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Optimal Control Problem in Hyperthermia by Heating Probe

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ABSTRACT

A mathematical investigation is performed in hyperthermia by inserting a conducting heating probe at the location of the tumour [1] so as to attain a desired rise of temperature in the deep tumour site of the tissue consisting of skin, fat, muscle, point tumour and muscle during total time of the operation of the process, by controlling the power of conducting heating probe and also by controlling optimally surface cooling temperature by using finite difference

Numerical calculation of temperature distributions of the tissue against the length of the tissue at different times on various value of total time of operation have been carried out which displayed the rise of temperature of the tumour. Here the switching time during which the heating power is operative has been obtained

Keywords: Maximal principle, tumour, auxiliary function, hyperthermia, inserting heating probe.

Notations:

χ = temperature $({}^0C)$

χ_1 = arterial temperature $({}^0C)$

χ_0 = initial temperature $({}^0C)$

ρ_i = density of tissue $(kg\ m^{-3})$ in i^{th} layer of the tissue.

c_i = specific heat of tissue $(J\ kg^{-1}\ K^{-1})$ in i^{th} layer of the tissue.

k_i = thermal conductivity of tissue $(\mathrm{W}\, m^{-1}\ K^{-1})$ in i^{th} layer of the tissue.

b_i = product of flow and heat capacity of blood $\mathrm{W}\, m^{-3}\ K^{-1})$ in i^{th} layer of the tissue.

χ^* = required rise of temperature (^0C) of tumour.

q_i = temperature (^0C) of tissue in i^{th} point of the tissue.

T = duration of the process (s)

t_2, t_1 = switching time (s).

Q_m = metabollic heat generate rate (Wm^{-3})

L = depth of tissue (m)

$h = \frac{L}{p}$ = length of equal subintervals of tissue segment $(0, L)$ (m).

p = number of division.

λ = heat convection coefficient between skin and surface ($Wm^{-2}\ K^{-1}$)

$u(t)$ = surface cooling temperature (^0C)

$Q(t)$ = heat source for unit volume (Wm^{-3})

Q_i = heating power for unit volume (Wm^{-3}) in i^{th} point of the tissue.

1.Introduction

In course of hyperthermia of cancer therapy the study of achieving a therapeutic temperature elevation in tumour by means of application of radiotherapy and / or chemotherapy without overheating the healthy normal tissue is generally useful form of treatment. To rise the temperature of the tumour, it's location as well as the anatomy of the patient alongwith patient's tolerance in course of heating patterns are very useful needs whether heat is generated either by invasive system, e.g., by small microwave antenna inserted into the tumour through hypodermic needles, or by non-invasive system with the aid of ultrasound transducers for superficial tumours.

The optimization problems to quantify the application of heat source and temperature of cooling on the surface are very important to form the strategy in hyperthermia treatment planning so as to achieve therapeutic rise of temperature of the tumour.

Deng et al [1] have performed several closed form of analytical solutions in bio-heat transfer problems, with space or transient heating on the skin surface or inside biological bodies by inserting a heating probe at the tumour region, using Green's function method. Dhar et al [2] investigated analytically optimal temperature control in hyperthermia by controlling artificial surface cooling using finite difference method.

Wagter [3] studied an optimization procedure to calculate transient temperature profiles in plane tissue by multiple electro-magnetic applicatiors. Analytical study by Butkovasky [4] had carried the fundamentals of optimal control problems in distributed parameter system. Dhar et al [5] had considered analytically an optimal control problem so as to attain a desired temperature throughout the tissue by induced heat source at least possible time.

The paper of Das et al [6] carried out an investigation for fast optimization computations in the application to a typical temperature objective function by finite element models. An optimization problem in hyperthermia of an electro-magnetic annular phased arrays (APA) was investigated employing non-invasive temperature estimation in Kowalski et al [7] by finite difference method. A thermal dose optimization in hyperthermia was studied by Loulou et al [8] using conjugate gradient method.

Kowalski et al [9] presented a hybrid proportional integral- in-time and cost minimization problem in space by feedback control system for electro-magnetic phased –array in hyperthermia using discretization both in time and space derivatives. An optimization problem on diseased tissue by generating heat with the aid of alternating magnetic fluid was investigated in Bagaria et al [10].

A successive over-relaxation finite difference method was applied by Cheng et al [11] in course of the study to build the foundation for facilitating real-time magnetic resonance image for heating systems with large number of physical sources in fast temperature optimization in hyperthermia. Kuznetsov [12] investigated an optimal control problem to maximize the tumor temperature at the end of the process by controlling spatial heat source.

In [13] Lee et al build up the concept of fundamentals of optimal control theory. A thermal therapy feedback control approach was the subject of study to control thermal dose using moving power deposition field in Arora et al [14].

In [15] Yuan et al applied conjugate gradient method in solving the tissue temperature distribution in bio-heat transfer equation. In the study of [16] Wren et al a hybrid equation that included both an increased thermal conductivity and a heat sink where temperature field in tissue was simulated.

An optimization problem of radio-immuno-therapy interactions with hyperthermia was developed in Kinuya et al [17]. Szasz et al [18] proposed a generalization of the Penne's- equation by inducing the entire energy balance.

With the aid of conjugate gradient method, a distributed optimal control problem for a system described by bioheat equation in a homogeneous plane tissue due to induced microwave was investigated by Dhar et al [19].

We would like to control optimally the heating power $Q(t)$ (Wm^{-3}) applied by inserting a conducting heating probe at $x = x_1$ (point of location of the tumour) and also surface cooling temperature u(t) (^oC) of the tissue consisting of skin, fat, muscle, point tumour and muscle according to Fig A during total time of the operation T of the process so as to attain a desired temperature χ^* at the tumour ($x = x_1$).

A numerical computation of temperature distributions of the tissue along the length of the tissue at different times on various values of total time of operation of the process have been worked out for investigation of desired rise of temperature of the

tumour after obtaining switching time during which the heating power is operative.

2. Mathematical analysis

The one-dimensional bio-heat equation [1,2] can be written as,

$$pc\frac{\partial \chi}{\partial t} = k\frac{\partial^2}{\partial x^2}\chi - b(\chi - \chi_1) + Q_m(x) + Q(t) \tag{1}$$

Boundary condition:

$$k\frac{\partial \chi}{\partial x} = \lambda\{\chi - u(t)\} \text{ on } x = 0 \tag{2}$$

$$\chi(x,t) = \chi_1 \text{ on } x = L \tag{3}$$

Initial condition:

$$\chi(x,o) = \chi_O \tag{4}$$

Let us reduce the system with distributed parameters to a lumped parameters using finite difference method by dividing the segment (O,L) on the X- axis into p equal intervals of length h for h = L/p. where we designated the temperature of the tissue at each point by quantities q_i=(i=o, 1, ... , p) on the basis of considering the parameters corresponding to current layers as soon as the solution point crosses the interface between the previous layer and the current layer. [2].

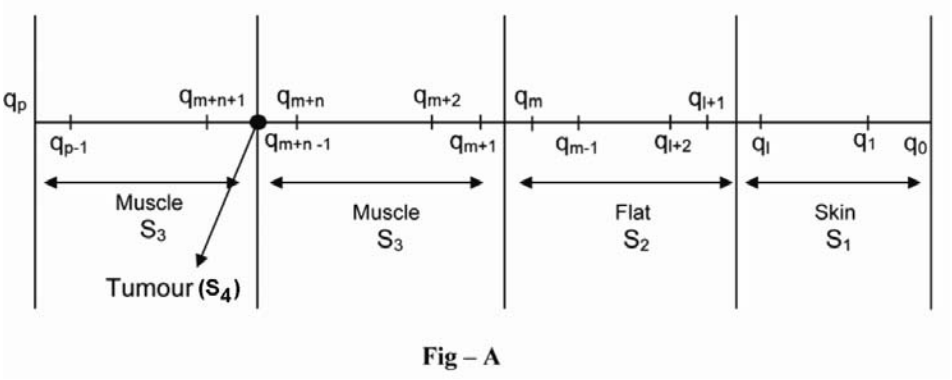

Fig – A

After dividing the layers consisting of skin, fat, muscle, a point tumour and muscle into equal sublayes of length h, given in Fig A, the equation (1) can be constructed as, [2]

$$\frac{dq_1}{dt} = {}^1F_{1,1} = \frac{1}{\rho_1 c_1}\left[\frac{k_1^2}{h^2(k_1 + \lambda h)} - \frac{2k_1}{h^2} - b_1\right]q_1 + \frac{k_1}{\rho_1 c_1 h^2}q_2$$

$$+ \frac{k_1 \lambda h\, u(t)}{\rho_1 c_1 h^2(k_1 + \lambda h)} + \frac{Qm_1}{\rho_1 c_1} + \frac{Q_1(t)}{\rho_1 c_1} \tag{5}$$

$$\frac{dq_j}{dt} = {}^{2}F_{j,s}\frac{k_s}{\rho_s c_s h^2}\left(q_{j+1} - 2qj + q_{j-1}\right) - \frac{b_s}{\rho_s c_s}\left(q_j - \chi_1\right) + \frac{Qm_j}{\rho_s c_s} + \frac{Q_j(t)}{\rho_s c_s} \tag{6}$$

$j = 2,.....,l-1;\quad j = l+2,.....,m-1,\quad j = m+2,.....m+n-2,\quad j = m+n+2,\ .....,p-1$

$s = 1 \qquad s = 2 \qquad s = 3 \qquad s = 3$

$$\frac{dq_j}{dt} = {}^{3}F_{j,s} = \frac{k_s}{\rho_s c_s h^2} q_{j+1} + \frac{k_{s-1}}{\rho_{s-1} c_{s-1} h^2}\left(q_{j-1} - 2qj\right) - \frac{b_{s-1}}{\rho_{s-1} c_{s-1}}\left(q_j - \chi_1\right) + \frac{Qm_j}{\rho_{s-1} c_{s-1}} + \frac{Q_j(t)}{\rho_{s-1} c_{s-1}} \tag{7}$$

$j = l \quad ; \quad j = m \quad ; \quad j = m + n - 1$

$s = 2 \qquad s = 3 \qquad s = 4$

$$\frac{dq_j}{dt} = {}^{4}F_{j,s} = \frac{k_s}{\rho_s c_s h^2}\left(q_{j+1} - 2q_j\right) + \frac{k_{s-1}}{\rho_{s-1} c_{s-1} h^2} q_{j-1} - \frac{b_s}{\rho_s c_s}\left(q_j - \chi_1\right) + \frac{Qm_j}{\rho_s c_s} + \frac{Q_j(t)}{\rho_s c_s} \tag{8}$$

$j = l + 1 \quad ; \quad j = m + 1$

$s = 2 \qquad s = 3$

$$\frac{dq_j}{dt} = {}^{5}F_{j,s} = \frac{k_{s-1}}{\rho_{s-1} c_{s-1} h^2}\left(q_{j+1} - 2q_j\right) + \frac{k_s}{\rho_s c_s h^2} q_{j-1} - \frac{b_{s-1}}{\rho_{s-1} c_{s-1}}\left(q_j - \chi_1\right) + \frac{Qm_j}{\rho_{s-1} c_{s-1}} + \frac{Q_j(t)}{\rho_{s-1} c_{s-1}} \tag{9}$$

$j = m + n + 1$

$s = 4$

$$\frac{dq_{m+n}}{dt} = {}^{6}F_{\overline{m+n,4}} = \frac{k_3}{\rho_3 c_3 h^2}(q_{m+n+1} + q_{m+n-1}) - \frac{2k_4 q_{m+n}}{\rho_4 c_4 h^2} - \frac{b_4}{\rho_4 c_4}(q_{m+n} - \chi_1) + \frac{Q_{m_{(m+n)}}}{\rho_4 c_4} + \frac{Q_{m+n}(t)}{\rho_4 c_4} \tag{10}$$

The equations (2) , (3) and (4) thus stands,

$$k_1\left\{\frac{q_1 - q_0}{h}\right\} = \lambda\{q_O - u(t)\} \tag{11}$$

$$q_p = \chi_1 \tag{12}$$

and $q_j(o) = \chi_O, \quad j = 0,1,2,\ldots.,p$ (13)

With the aid of Maximal Principle, we would like to attain desired temperature χ^* at the point of location of the tumour at $x = x_1$ embedded inside the tissue consisting of skin, fat, muscle, tumour and muscle according to Fig-A during total time of operation of the process T by controlling optimally time dependent heating probe of power $Q(t)$ inserted in the deep tumour site at x =x_1 and also controlling optimally surface cooling temperature u(t).

Thus the functional stands after discretizing given by [2,4], according as Fig A,

$$\frac{1}{2}\int_0^T \left\{\chi^* - q_{m+n}(t)\right\}^2 dt \text{ is to be minimized} \tag{14}$$

The Hamiltanian of the problem following [2,4,13] under 'Maximal Principle',

$$\begin{aligned} H = -\frac{1}{2}\left\{\chi^* - q_{m+n}(t)\right\}^2 &+ \sum_{j=2}^{l-1} \varphi_j {}^2F_{j,1} + \varphi_l {}^3F_{l,2} + \varphi_1 {}^1F_{1,1} \\ &+ \varphi_{l+1} {}^4F_{\overline{l+1},2} + \sum_{j=l+2}^{m-1} \varphi_j {}^2F_{j,2} + \varphi_m {}^3F_{m,3} + \varphi_{m+1} {}^4F_{\overline{m+1},3} \\ &+ \sum_{j=m+2}^{m+n-2} \varphi_j {}^2F_{j,3} + \varphi_{m+n-1} {}^3F_{\overline{m+n-1},4} + \varphi_{m+n} {}^6F_{\overline{m+n},4} \\ &+ \varphi_{m+n+1} {}^5F_{\overline{m+n+1},4} + \sum_{m+n+2}^{p-1} \varphi_j {}^2F_{j,3} \end{aligned} \tag{15}$$

Here the values of ${}^1F_{1,1}$, ${}^2F_{j,s}$, ${}^3F_{j,s}$, ${}^4F_{j,s}$, ${}^5F_{j,s}$ and ${}^6F_{\overline{m+n},4}$ given in equations (5), (6), (7), (8), (9) and (10) respectively are considered in terms of different values of parameters ρ, k, c and b as specified in skin, fat, muscle and tumour layers.

The auxiliary function φ_j $(j = 1,2,3,.....p-1)$ can be written as,

$$\frac{d}{dt}\varphi_j = -\frac{\partial H}{\partial q_j}, \; j = 1,2,\ldots.,p-1 \tag{16}$$

with terminal condition $\varphi_j(T) = 0, j = 1,2,\ldots\ldots,p-1$ (17)

According to the problem and considering the Fig A we note that

$$Q_j(t) = 0,\ j = 1,2,3,.....,m+n-1,m+n+1,.....,p-1; \tag{18}$$

and we write,

$$Q_{m+n}(t) = Q(t); \tag{19}$$

where $x_1 = (m+n)h.$

From the relations $\frac{\partial H}{\partial Q(t)} = 0$, and $\frac{\partial H}{\partial u(t)} = 0$ we note that the controls are singular, and thus one can construct the optimal controls $Q(t)$ and $u(t)$ given by,

$$Q(t) = \frac{1}{\rho_4 c_4} sign\ \varphi_{m+n}(t) \tag{20}$$

and

$$u(t) = \frac{k_1 \lambda h}{\rho_1 c_1 h^2 (k_1 + \lambda h)} sign \varphi_1(t) \text{ [vide equation (5)]} \tag{21}$$

Equations (20) and (21) for switching times, $t = t_1$ and $t = t_2$ respectively, taking for the sake of simplicity, stand as,

$$\varphi_{m+n}(t_1) = 0 \text{ and } \varphi_1(t_2) = 0 \tag{22}$$

where $\varphi_{m+n}(t_1)$ and $\varphi_1(t_2)$ can be obtained from Equations (15), (16) and (17) with the help of Equations (5) - (13) for obtaining $q_j(t)$ $(j = 1,2,.....,p-1)$

Here we have assumed time dependent induced incident power of electro-magnetic field per unit volume $Q_{m+n}(t)$ (wm^{-3}) and surface cooling temperature u(t) (^{0}c), both taken as controllable inputs, are piecewise constant functions of time that change values at certain specified discrete instants considered as switching times [3].

3. Numerical Calculation:

For numerical calculations we have taken the data as given in [2,3]

	ρ c($Jm^{-3}K^{-1}$)	k($Wm^{-1}K^{-1}$)	b($Wm^{-3}K^{-1}$)	Qm(wdm^{-3})
Skin	3.4 x 10^6	.44	7500	1
Fat	2.5 x 10^6	.23	0	0
Muscle	3.4 x 10^6	.50	5550	3
Tumour	3.00 x 10^6	.30	2000	3
Muscle	3.4 x 10^6	.50	5550	3

h=length of each division of tissue layer = 0.5mm, χ_0 = 25^{o}C (initial temperature), χ_1 = 37^{o}C, λ = 200 $Wm^{-2}K^{-1}$, χ^* = 43^{o}C, T = 600s, 800s, 1000s, L = .01m,p=20.

Table 1

For calculating the temperature distribution of the tissue according as specified controls $Q(t)$ and $u(t)$ we have considered the lengths of skin, fat, muscle, located tumor and muscle, given by, 1mm, 2mm, 3mm, tumour situated at the point $x = 6$ mm and 4mm respectively as indicated in Fig A.

In course of drawing all the figures we have obtained the control input variables $Q(t)$ (Wm^{-3}) and u(t) (^{0}C) so as to satisfy the conditions given in equation (22) adjusting by simulation.

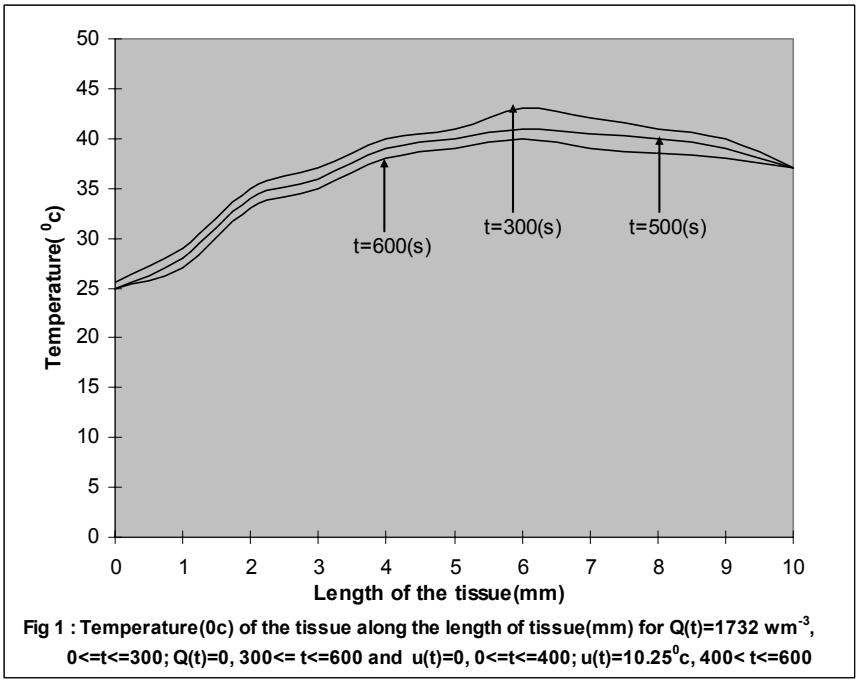

Fig 1 : Temperature(0c) of the tissue along the length of tissue(mm) for Q(t)=1732 wm^{-3}, 0<=t<=300; Q(t)=0, 300<= t<=600 and u(t)=0, 0<=t<=400; u(t)=10.25^{0}c, 400< t<=600

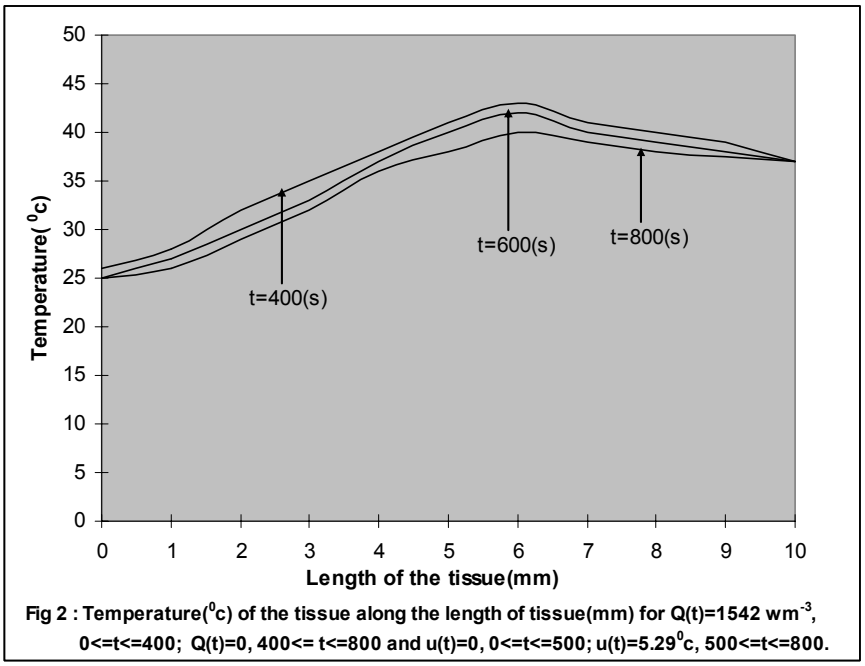

Fig 2 : Temperature(^{0}c) of the tissue along the length of tissue(mm) for Q(t)=1542 wm^{-3}, 0<=t<=400; Q(t)=0, 400<= t<=800 and u(t)=0, 0<=t<=500; u(t)=5.29^{0}c, 500<=t<=800.

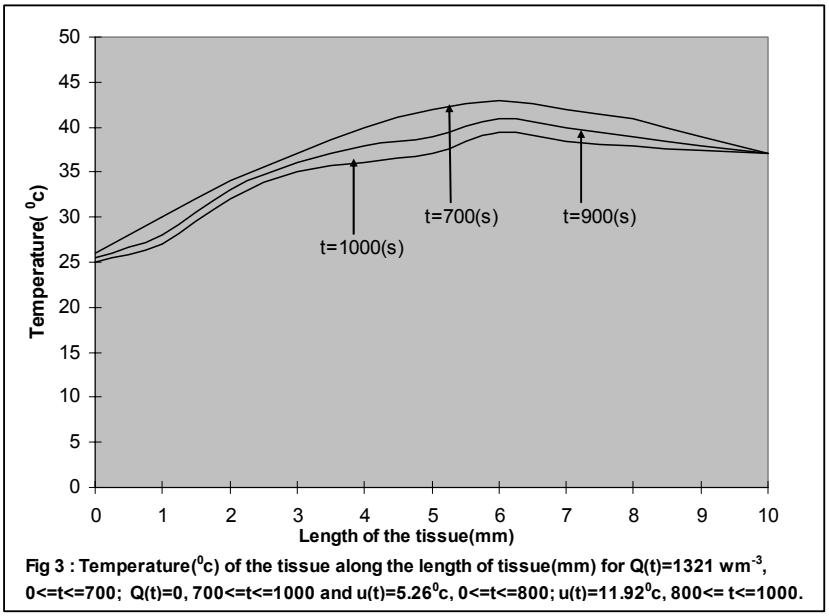

Fig 3 : Temperature(^{0}c) of the tissue along the length of tissue(mm) for Q(t)=1321 wm^{-3}, 0<=t<=700; Q(t)=0, 700<=t<=1000 and u(t)=5.26^{0}c, 0<=t<=800; u(t)=11.92^{0}c, 800<= t<=1000.

4. Results and discussion

Fig 1,Fig 2 and Fig 3 display the temperature of the tissue along the length of the tissue for

$$Q(t) = 1732\ Wm^{-3},\ 0 \le t \le 300(s);\ Q(t) = 0,\ 300 \le t \le 600(s);$$

u(t)=0, $0 \le t \le 400(s)$; u(t)= 10.25^0C, $400(s) \le t \le 600(s)$ in Fig 1

$Q(t) = 1542\ Wm^{-3}$, $0 \le t \le 400(s)$; $Q(t) = 0$, $400 \le t \le 800(s)$;

u(t)=0, $0 \le t \le 500(s)$; u(t)= 5.29^0C, $500(s) \le t \le 800(s)$ in Fig 2

and $Q(t) = 1321\ Wm^{-3}$, $0 \le t \le 700(s)$; $Q(t) = 0$, $700 \le t \le 1000(s)$;

u(t)=5.26°C, $0 \le t \le 800(s)$; u(t)= 11.92^0C, $800(s) \le t \le 1000(s)$ in Fig 3

In Fig 1, Fig 2 and Fig 3 it is observed that the temperature of the tumour at x = 6mm attain 43^OC (desired temperature) at t = 300s, 400s, and 700s (switching times) for T = 600s, 800s, 1000s respectively. The temperature of the tissue on the left side of the tumour increases steadily and after attaining 43^OC it decreases on the right side of the tumour with rapidity till the end of the process, which can be accounted for due to cutting off the heating power in the second time segment of operation of the process. Thus, all together, it is seen from Fig 1, Fig 2 and Fig 3 that the overheating of the healthy tissue above 43^OC are being avoided.

However, it is found that as the total time of operation of the process increases from $600s$ to $1000s$, the values of $Q(t)$ appear in the first segment of operation decreases with corresponding increase of the switching time, *i.e.*, increase of duration of application of $Q(t)$ in the first time segment.

It is also seen that the values of u(t) in the first time segment is always less than that of in the second time segment of operation.

5. Conclusion

This analytical study may provide an initiating background in focusing further developments for the cases of different structures of the tissue having different times of operation with different point of locations of the tumour with different lengths of the tissue.

But for the purpose of practical application the investigation of this analytical study must be performed in terms of clinical trials in hyperthermia.

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