



Intensity Based Simulation of the Temperature Prediction in the Focal Region of Liver Using MRI-Guided High Intensity Focused Ultrasound (HIFU)

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In this research paper a new temperature prediction method is proposed to predict the temperature in liver during thermal ablation which also takes in to account the blood flow cooling. The proposed method suggest a modification of Pennes bioheat transfer equation (PBHTE) inorder to more accurately predict the treatment temperature. The temperature elevation by the proposed heat transfer model is compared with the PBHTE model and the other two heat continuum models by Wulff and Klinger. Appropriate temperature prediction is useful in treatment planning. This may reduce the recurrence level of cancer. Further the reduction in treatment time increases patient safety.

Keywords: Bio Heat Transfer Equation, Temperature Prediction, Pixel Intensity, Convective Cooling, Thermal Models, Blood Perfusion.

1. INTRODUCTION

Liver cancer is one of the most common cause of cancer death in the world.¹ Hyperthermia is one of the treatment modality for cancer and it can be applied in two different ways as local hyperthermia and regional hyperthermia. Thermal modeling during heat therapies such as hyperthermia or ablation is challenging and very important task. In order to achieve therapeutic effect the whole tumor volume must be heated by a prescribed temperature which gives the thermal dose to be given to the patient. Heating of the tumors close to blood vessels is however difficult, due to the heat exchange between tumor and blood vessels, which act as a heat sink. When high temperatures are used to destroy a small area of cells like tumor it is called local hyperthermia or thermal ablation. When the temperature of the whole body is raised above the normal body temperature it improves the results of cancer treatments like radiation, immunotherapy or chemotherapy. This treatment is regional hyperthermia or whole body hyperthermia.² During hyperthermia the region of tumor along with the nearby healthy region gets heated. The temperature in the focal spot increases rapidly from 60 °C–90 °C causes tissue ablation without damage of surrounding tissue.³ The Liver is a highly perfused organ with large number of blood vessels. The major blood vessels flowing through the

liver are hepatic artery, portal vein and hepatic vein.⁴ The most effective diagnostic tools in medicine were developed due to the discovery of imaging techniques such as X rays, ultrasound, radioactivity and magnetic resonance.⁵ High Intensity Focused Ultrasound (HIFU) is a non-invasive method and it uses non-ionizing radiation for treating tumor affected tissues. Ultrasound beams focused on a tissue guided and controlled using Magnetic Resonance (MR) thermal imaging is known as Magnetic Resonance guided focused ultrasound (MRgFUS) technique.⁶ Due to the significant energy deposition at the focus, temperature within the tissue rises to more than 60 °C and completely destroys the tissue.⁷ Accuracy in thermal dose depends on the results from the Computer aided diagnosis. An accurate dose prevents damage to the nearby organ or tissue. Cell death or plasma membrane rupture is caused due to necrosis during HIFU treatment.⁸ It is proven that after the HIFU treatment, percentage of necrosis obtained was only 50%. Partial necrosis may lead to recurrent cancer. One of the main causes of the partial necrosis is convective cooling. Convective cooling occurs due to the effect of heat carried away by the blood vessel or acoustic streaming.^{9,10} The temperature on the surface at a point where therapeutic ultrasound is applied is calculated using PBHTE.¹¹ Diagnostic ultrasound transducer delivers ultrasound with intensities of 0.1 to 100 mW/cm². In contrast, HIFU transducers deliver ultrasound with intensities in the range of

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100 to 10,000 W/cm² to the focal region.¹² Temperature of normal human body is 37 °C.¹³ As per the experimental results proven by Solovchuk et al.¹⁴ for temperature above 85 °C, preboiling or cavitation occurs. Various thermal models are used to predict the temperature fields during HIFU treatment.

The tradition and the basic equation for Bio-heat transfer is framed by Pennes. Pennes Bio-Heat Transfer Equation (PBHTE) is used to calculate the temperature elevation in the tissue.¹⁵ The advantage and limitation of PBHTE are discussed by Khanafer and Vafai.¹⁶ The advantage is that it predicts temperature of the tissue at the focus, and its limitation is that it does not consider the effect of the direction of blood flow. Since the PBHTE do not consider the direction of blood flow, the predicted temperature are often inaccurate. Other thermal models of bio-heat transfer are the extended and modified versions of the original work of Pennes. The limitation of PBHTE is overcome by other heat equations models like Wulff Continuum model and Klinger continuum model.^{17,18} As per Wulff continuum model the blood perfusion term has been considered proportional to the temperature difference between blood and tissue rather than between the two blood streams. The limitation of this model is that, finding the local blood mass flux (v_h) is difficult. In Klinger continuum model the convective heat caused by blood flow inside the tissue is considered during temperature prediction. Hence Klinger continuum model is called as modified Pennes model.

Liver is a highly perfused organ with a large number of blood vessels. When the tumor is located close to the large blood vessels, the well known Pennes bioheat equation can not be used to model the temperature elevation during focused ultrasound therapy. In this case the effect of convective cooling in the blood vessel should be taken into account. To overcome this problem and to predict the temperature in an efficient way, it is proposed to implement a new temperature prediction method based on altering the blood perfusion term. In the proposed method the perfusion rate and viscosity terms of the blood are also taken into consideration.

2. METHODS

Heat transfer within a living tissue has been explained by various thermal models. Standard bio-heat equation was formulated by Pennes. This thermal model roughly predicts the heat transfer within the tissue. Certain shortfalls in Pennes thermal model were overcome by Wulff and Klinger by adding terms for heat convection and blood perfusion.

2.1. Pennes Bio-Heat Transfer Model

Pennes has formulated the very old and standard equation for heat transfer in the tissue. The temperature and the

thermal dose fields are calculated using Pennes bio-heat transfer equation,

$$\rho C_p \frac{\partial T_t}{\partial t} = \nabla \cdot (k \nabla T_t) + q_p + q_m \quad (1)$$

where, ρC_p is the volumetric heat capacity, C_b and C_p are the specific heat of blood and tissue respectively, T_t is the temperature of the tissue, k is the thermal conductivity of tissue, t the time, q_p is perfusion heat, q_m is volumetric metabolic heat generation rate.

$$q_p = \omega \rho_b C_b (T_{ain} - T_{vout}) \quad (2)$$

where ω is the volumetric blood perfusion rate in tissue per unit volume, ρ_b is blood density, T_{ain} and T_{vout} are the temperature of the blood entering the artery and blood leaving the vein respectively. Prior to Pennes model the heat transfer from human body to the surrounding area is found by the thermal conductance and the thermal gradient value. Pennes theoretical contribution was that the rate of heat transfer between blood and tissue is proportional to the product of the volumetric perfusion rate and the difference between the arterial blood temperature and the local tissue temperature. By neglecting the non-unidirectional blood flow, PBHTE produces errors in predicted temperature.

2.2. Wulff Continuum Model

In Wulff continuum model the heat transfer between blood and tissues is proportional to the temperature difference between these two media rather than between the two blood stream temperature. Wulff's equation is given as,

$$\rho C_p \frac{\partial T_t}{\partial t} = K_t \nabla^2 T_t - \rho_b C_b U_h \cdot \nabla T_t + q_m \quad (3)$$

Where U_h is the local mean blood velocity associated with enthalpy flux. The disadvantage of Pennes model was overcome by considering the blood flow direction by accounting the local blood mass flux $\rho_b U_h$.

2.3. Klinger Continuum Model

In Klinger continuum model the convective heat transfer caused by blood flow in the tissue was considered. The spatial and temporal variations of the velocity (v) and heat source, assuming constant physical properties of the tissue and incompressible blood flow the modified Pennes model was expressed as,

$$\rho C_p \frac{\partial T_t}{\partial t} = K_t \nabla^2 T_t - (\rho C)_b v \cdot \nabla T_t + q_m \quad (4)$$

Where k_t , T_t , q_m are the thermal conductivity, tissue temperature (convective heat caused by blood flow inside the tissue) and metabolic heat transfer respectively and v is the velocity of blood considering the spatial and temporal variations.

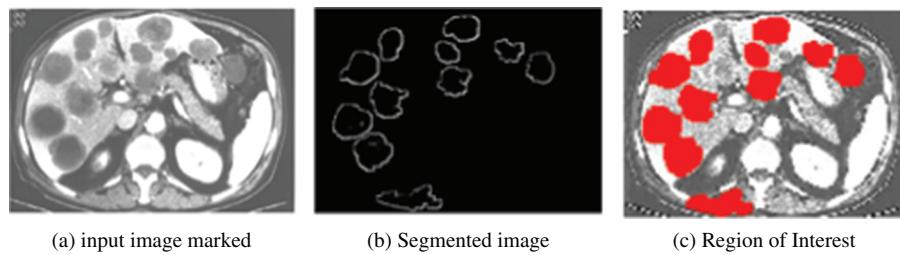


Fig. 1. The region of interest marked after segmentation of the input image



Fig. 2. A portion of the tumor marked in the input image

2.4. Proposed Model

In the proposed model the limitation of PBHTE is overcome by considering the vascular structure of the liver tissue. The three major blood vessels passing through the liver are also taken special consideration because they cause convective cooling. Also applying over dosage of temperature may cause destruction of the vessel wall. So the proper prediction of temperature to be applied on tumor tissue in the liver is the constraint considered in the proposed model. In the existing algorithm the effect of blood flow within the tissue is neglected and so the proposed heat transfer equation of temperature prediction is made by adding the terms from two different bioheat equations and one extra term for dynamic viscosity of blood (μ).^{19,20} Viscosity of blood is a dynamic quantity. It is a

direct measure of the ability of blood to flow through the vessels. Viscosity in normal tissues is lower than in solid tumors.²¹ Hence it has been included to calculate the heat prediction in the proposed method. Equation of the proposed method is,

$$\rho C_p \frac{\partial T_t}{\partial t} = K_t \nabla^2 T_t - (\rho C)_b (V_h + \omega_b + \mu) \nabla T_t + q_m \quad (5)$$

Where V_h is the average blood velocity, ω_b is the perfusion rate of the blood flow and μ is the viscosity of blood. The input image is a CT image of a metastatic liver where cancer has spread from the colon as shown in Figure 1. The Region Of Interest (ROI) is segmented by using a thresholding algorithm after preprocessing steps like edge detection, adding luminance, dilate and erode operations.

MATLAB R2011 a tool is used for simulation. The Gray level intensities of the input image are obtained and tabulated in a $350 * 250$ table. Pixel values other than the ROI are made zero. Temperature prediction is done in the Region Of Interest and the results are obtained. Pixels with low intensities are dark which denotes the region affected with tumor and the healthy region is denoted by high intensity bright pixels. A portion of the tumor region from the input image is marked and shown in Figure 2. The corresponding intensity values of the marked portion is shown in matrix format in Figure 3. The boundary of the ROI is highlighted in the Figure 3. The Portion of the tissue

Fig. 3. The intensity values corresponding to the marked tumor area in Figure 2.

is analyzed by PBHTE, Klinger and Wulff algorithms and the results are compared with the proposed thermal model for proper temperature prediction. The blood and tissue parameters are as discussed in the research papers by Shehata and Tzu-Ching shih.^{22,23}

3. RESULTS AND DISCUSSION

The gray scale pixel intensity shows the variation between the tumor and healthy pixels. Depending on the intensity variation the relevant heat to ablate the tumor tissue is predicted. The simulation results show that the pixel intensities in the range 213 to 73 has temperature elevation from 45.55 °C to 71.01 °C. The lowest pixel intensity in the ROI is 73 and the heat predicted for this pixel is 41.24 °C by PBHTE, 61.5 °C by Klinger, 63.71 °C by Wulff and 71.01 °C by the proposed method. The predicted temperature values show 16.65 °C, 5.23 °C, 4.01 °C rise when compared to the base PBHTE, Klinger and Wulff heat prediction methods. Due to increased temperature the percentage of ablation will also improve. The comparison of heat for the individual pixel intensity values by various temperature prediction models are listed in Table I. As the temperature values above 85 °C causes unwanted effects like preboiling and cavitation, the results obtained shows the safe limit in temperature. Temperature increases with respect to time during HIFU treatment. The predicted temperature values for the proposed thermal model are showing increased values compared to other thermal models. The temperature predicted by the proposed heat prediction model for the lowest intensity pixel value 73 is 71.01 °C and for the high intensity pixel value 213 is 45.55 °C. The graph for the increase in temperature with respect to pixel intensity is shown in Figure 4. The comparison of predicted temperature values for proposed and other heat models are shown graphically in Figure 4. In Table II the temperature elevation predicted by various thermal models are tabulated with respect to time for a single pixel intensity 73. The values are listed only for the pixel intensity 73, as the least pixel intensity value has the highest temperature values predicted. The temperature is predicted for every

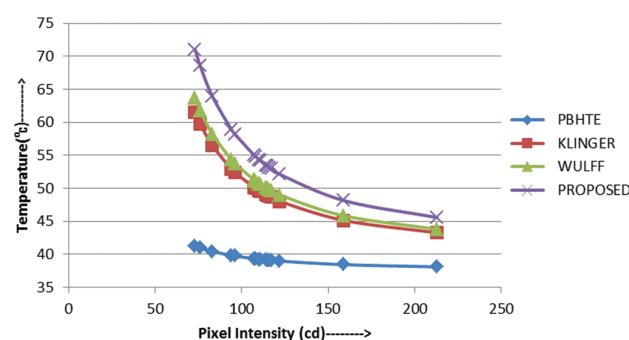


Fig. 4. Comparison of predicted temperature values for proposed and other heat models.

Table I. Predicted temperature values for various thermal models for individual pixel intensities.

Pixel intensity (candela)	Predicted temperature (°C)			
	PBHTE	Klinger	Wulff	Proposed
213	38.07	43.23	43.77	45.55
159	38.42	45.12	45.82	48.13
122	38.95	48	48.96	52.1
117	39.06	48.62	49.63	52.95
116	39.08	48.75	49.78	53.14
115	39.11	48.89	49.93	53.32
114	39.14	49.03	50.08	53.52
111	39.22	49.47	50.56	54.13
110	39.24	49.63	50.73	54.35
108	39.30	49.95	51.08	54.8
107	39.33	50.13	51.27	55.04
96	39.73	52.39	53.75	58.2
94	39.81	52.9	54.3	58.91
83	40.42	56.47	58.2	63.92
76	40.96	59.74	61.78	68.53
73	41.24	61.5	63.71	71.01

0.8 sec. It is seen that the temperature reached in 6.4 sec is 41.24 °C, 61.5 °C, 63.71 °C and 71.01 °C by PBHTE, Klinger continuum model, Wulff continuum model and the proposed heat model. Better removal of tumor tissue can be reached at increased temperature levels for short duration than for low temperature values.

The raise in the temperature predicted by the proposed thermal model is by considering the convective cooling effect caused by the blood vessels passing through the liver. The heat transfer depends on the blood flowing through the blood vessels. As the blood vessels carry away the heat given by the HIFU, the cancer tissue above the blood vessel may need more heat than the other portion without blood vessels. Hence the temperature predicted must be more to compensate the convective cooling. Also, it is seen that the temperature predicted are within the safety range and will not cause any boiling effects to the cancer region. The predicted temperature values are plotted for the corresponding gray scale pixel intensity values. The proposed model results are compared with Pennes BHT, Klinger and Wulff thermal model in Figure 5. The maximum heat predicted by the proposed model is 71.01 °C.

Table II. Increase in temperature with time for various thermal models.

Time (sec)	Predicted temperature (°C)			
	PBHTE	Klinger	Wulff	Proposed
0.8	38.61	38.82	38.83	38.86
1.6	38.67	39.26	39.29	39.38
2.4	38.79	39.9	39.97	40.15
3.2	38.97	40.87	41	41.35
4	39.25	42.44	42.66	43.33
4.8	39.66	45.13	45.57	46.89
5.6	40.28	50.27	51.18	54.06
6.4	41.24	61.5	63.71	71.01

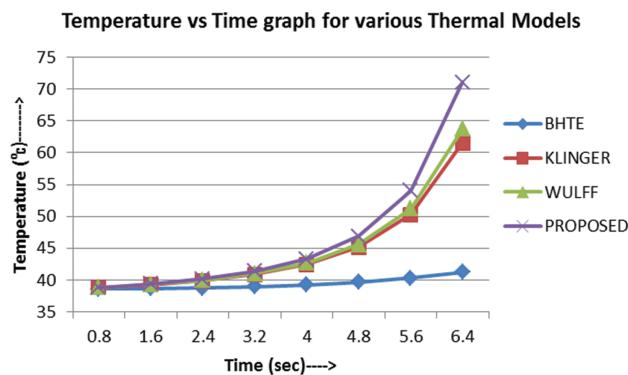


Fig. 5. Temperature versus time plot for various thermal models.

4. CONCLUSION

An intensity based simulation thermal model has been proposed in this research paper. This method predicts the temperature values for the corresponding intensity values and therefore avoids heat applied to the healthy tissues. This model takes into account the convective cooling in the large blood vessel and the perfusion due to capillary flow. The effect of convective cooling may reduce the temperature applied to the tumor tissue. In the proposed thermal model the perfusion rate and viscosity of blood are considered. Therefore the heat carried away by the blood vessels can be compensated by the increase in predicted temperature values. Hence sufficient amount of heat can be applied to the tumor cells for complete ablation. The results can be further used in surgical planning platform for the non-invasive HIFU tumor ablating therapy in real time using MRI liver images.

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