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Optimizing the Power Required In Hyperthermia Treatment Using Magnetic Nanoparticles

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Abstract

Hyperthermia is the name given to the technique involving selective heating of magnetic particles using high frequency magnetic field. The present paper uses the fact that tumor in the affected area can be removed by heating it up to temperatures, in range of 41°C - 46°C. We propose the power range of 2.75W - 6.5W applied to the magnetic nanoparticles up to time intervals till 10 seconds for a tumor with diameter up to 5cm for its removal. Temperature in the affected area has been studied as a function of magnetic nanoparticle diameter, exposure time of nanoparticles by alternating magnetic field and power.

Keywords*: Hyperthermia, magnetic nanoparticles*

1. Introduction

According to the studies conducted [1], cancer deaths in the world have declined considerably but it is still unconquerable. It is still one of the leading causes of death in developed and developing countries. Usual therapy like radiation, surgery, immunotherapy in addition to chemotherapy have challengeslike ease of access to the tumor cells, danger of operating on a vital organ to name some[2].Uses of nanoparticles have been reported for the detection and drug delivery in treatment of various diseases [3-7]. Their use minimizes the side-effects encountered in conventional therapies at cellular and tissue level. Their widespread use is accounted by their size.

The presented paper uses the concept of 'magic bullet' by Paul Ehrlich (1854-1915), who received Nobel Prize in 1908, in medicine for his work in the field of immunity. His Magic Bullet idea proposes selective targeting of disease causing organism in addition to delivery of toxin for the affected area [8]. A number of hyperthermia techniques have been suggested [9-15] since 1970. Zimmermann and Pilwat in 1976 used magnetic erythrocytes for drug delivery. Freeman *et al*. [16] proposed in 1960, that magnetic nanoparticles could be transported through the vascular system and grouped in a specific part of the body using magnetic field.Boris Polyak and Gary Friedman in 2009, proposed applications and clinical potential of magnetic targeting for site-specific drug delivery [17].The treatment of hyperthermia involves heating of injected cancer-specific biomolecules coated magnetic nanoparticles at the affected area. It involves selective

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heating of magnetic particles, which are positioned at the affected site, using high frequency magnetic field, the present paper uses the fact that tumor in the affected area can be removed by heating it up to temperatures, in range of 41°C - 46°C. We propose the power range of 2.75W - 6.5W, when applied to the magnetic nanoparticles (present at the tumor site), for duration of (up to) 10 seconds, a tumor with diameter size of 5cm can be efficiently removed. Study of temperature in the affected area as a function of magnetic nanoparticle diameter along with exposure time of magnetic nanoparticles by alternating magnetic field and power is presented. Removal of tumor (different diameter sizes) located in liver is studied by varying power applied for different exposure times theoretically using heating model given by Tsafnat *et al*. [18].

2. Approach Followed

The work presented carries forward the results of [19], which shows that for a applied power to magnetic nanoparticles of 6.5W, if heat is applied for a duration of 10 seconds, it leads to removal of tumor (up to radius size of 10cm). The presented paper explores the variation in applied power within which the desired results can be obtained, which in turn leads to minimizing the running cost and undue heating of healthy tissue/cell in the vicinity of the affected area.We present case of tumor in liver. Tsafnat *et al*. [18]gave model for heating of liver tumors. According to their study affected area demonstrates lower levels of blood perfusion in comparison to a healthy one. This results in partial safety for the healthy liver tissue during localized hyperthermia treatment. The mathematical model used in the present paper simulates the practical heat diffusion from the affected area (tumor) to its surrounding (unaffected) tissue. It is assumed that temperatures in the two respective areas have an effect on each other at the boundary interface.

3. The Mathematical Model

We assume the tumor to be spherical tissue with radius a , and the surrounding normal tissue to be a bigger concentric sphere with radius b(see Figure 1). We also assume that the heat source of constant power density P is concentrated within the small sphere of radius a surrounded by a medium of homogenous heat conductivity. Because of the spherical symmetry of the system and the homogenous time-independent power density P inside the sphere, the temperature distribution depends only on distance r from the center of the sphere and on time t. Differential equations of heat conduction [11, 19,23] are used for defining the required mathematical model given by,

$$c_1\rho_1 \frac{\partial T_1}{\partial t} = \frac{k_1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial T_1}{\partial r}\right) + P, \text{ for } 0 \le r < a, \text{ interior of tumor} \quad (1)$$

$$c_2\rho_2 \frac{\partial T_2}{\partial t} = \frac{k_2}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial T_2}{\partial r}\right) \text{ for } a \le r \le b, \text{ exterior of tumor} \quad (2)$$

The subscript “1” refers to tumor tissue, while the subscript “2” refers to normal tissue and the various parameters in these equations are defined as follows:

T represents the temperature

$c$is the specific heat capacity

$\rho$is the density

$k$is the heat conductivity

Based on the assumption that the temperature and flux at the boundary are fine and continuous, the boundary conditions can be written as

$$T_1(a,t) = T_2(a,t) \quad (3)$$

$$k_1 \frac{\partial T_1(a,t)}{\partial r} = k_2 \frac{\partial T_2(a,t)}{\partial r} \tag{4}$$

$$T_1(0,t) \text{ isfinite} \tag{5}$$

$$T_1(r,0) = T_0 \tag{6}$$

$$T_2(r,0) = T_0 \tag{7}$$

To solve the above system of equations,we discretize it using the Euler's method.

Let $h > 0$ and $k > 0$ be the step lengths in the space and time directions, respectively. Let N_1 and N_2 be integers such that $hN_1 = a$ and $hN_2 = b$. We replace the region $\Omega = \{(r,t) \mid 0 \le r \le b, t \ge 0\}$ by a set of grid points (r_l, t_j),denoted by (l, j), where $r_l = lh, \quad t_j = jk$, $j = 0,1,2,\ldots, J$ and $l = 0,1,\ldots, N_2$ where *J*is a positive integer.

Let $(T_1)_l^j = T_1(r_l, t_j)$ and $(T_2)_l^j = T_2(r_l, t_j)$ denote the solution of (1) and (2), respectively at the grid point (*l*, *j*).

We approximate the solution of (1), (2) at the grid point (*l*, *j*) by the scheme

$$(T_1)_l^{j+1} - (T_1)_l^j = \frac{k_1 k}{c_1 \rho_1 h^2}\left[\left((T_1)_{l+1}^{j+1} - (T_1)_l^{j+1}\right) - \left(1 - \frac{2k}{r}\right)\left((T_1)_l^{j+1} - (T_1)_{l-1}^{j+1}\right)\right] + \frac{Pk}{c_1 \rho_1},$$

$$0 < l < N_1 \tag{8}$$

$$(T_2)_l^{j+1} - (T_2)_l^j = \frac{k_2 k}{c_2 \rho_2 h^2}\left[\left((T_2)_{l+1}^{j+1} - (T_2)_l^{j+1}\right) - \left(1 - \frac{2k}{r}\right)\left((T_2)_l^{j+1} - (T_2)_{l-1}^{j+1}\right)\right] + \frac{Pk}{c_2 \rho_2},$$

$$N_1 < l < N_2 \tag{9}$$

$$(T_1)_0^{j+1} - (T_1)_0^j = \frac{k_1 k}{c_1 \rho_1 h^2}\left((T_1)_1^j - (T_1)_0^j\right) + \frac{Pk}{c_1 \rho_1}, \tag{10}$$

From the boundary condition at the tumor-healthy tissue edge we can write the approximation at the grid point(N_1, *j*) as

$$(T_1)_{N_1}^j = (T_2)_{N_1}^j = \frac{k_1 (T_1)_{N_1 - 1}^j + k_2 (T_2)_{N_1}^j}{k_1 + k_2} \tag{11}$$

Solving scheme (8)-(11), using values of the different constants from Table 1[11, 20-22], the graphs were plotted studying dependency of temperature in and around tumor on radius (of tumor), time (of heat exposure) and power applied (on magnetic nanoparticles).

4. Results and Discussion

Using various parameters listed in Table 1 and varying *r* from center (zero cm) to the boundary of the affected area (=*a*), time of exposure up to 10 seconds with power ranging from 2.75 W - 6.5 W, Figures 2-6 were obtained using MATLAB.In the given model, it was assumed that magnetic nanoparticles used were of the size upto10nm in radius.Figure 2 is a surface plot where temperature in the affected area is plotted as a function of hyperthermia time (*t* in seconds) and radius of the tumor (r in cm). It can be seen from the plot that on application of 5W power, temperature in tumor rises to 46°C at the center of the tumor and gradually reducing to body temperature at the interface (of affected and healthy area), thus, causing minimal effect to the unaffected area and hence reducing the side effects due to the treatment. Same result can be deduced by Figure 3. Figure 4 and 5 depict the temperature variation at the center of the tumor on varying power of magnetic nanoparticles and time of heat exposure. It can be observed that temperature at the center

gradually rises from body temperature at the interface (r=*a*) to 48°C for a power range of 2.75W- 6.5W. If we study Figure 6, it can be further noticed, that for a standard time of exposure (*t* = 7seconds) if power is varied from 2.75W- 6.5W over a radius of 2.5 cm, it leads to annihilation of the tumor.

Thus it can be concluded from the above graphical results that hyperthermia treatment involving magnetic nanoparticles can be used for the removal of tumorous cell/tissue, if we use nanoparticles with power in the range of 2.75W-6.5W with a heat exposure time up to 10 seconds. This will make treatment more effective with fewer side-effects and less cost.

Table 1. Liver Tissue and Nanoparticle Parameters [11,20-22]

Parameter	Constant	Value
Radius of liver tumor	*A*	2.50 cm
Tumorous liver tissue specific heat	c_1	3.758 KJ/kg. K
Healthy liver tissue specific heat	c_2	3.617 KJ/kg. K
Liver tissue heat conductance	$k_1=k_2$	0.5122 W/m. K
Liver Density	$\rho_1 = \rho_2$	1.0492 g/mL

5. Conclusion

Thus it can be concluded that power applied to the magnetic nanoparticles in hyperthermia treatment when optimized in the range of 2.75W-6.5W results in effective removal of tumor,with diameter up to 5 cm and exposure time till 10 seconds, minimizes undue damage of surrounding tissue/cell in addition to being cost effective.

Figure Captions

1. Spherical tumor tissue surrounded by concentric sphere containing normal tissues.
2. Surface plot showing temperature in the tumorous cell/tissue as a function of hyperthermia time (*t*, in seconds) and distance from the center of the tumor (*r*, in cm) for a constant magnetic nanoparticle power of 5W.
3. Temperature inside the tumorous cell/tissue as a function of distance from the center of the tumor (*r* in cm) and hyperthermia time (*t*, in seconds) for a constant magnetic nanoparticle power of 5W.
4. Surface plot showing temperature at the center of the tumorous cell/tissue as a function of hyperthermia time (*t* in seconds) and a magnetic nanoparticle power (*p*, in watts).
5. Temperature at the center of the tumorous cell/tissue as a function of magnetic nanoparticle power (*p*,in watts) and hyperthermia time (*t*, in seconds).
6. Surface plot showing temperature in the tumorous cell/tissue as a function of distance from the center of the tumor (*r*, in cm) and magnetic nanoparticle power (*p*, in watts) for a constant exposure time (*t*= 7 seconds).

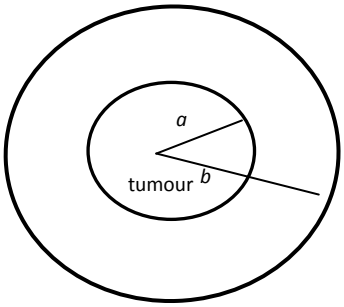


Figure 1

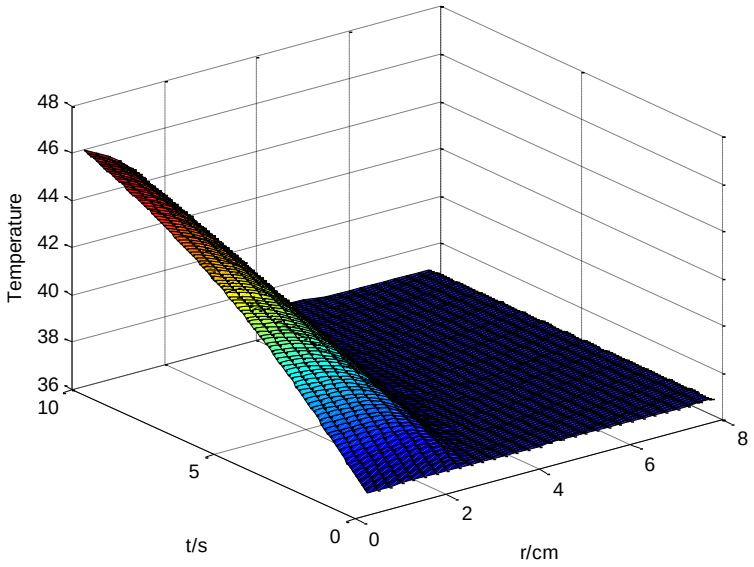


Figure 2

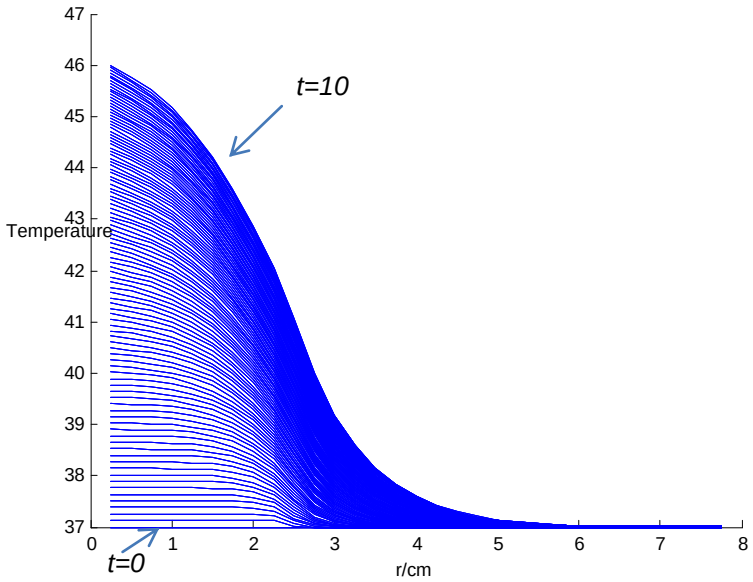


Figure 3

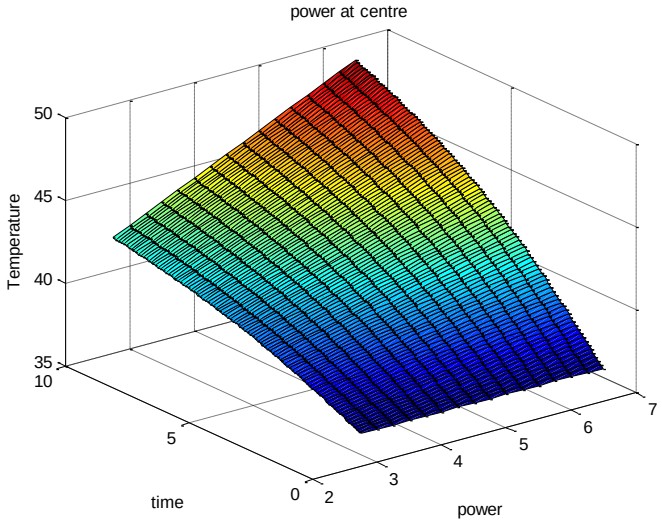
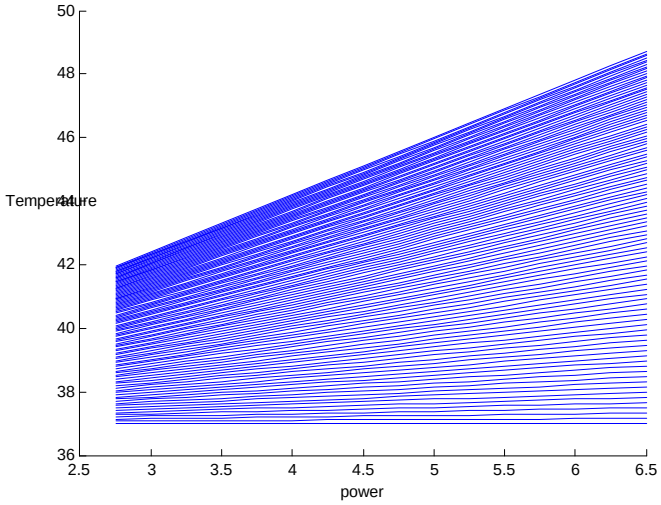


Figure 4



t=10

t=0

Figure 5

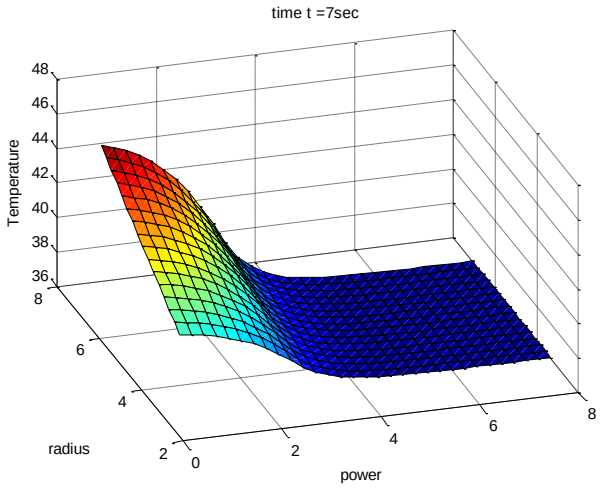


Figure 6

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