TEMPERATURE DISTRIBUTION DURING HIFU TREATMENT AND EFFECT OF LARGE BLOOD VESSEL

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Abstract. Thermal models are used to predict temperature distributions of heated tissues during thermal therapies. High intensity focused ultrasound (HIFU) is a non-invasive treatment modality for a variety of cancers. Computer models have been used to determine tissue temperatures during ultrasound hyperthermia. In this work, we consider a liver tissue with a tumor at its center. We calculated temperature distribution in the presence a large blood vessel. The distance between the vessel and the tumor tissue varied from 1 to 3 mm. We used the Pennes bioheat equation for modeling heat transfer. A finite element method (FEM) was used to obtain the temperature distribution for a heat transfer equation. A 3-D model for simulation of tumor tissue utilized a cylinder with 4-mm diameter and 10-mm height located in the center of the cylindrically modeled liver tissue. Temperature distribution to the center of the tumor in HIFU treatment increases during the heating duration and after that temperature reduces. By increasing distance from the vessel to tumor, temperature slightly increased. Simulation results demonstrate that with the use of more absorbed power density, the temperature at the centre of tumor increases.

1 Introduction

The therapeutic applications of ultrasound are hyperthermia treatment and ultrasound surgery. These applications are based on absorption of ultrasound which produce localized temperature rise in tissue. The hyperthermia treatment is used to enhance the response to radiotherapy and chemotherapy. High temperature hyperthermia, which is itself used for tissue destruction, is called HIFU treatment. HIFU is used to destroy tumors noninvasively and the basic idea is to heat the tumor tissue so that the temperature of the tissue will be raised over level that causes necrosis and tumor will be destroyed. Usually, in HIFU tumor tissue is heated to temperatures greater than 50°C [1, 2, 3].

Ultrasound hyperthermia is a treatment modality that uses heat to destroy cancer cells by localized heating of tumors. Ultrasound hyperthermia is used for liver cancer, with increasing use in other organs such as kidney, lung, bone, and adrenal gland [1]. Ultrasound is mostly utilized for those tumor patients who are not candidates for surgical resection due to complications such as awkward size and location of the tumor. The heat due to ultrasound hyperthermia causes tissue necrosis at predictable temperatures in relatively predictable volumes. The goal of hyperthermia treatment is to define the power deposition pattern such that while the tumor is adversely affected, there would be only minimal impingement on the normal tissue.

HIFU is a non-invasive method for hyperthermia. This technique creates short and local elevations of temperature at the focus. The main goal of HIFU is to maintain a temperature between 50 and 100 °C for a few seconds (typically less than 10 s), in order to cause tissue necrosis. Typically, focal peak intensity between 1000 and 10,000 W/cm^2 is used with pulse duration between 1 and 10 s and a frequency of 1 to 5 MHz [2,3]. HIFU has the advantage of no-invasiveness, better penetration, better selectiveness and ease of power control, over other physical methods such as lasers, microwaves, or radio frequency (RF) fields.

The liver is a highly perfused and the largest organ in human body and is located in the right upper quadrant of the abdomen. Presence of a large blood vessel next to the tumor is often seen in liver tumors [4]. When ultrasound is focused on tumor adjacent to large vessels, the blood flow would drag thermal energy away from the tissue [5]. These vessels can change the shape of the zone of necrosis. Distance of the blood vessels from the tumor can change the amount of the maximum tissue temperature. Heat transfer between tissue and blood vessel has been investigated by a number of various models [6-9]. However, it seems that previous studies have hardly considered a 3D HIFU treatment which includes the effect of large blood vessel presence in the vicinity of tumors for liver tumor.

Most computational models of ultrasound hyperthermia used Pennes equation [6]. Frequently simulations consider effect of large vessels by either assigning constant temperature at the surface of the vessel [5,7] or applying a constant convective heat transfer coefficient (h) [8]. We preformed simulations to clarify the essence of flow distribution in vessels. Our study implied that the flow in the vessel is laminar and the thermal boundary layer is fully-developed, thereby resulting in a constant h throughout the procedure. However, since the heated region

during the procedure varies in time and the vessel heated length is small, the thermal boundary layer is not fully-developed.

The purpose of this study is to investigate the effects of presence and various locality scenarios of a blood vessel to tumor and evaluating its effect on the thermal distribution within the target during HIFU therapy. We created a 3-D FEM model which included a 4-mm diameter, 10-mm height cylindrical tumor tissue model and a large blood vessel located at selected distances to it. Using the FEM approach we studied the effect of varying the distance between the blood vessel and the tumor, the exposure time, and the diameter of the blood vessel.

2 Temperature Model

To generate the finite element model, we used the software FEMLAB (COMSOL)[10]. This software performs thermal field analysis and provides all the elements needed to build the model. In tissue, heat is transferred due to conduction and convection. For example in regions where perfusion is remarkable, heat transfers from tissue to blood (conduction) and blood flow transfers heat to other parts of the body (convection). The temperature distribution in tissue is normally calculated using Pennes bioheat transfer equation BHTE, Eq. (1) [6].

$$\rho c\frac{\partial T}{\partial t} = \nabla .k\nabla T - \rho_b c_b \omega_b (T - T_b) + Q_{met} + Q_{ext}, \qquad (1)$$

where ρ is the tissue density (kg/m^3), C is the tissue's specific heat (J/kg°C), and k is its thermal conductivity (W/m°C), ρ_b is the blood's density (kg/m^3), c_b is the blood's specific heat (J/kg°C), wb is its perfusion rate (1/s), Tb is the arterial blood temperature (°C), while Qmet and Qext are the heat sources from metabolism and the absorbed power density from HIFU, respectively (W/m^3). Here we considered the effect of Q_{met} contrary to the usual practice of ignoring it due to its small contribution in comparison to Qext.

The first term on the right hand side of the equation is thermal conduction. The second term is convection or heat transfer to the tissue by perfusion and considered as a heat sink term representing the removal of heat by blood in the microvasculature.

Pennes' primary hypothesis was that energy exchange between blood vessels and the surrounding tissue occurs mainly across the wall of capillaries that are blood vessels with 0.005-4.015mm in diameter, where blood velocity is very low. He assumed that the thermal contribution of blood can be modeled as if it enters an imaginary pool (the capillary bed) at the temperature of major supply vessels, Ta, and immediately equilibrates (thermally) with the surrounding tissue. Thus it exits the pool and enters the venous circulation at tissue temperature, T. He claimed that the total energy exchange by the flowing blood can be modeled as a nondirectional heat source, whose magnitude is proportional to the volumetric blood flow and the difference between local tissue and major supply arterial temperatures[11].

Blood perfusion rate is the mass flow rate of blood per unit volume of tissue, given in units of (kg/m^3) and the blood perfusion in liver tissue is 6.4*10^{-3} 1/s [12,13]. The tissue parameters for the various materials are listed in Table 1[14].

Material	Density, ρ	Thermal conductivity, k	Specific heat, C	Q_{met}
Liver	1060	0.512	3600	400
Blood	1000	0.543	4180	-

Table 1. Tissue parameters used in calculations

A three dimensional view of the model and distances are shown in Fig. 1 Liver tissue was modeled as a cylinder (100 mm diameter × 120 mm length). The temperature on the boundary of the model and the initial temperature of tissue were set to 37°C. Since the vessel was located out of the focal zone, we set the temperature of the blood and the vessel wall to 37°C as an additional boundary condition in our initial model. The estimation of the heat transfer coefficient h was based on the assumption that h between vessel and tissue is constant and is about 1000 W/ (m$^{2\circ}$ K) [15, 16].

The heat flux condition accounts for general heat flux as well as that from convection as defined by a convective heat transfer coefficient. The boundary condition on vessel was accounted by heat flux.

$$-n.(-k\nabla T) = q_0 + h(T_{\inf} - T), \qquad (2)$$

where q_0 represent a heat flux that enters the domain, $h(T_{inf} - T)$ models convective heat transfer with the surrounding environment, where h is the heat transfer coefficient and T_{inf} is the external bulk temperature(37° C). The value of h depends on the geometry and the ambient flow conditions. For a thorough introduction on how to calculate heat transfer coefficients, see Ref 17.

The convective boundary condition was considered in the tissue-vessel interface. Thus, the heat sink effect of the blood flow inside the vessel was modeled by a convective boundary condition at the tissue-vessel interface. The value of convective coefficient was set in the model according to h, which assumes that the blood behaves as a Newtonian fluid in large vessels, the flow is laminar and the geometry of the vessel is linear [18].

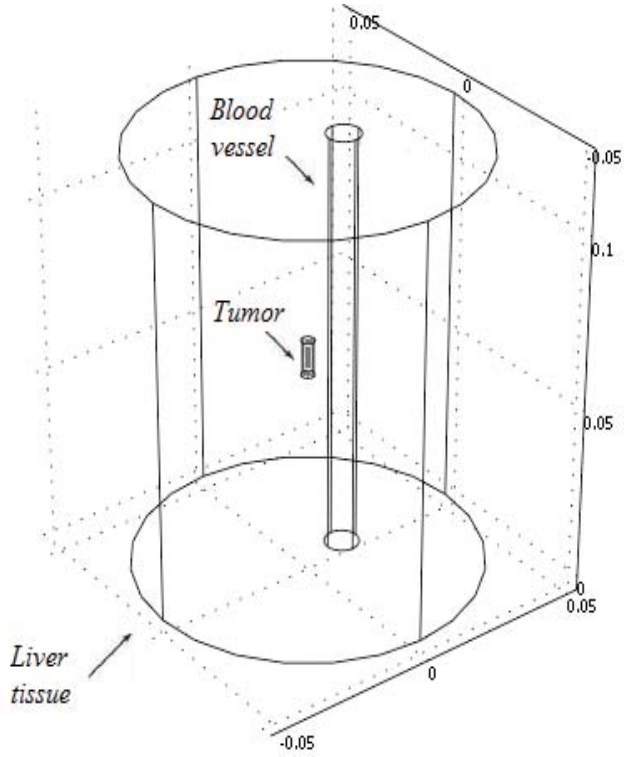


Figure 1. A three dimensional view of the model

3 Results and Discussion

Computer simulations were performed for different heating durations and waiting times with a total time of 10 seconds, such as 3+7, 4+6, 6+4, and 7+3. In this work heating durations were considered for 3, 4, 6, and 7 second. Maximum temperature with absorbed power density of $13W/cm^3$ for four heating durations on the tumor is listed in Table 2.

Heating duration	3	4	6	7
Maximum Temperature	45.07	48.07	51.127	55.14

Table 2. Maximum temperature for different heating durations

Cancer cells die when the temperature is at least 50°C. So, according to Table 2, cancer cells die when heating duration is approximately 6 second long. Figure 2 shows the temperature distribution after 6 second with absorbed power density of $13W/cm^3$. Figure 3 shows the temperature distribution in the 2D model(Y-Z) after 7s with absorbed power density of $13W/cm^3$. For both conditions, the vessel diameter is 10mm and the distance of vessel to the tumor is 2mm. Effect of the heating durations on the profiles of the temperature at the center of the tumor for absorbed power density of $13W/cm^3$ was depicted in Figure 4.
Figure 5.a shows temperature distribution with different distances after 7s and absorbed power density of $13W/cm^3$. It depicts the fact that temperature at the center of the tumor would increase during the heating process. For different distances, the peak temperature sounds about the same and is independent of the distance from the vessel to tumor. In this figure d is distance from the vessel to tumor.

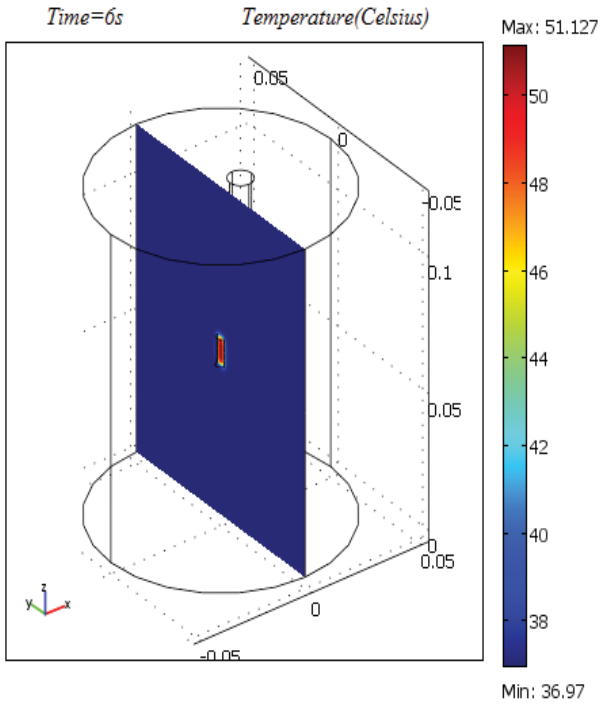


Figure 2. Temperature distribution in the tissue 3D model after 6s and absorbed power density of 13W/cm^3.

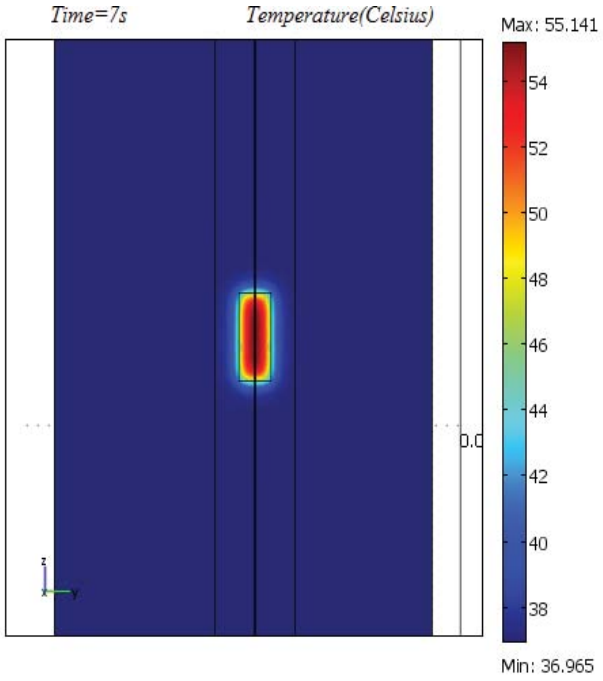


Figure 3. Temperature distribution in the tissue 2D model(Y-Z) after 7s and absorbed power density of 13W/cm^3.

When distance of vessel to the tumor is reduced, the blood flow would drag more thermal energy away from the tissue and as a result, temperature has to reduce. More accurate changes of temperatures for different distances near t=7s is shown in figure 5.b. For constant distance of the blood vessels from the tumor 2mm and constant time 7 s, relationship between absorbed power density and maximum temperature in Figure 6 is depicted. This figure shows that with increasing amount of absorbed power density, maximum temperature in center of the tumor increased.

Under the same heating duration, maximum temperature is earned for the higher absorbed density. For constant absorbed power density, maximum temperature is for the most heating duration. For the constant absorbed power density and heating duration, the thermal dose profiles are similar and the peak thermal dose levels are almost the same.

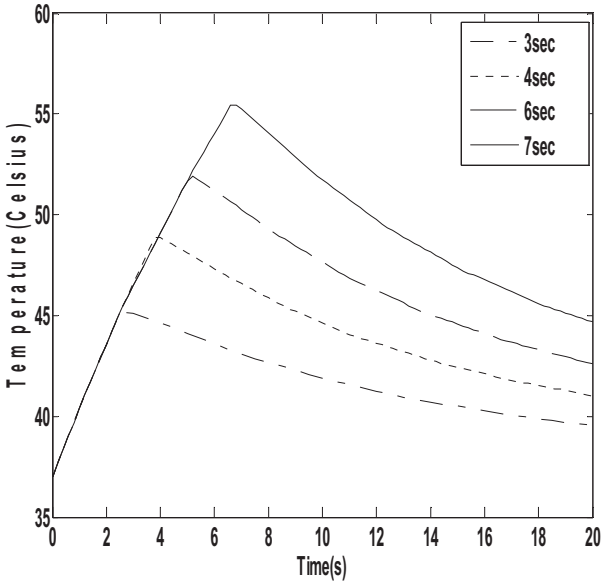
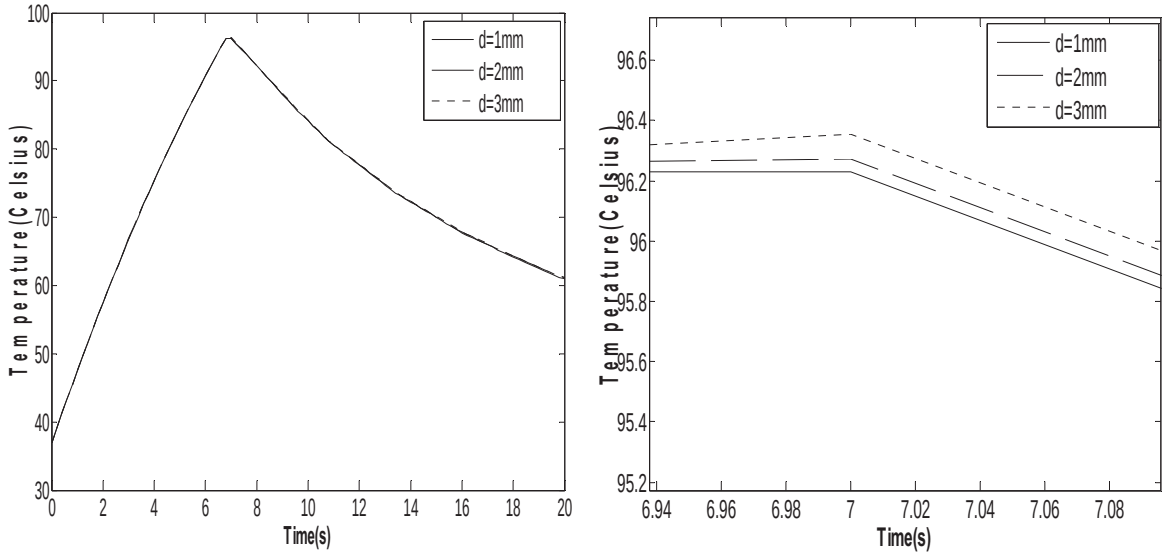


Figure 4. Temperature distributions to the center of the tumor with different heating durations for absorbed power density of 13W/cm^3.



(a) (b)

Figure 5. Temperature distributions to the center of the tumor with different distances for absorbed power density of 40W/cm^3 and t=7s a). total view b). accurate view of peak.

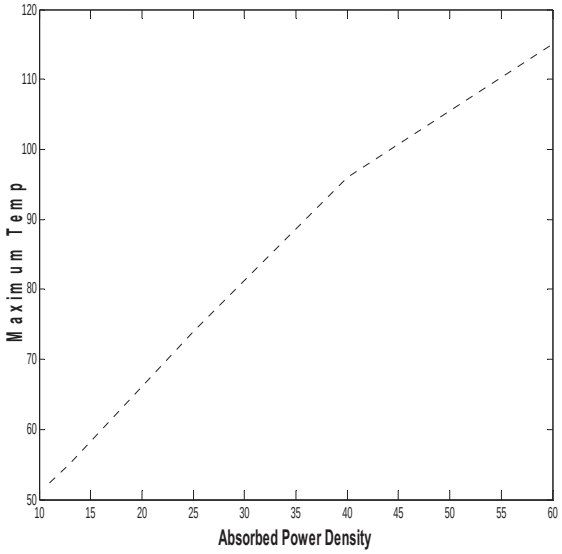


Figure 6. Relationship between absorbed power density and maximum temperature for d=2mm and t=7s.

4 Conclusion

This work presented the analysis of the thermal output produced by HIFU treatment. By increasing distance from the blood vessel to tumor, temperature slightly increased. In our models, the diameter of the large blood vessel is 10mm, which is the typical size of the portal vein. Presence of a large blood vessel next to the tumor is often seen in liver tumors. When ultrasound is focused on tumor adjacent to large vessels, the blood flow would drag thermal energy away from the tissue. Since the vessel was located out of the focal zone, we set the temperature of the blood and the vessel wall to 37°C as an additional boundary condition in our initial model. The temperature on the boundary of the model and the initial temperature of tissue were set to 37°C. Simulation results demonstrated that with the use of HIFU, the temperature at the centre of tumor had most temperature and with the use of more absorbed power density, the temperature at the centre of tumor increased. A shortage of this work is lack of experimental validation of the developed model. When considering the results of this work we have to be aware of the uncertainties and approximations which are associated with modelling complex biological situations with bio heat transfer models. It has to be emphasised that the results only work as a prediction of the used model; the results can't in any way be extrapolated to the real in vivo situation without performing any verifying in vivo experiments. In spite of this the work can be seen as guiding in a qualitative manner when considering HIFU heating and heat transfer in the vicinity of large vessels. Strengthening for the developed model is the attempt to bring together a tissue perfusion model with modelling of blood flow within large vessels.

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