t \frac{\partial T\left(r,z,t\right)}{\partial t} = K_t\left(\nabla^2 T\left(r,z,t\right)\right) + w_b \rho_b C_b\left(T_c - T\left(r,z,t\right)\right) + Q_{met} + Q_{ab} \tag{5}$$

where Q_{met} is heat generation due to metabolism of the body, Q_{ab} is the amount of heat absorbed by nanoparticles due to intensity attenuation within the tissue, T (r,z,t) is the tissue temperature as a function of r,z co-ordinates, T_c is the core body temperature, C_t is the specific heat of the tissue, C_b is the specific heat of the blood, ρ_t is the density of the tissue and ρ_b is the density of the blood.

The thermophysical properties of the healthy tissue and the tumour are presented in table 1.

Table 1. Thermophysical properties of healthy tissue

For Healthy tissue	
Thermal conductivity (K_t)	0.5 $W.m^{-1}.K^{-1}$
Density (ρ_t)	1000 $kg.m^{-3}$
Heat capacity (C_{pt})	4200 $J.kg^{-1}K^{-1}$
Absorption coefficient (α_t)	0.02 m^{-1}
Arterial blood temperature	37 °C
Heat capacity of blood (C_{pb})	4200 $J.kg^{-1}K^{-1}$
Blood perfusion rate (s^{-1})	1×10^{-3}
Density of blood (ρ_b)	1000 $kg.m^{-3}$

Table 2. Thermophysical properties of tumour

For Tumour	
Thermal conductivity (K_t)	0.55 $W.m^{-1}.K^{-1}$
Density (ρ_t)	1100 $kg.m^{-3}$
Heat capacity (C_{pt})	4200 $J.kg^{-1}K^{-1}$
Absorption coefficient (α_t)	0.06 m^{-1}
Blood perfusion rate (s^{-1})	9.1×10^{-3}
Density of blood (ρ_b)	1000 $kg.m^{-3}$

2.3 Skin Tumour and distribution of nanoparticles

The skin tumour case in the 3D module has been selected for the study. For the study, both healthy tissue and tumour have been considered cylindrical (as shown in figure 2).

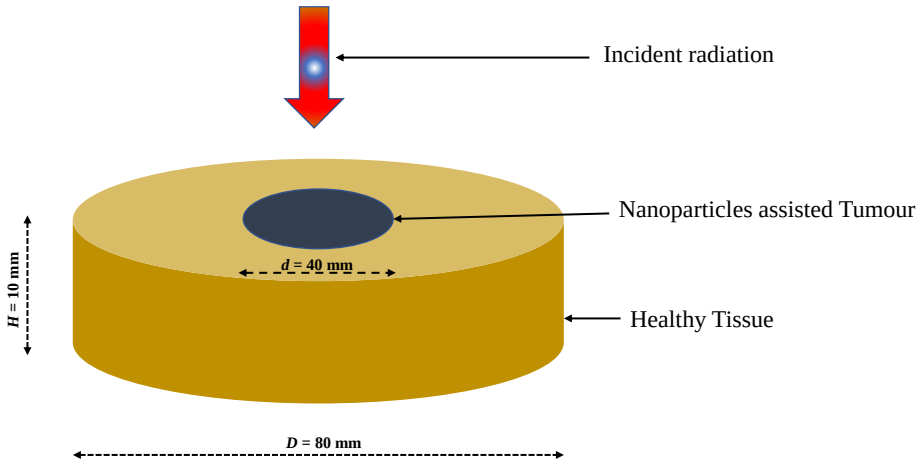

Figure 2. Schematic of the healthy tissue and the tumour irradiated with electromagnetic waves.

For the numerical analysis, it has been assumed that the tumour has a diameter of 40 mm and the height of the tumour is 5 mm. This tumour is surrounded by healthy tissue having a diameter of 80 mm and a height is 10 mm. Further, it has been assumed that gold nanorods have impinged on the tissue. The irradiation is normal to the tumour and gets absorbed by the nanoparticles.

3. RESULTS AND DISCUSSIONS

3.1 Optical properties of nanorods

The absorption coefficient for the gold nanorods has been shown in Fig. 3. For the absorption coefficient, a diameter of 25 nm and aspect ratio (AR) of 1.5, 3.5 and 5.5 has been considered. To understand the effect of volume fraction, two different volume fractions have

been considered i.e. 0.001 and 0.002% respectively (see Fig. 3a and 3b). From these figures, we found that the absorption increases with the increase of volume fraction. Further, the aspect ratio shows there are three peaks, and the highest peak has been achieved with AR of 3.5. At AR 3.5, the absorption peak is at the wavelength of 725 nm and this maximum peak is because of the local surface plasmon resonance (LSPR) effect. To ablate the tumour, the incident radiation will be at the wavelength of 725 nm and maximum irradiation will get absorbed by the nanoparticles. Maximum absorption results in more heating and thus ablation of the tumour takes place.

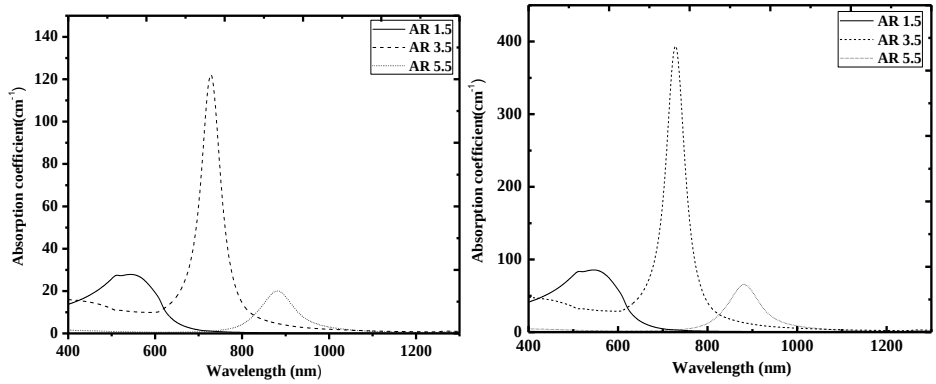

Figure 3. Optical signature of the gold nanorods at different aspect ratio (a) for volume fraction of 0.001% and (b) 0.002%.

3.2 Effect of volume fraction on the ablation of tumour

Figure 4 shows the effect of volume fraction on the temperature rise of the tumour. It shows that with the increase of absorption coefficient (which depends on the volume fraction), the average temperature in the tumour increases, reaches a stagnant point and with further increase of absorption coefficient, the temperature starts decreasing. This is because, at a low volume fraction, the whole irradiation is not absorbed by the nanorods. On the other hand, at a higher volume fraction, the irradiation is absorbed by nanorods in the top layer, thus the irradiation does not reach the whole volume of the tumour, thus there will be no complete damage to the tumour. Due to this fact, the optimum volume fraction of the nanoparticles needs to be added to the tumour for complete ablation of the tumour.

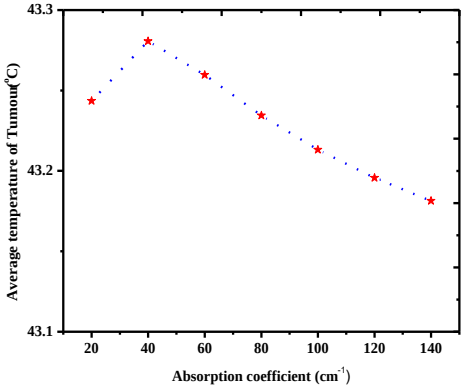

Figure 4. Effect of absorption coefficient on the average temperature of the Tumor

3.3 Effect of irradiation time and irradiation intensity

The effect of irradiation intensity and irradiation time on the damage of the tumour has been shown in Fig. 5. From figure 5 it can be seen that the average temperature rise of the tumour directly depends on the irradiation intensity. So, according to the size of the tumour, the intensity needs to select. Further, the ablation temperature also increases with irradiation time. As we know, for complete damage to the tumour, the temperature should be in the range of 50-60 ºC. So, this temperature can be achieved with an irradiation intensity of 5000 Wm-2 (see Figures 6a and 6b). Further, to illustrate the effect of irradiation intensity on the damage to the tumour, isosurfaces have been shown in figure 6b, which confirms that the tumour ablated with the irradiation time. Further, care is needed when selecting the irradiation intensity because more irradiation time and irradiation intensity damage the healthy tissue.

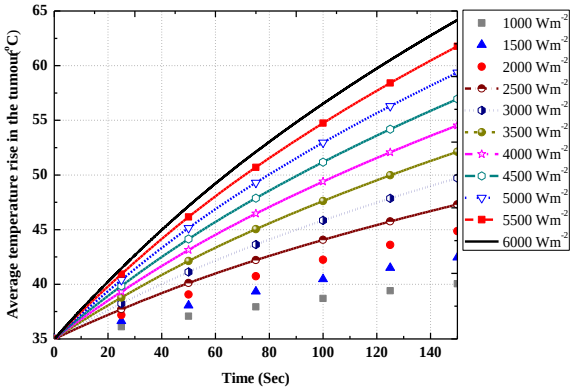

Figure 5. Effect of irradiation intensity on the temperature rise in the tumour

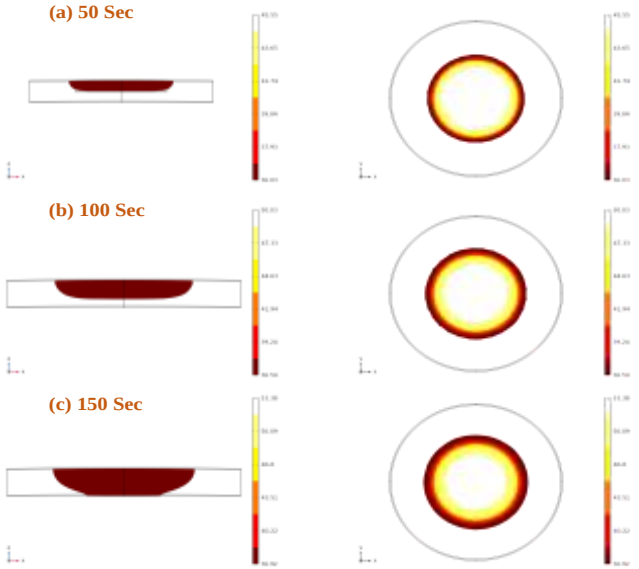

Figure 6(a)

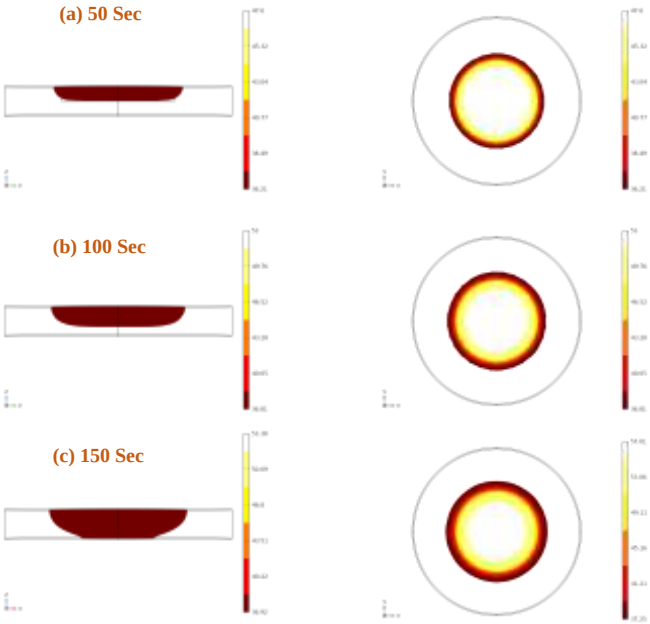

Figure 6(b)

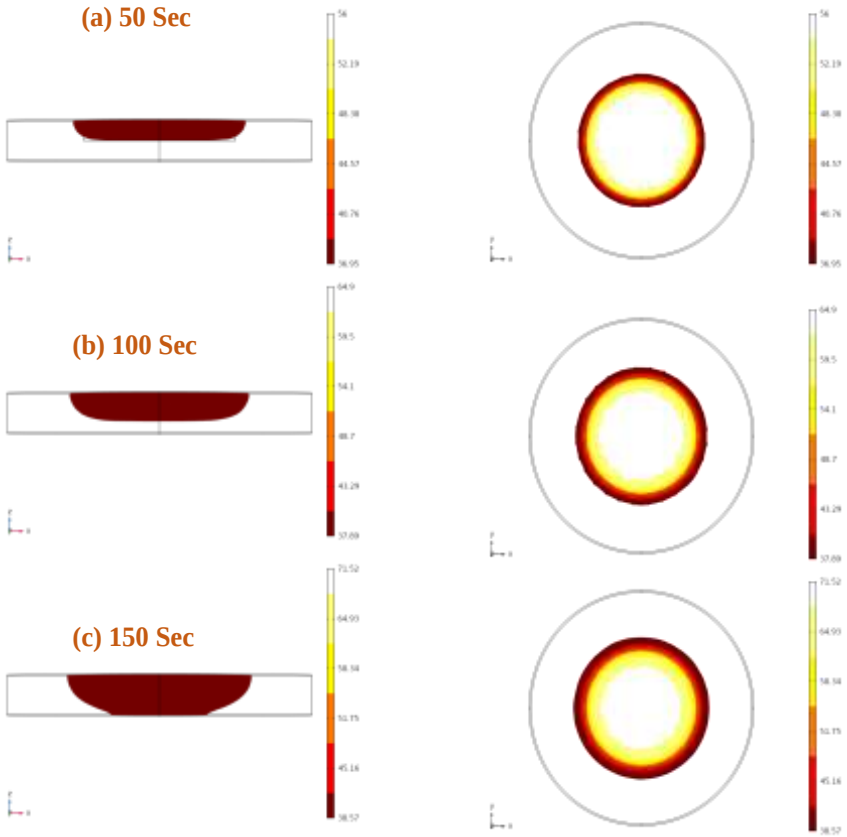

Figure 6(c)

Figure 6. Temperature contours for the ablation of the tumour at different intensities (a) 2500 Wm^{-2} (b) 3000 Wm^{-2} and (c) 5000 Wm^{-2}

3.4 Effect of temperature along the diameter of the tumor

The temperature variation along the radius of the tumour has been shown in Fig. 3.4. From the figure, it can be seen that the temperature is maximum in the centre of the tissue and decreases at the outer periphery. This is because the flowing blood in the healthy tissue near the tumour takes away the heat, which cools it down. Further, the same trend has been seen at different depths along with the tumour.

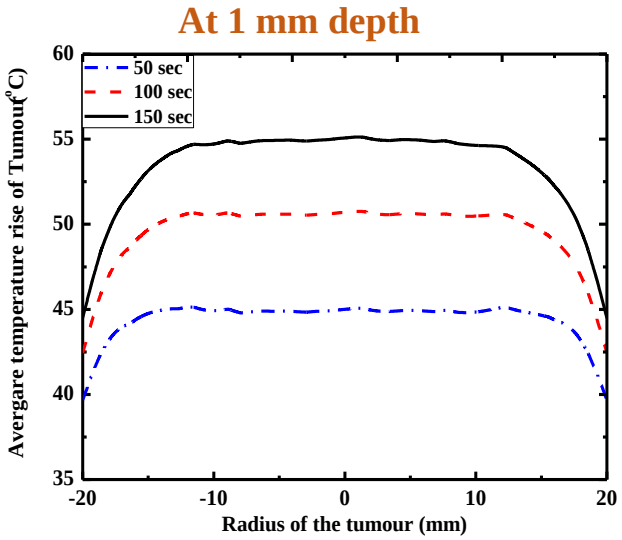

Figure 7(c)

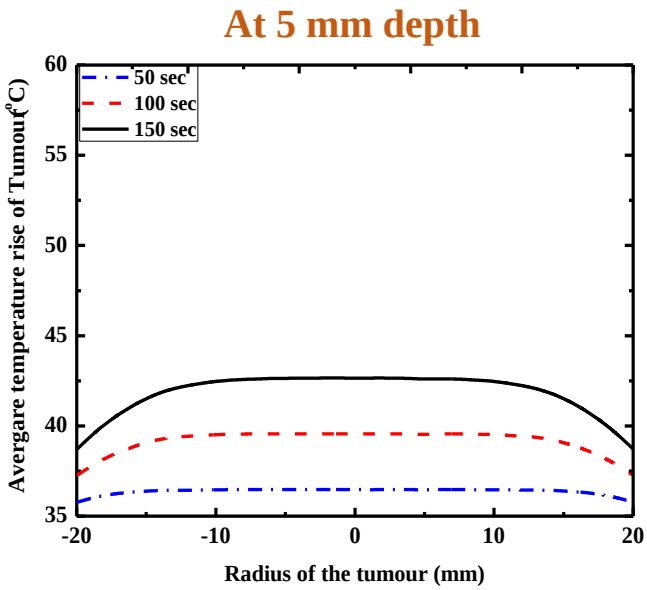

Figure 7(b)

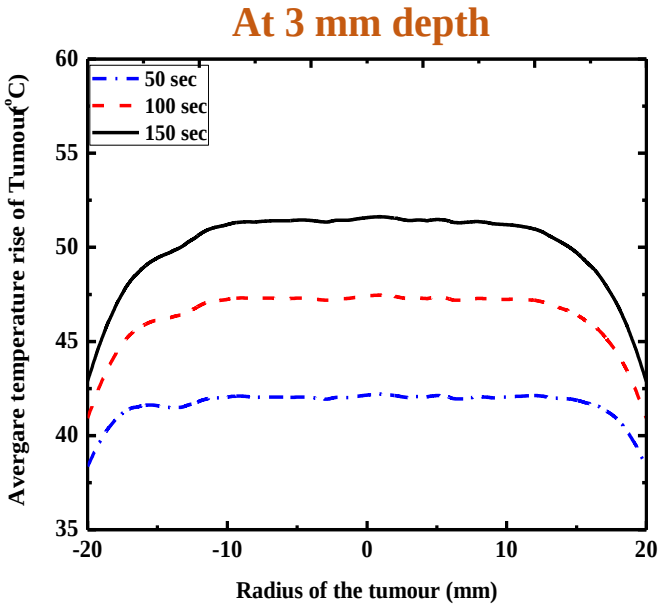

Figure 7(c)

Figure 7. The temperature rise in the tumour along the radius of the tumour at different depths (a) 1 mm (b) 3 mm and (c) 5 mm

4. CONCLUSION

From the results, it has been found that for the damage to the tumour, the temperature required is around 50-60 ºC. The ablation temperature depends on various factors like volume fraction of the nanoparticles, irradiation time and irradiation intensity. From the study, it has been found that the absorption coefficient depends on the volume fraction and it increases with the increase of volume fraction. Further, an intensity of 5000 Wm-2 is required for ablation of the tumour in 50-60 sec. The temperature in the outer periphery of the tumour is less than the inner part because due to blood perfusion, the heat is lost from the tumour to the healthy tissue. It is very important to maintain the optimum irradiation time and irradiation intensity, otherwise, it can damage the healthy tissue.

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Biographies

Dr. Vishal Bhalla holds B.Tech degree in Mechanical Engineering from P.T.U, M.E degree in Thermal Engineering from Thapar University, and a PhD in Mechanical Engineering from IIT Ropar (2018). His interests are in the field of heat transfer and thermal analysis. After completing his PhD he worked at NIT Hamirpur, and later at Brunel University London, U.K. as a Post-Doctoral research scholar. Currently he is working as Assistant Professor at College of Engineering Pune, Maharashtra, India. He is the reviewer of many reputed research papers.

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