Simulation of Pixel wise temperature prediction for Liver Tumor by High Intensity Focused Ultrasound Ablations.

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Abstract:- Medical imaging has become more challenging in the research field. High-intensity focused ultrasound (HIFU) is a developing medical technology, which allows non-invasive ablation of tumors. Magnetic Resonance Imaging (MRI) plays a vital role in guiding the focused ultrasound. Research in the abdominal area is complicated due to various reasons like respiration, bowel movement, air gaps, vascular pulsations etc. Segmentation of the liver and identifying the region of interest is difficult because of the similarity in the gray level between the liver and the liver lesion. Also in the adjoining regions the gray levels are similar and the lesion types vary from person to person. Thresholding is the simplest and, most commonly used techniques in image segmentation. This technique can be used to detect the contour of the tumor in the Liver. The nonlinear absorption of the biological tissues during HIFU is solved numerically using Kuznetsov, Zabolotskaya and Khokhlov (KZK) equation. The temperature changes in the tissues and the thermal dosage to be applied are determined by the Pennes Bio-Heat Transfer Equation (PBHTE). Other thermal models of bio heat transfer are discussed. They are the extended and modified versions of the original work of pennes. Comparing the Pennes BHTE, Wulff and Klinger the proposed model of heat equation is formed. Thus the temperature and thermal dose to be applied to the region of interest is calculated. Other models for Bio-Heat transfer are compared and the proposed model is derived. The present study aims at improving the accuracy of the thermal dose applied to the region of interest for HIFU thermal ablation, thereby improving the patient's safety, by making significant changes in the present model of heat transfer.

Keywords: MR guided HIFU, Temperature prediction, PBHTE, Thresholding based segmentation, Pixel intensity based prediction, thermal dose .

1. Introduction

Due to the discovery of seminal physical phenomena such as X rays, ultrasound, radioactivity and magnetic resonance and the development of imaging instruments that harness them have provided some of the most effective diagnostic tools in medicine. Data sets in two, three or more dimensions convey increasingly vast and detailed information for clinical or research applications. The diagnostic information when sent in a timely, accurate manner will help the radiologist and the health care systems to give an accurate dosage of medicine without causing any harm to the adjacent organs or tissues. High Intensity Focused Ultrasound is a non-invasive method of treating tumor affected tissues. Magnetic Resonance Imaging (MRI) is a medical imaging technique used in radiology to investigate the anatomy and function of the body in both healthy and diseased environment. This technique is used for medical diagnosis, staging of disease and for follow-up without exposure to ionizing radiation. Hence it is recommended in reference to CT when either modality could yield the same information.

MR images are affected by intensity inhomogeneity, weak boundary, noise and the presence of similar objects close to each other. Applying HIFU to the organs like liver in the abdominal region is complicated due to the major blood vessels passing through. The target organ is below the ribs and so the left liver lobe is easily accessible than the right lobe. Other reasons like air bubbles, normal respiration of patients, bowel or fat as a hindrance to the ultrasonic rays are also

reducing the accuracy of diagnosed heat to be applied. The large blood vessels carry away the heat applied to treat the affected area, and it becomes problematic to achieve complete necrosis of tumors. Magnetic Resonance guided High Intensity Focused Ultrasound (MRgHIFU) is a technique where HIFU beam heats and destroys the targeted tissue in non-invasive way and MRI is used to visualize patient's anatomy and controls the treatment by monitoring the tissue effect in real time. Thermal ablation is related to exposure time. To predict the temperature elevation in the tissue thermal models should be applied. Bio-Heat transfer Equation (BHTE) is the basic and often used model for prediction and the prediction is done based on applied acoustic pressure, absorption rate, Heat diffusion coefficient and Perfusion value [1].

Section 2 presents the literature review of segmentation, liver lesion calculation, Treatment considerations during HIFU and bioheat transfer. Section 3 discusses about the Heat equations and the thermal dose calculation. Results and discussion are made in Section 4. Finally, conclusions are made in section 5.

2. Literature Review

2.1. Liver tumor

Liver tumor is the abnormal growth in the liver [2]. Any tumor can be classified as primary or secondary tumor. Tumors are groupings of abnormal cells that cluster together to form a mass or lump. The unwanted growth of mass or lump disturbs the normal functionality of the human body. Tumors that originate in the liver may be benign and malignant known as primary tumors and the tumor that has spread to the liver from its original source of origin in another part of the body is a secondary tumor.

2.2. Segmentation of the lesion region.

Automatic threshold based liver lesion segmentation method for 2D MRI images are proposed in this paper to determine the Region of Interest (ROI). Although Threshold based segmentation methods produce only rough results in liver tumor segmentation, they can be used to segment the lesion area as the contrast between the lesion and the liver is more significant. In [3,4] threshold based segmentation was used as the main method to segment the tumor. The values for thresholding (i.e.) the higher and the lower limits are identified from intensity information of the grayscale input image. These values are used to isolate tumor directly. Morphological filter was used to mark the tumor from liver tissue. This is done as post-processing. As the output is sensitive to noise the neighborhood pixel values are used to reduce the false detection.

2.3. Lesion value calculation

The liver region is segmented and the morphological operators Dilate and Erode are used to filter the lesion values roughly. After creating morphological structuring element the dilate function returns the maximum value of all neighboring elements, whereas the erode function returns the minimum value. Now the connected components are identified in the binary image. Finally the label matrix is found for further processing. The canny edge detector is used for edge detection in gray scale images. Edge starts with the low sensitivity result and then grows it to include connected edge pixels from high sensitivity result. This helps to fill gaps in connecting edges.

2.4. Treatment with HIFU

The treatment process is classified as pretreatment preparation, treatment planning, ablation strategies and aftercare [5].

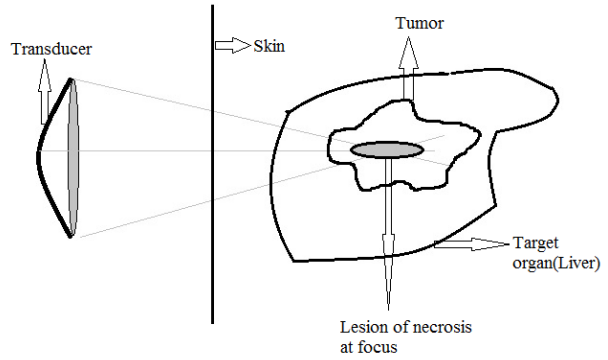

Fig 1: HIFU Treatment (Focusing of target organ using transducer)

During treatment the parameters to be considered are the heat at the focus and focal length of the transducer. The focusing of the target organ using a transducer is shown in the Fig 1. The ideal focal length of transducer is calculated as the sum of the distance from the deepest layer of the tumor to the skin surface and 1 cm safety margin.Treatment to the patients can be given in two ways, one is the linear mode where the transducer moves in linear motion over the treatment area and the ultrasound pulses are shot continuously without interruption as shown in Fig 2. Whereas in the dot mode the ultrasound pulses are shot with time gap as shown in Fig 3. The acoustic power applied to the target area can be varied in the case of dot mode. The linear mode has more risk of skin injury than dot mode where the pulses are shot with time gap.

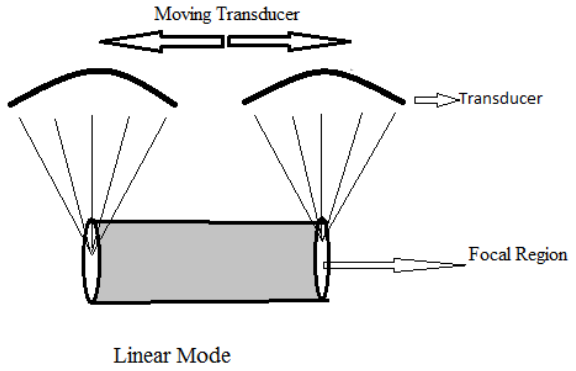

Fig 2: Linear mode of ablation.

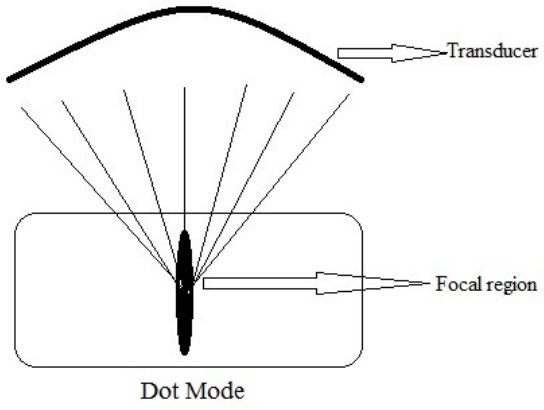

Fig 3: Dot mode of ablation

Thermal therapy like HIFU causes protein denaturation of the infected cells. Cell killing is proportional to the temperature and length of exposure. The amount of damage caused in the tissue can be modeled using Cumulative equivalent minutes (CEM) [6],

$$\text{CEM} = \int_{t0}^{tf} R^{T-Tref}\, dt \qquad (1)$$

R = 0.25 when T < 43^0 and R = 0.5 when T $\geq$ 43^0

T_{ref} is chosen as 43^0 c because this temperature is near the breakpoint during Arrhenius analysis [7]. Arrhenius plot deals with rate of cell killing. 43.5^0c is the thermotolerence for human tissue. R is the number of minutes needed to compensate for a 1^0c temperature change either above or below the breakpoint. The reduction in temperature maxima will reduce the risk of thermal injury, while an increase in temperature minima will increase the tumor response. HIFU ablation is a necrosis process where the coagulation occurs within the time frame of the HIFU treatment. This can be observed immediately after the post treatment in MR imaging. The effects of some common clinically used thermal treatments are listed in the table 1 [8],

Table 1. Thermal effects of various treatments on biological tissues.

Therapy	Temperature Range (°C)	Time requirement	Physical effects
Cryoablation	<-50	<10 min	Complete cellular destruction Freezing
Hyperthermia	41-50	30-60min	Weaken the tumor cells/Increased perfusion
HIFU	50-70	A few sec to 1 min	Protein denaturation / coagulation of

Ablation	>70	A few sec	cellular proteins Membrane rupture/ cell shrinkage

2.5. Bioheat Transfer during HIFU

The three primary heat transport modes are thermal conduction, convection and radiation . Conduction occurs due to temperature gradients in living tissues. Convection involves movement of heat from one place to another via the motion of blood through the circulatory system. Radiation occurs in the treated region due to the heat radiated in all directions. Heat is absorbed during HIFU treatment and Kuznetsov, Zabolotskaya and Khokhlov (KZK) equation is a generalized equation for calculating the frequency dependent absorption in the tissue. The temporal average intensity and heating rate calculated using the KZK equation. The heat transfer in the tissue and the temperature rise is modeled based on Penne's Bio-Heat Transfer Equation (PBHTE). Thus the temperature and thermal dose to be applied to the region of interest are calculated.

3. Heat equations and thermal dose calculation

The Kuznetsov, Zabolotskaya and Khokhlov (KZK) equation is solved numerically in frequency domain and so it is replaced by a coupled set of nonlinear partial differential equations [9]. The physical phenomena of the living tissues are studied by the Bio-Heat Transfer Equations (BHTE). The traditional and the basic one is the Penne's bio-heat transfer equation. Other thermal models of bio heat transfer are the extended and modified versions of the original work of penne's [10]. Thus the temperature and thermal dose to be applied to the region of interest is calculated. Various methods are analyzed for studying the temperature of the tissue during treatment planning. The Penne's bio - heat transfer equation for blood perfused tissues is written as,

$$(\rho C_\rho)_t \frac{\partial Tt}{\partial t} = \nabla.(K_t \nabla T_t) + q_p + q_m \quad (2)$$

Where q_p, q_m, ρ_t ,C_ρ,T_t , K_t ,t are the heat convention, metabolic heat transfer, tissue density, specific heat of blood, temperature of tissue, thermal conductivity and time respectively. The advantage of BHTE is that it predicts temperature fields and it is used in hyperthermia modeling. The limitation of BHTE is that it does not consider the effect of the direction of blood flow. The limitation of BHTE is overcome by Wulff Continuum model and Klinger continuum model [11]. In Wulff continuum model the heat transfer between blood and tissues is proportional to the temperature difference between these 2 media rather than between the two bloodstreams temperatures. Wulff's equation is given as,

$$(\rho\, C_\rho)_t \frac{\partial \mathbf{Tt}}{\partial \mathbf{t}} = \boldsymbol{\nabla}.(\mathbf{k}_t \boldsymbol{\nabla} \mathbf{T}_t) - \rho_b V_h C_b \boldsymbol{\nabla} T_b - \boldsymbol{\nabla} H_b \boldsymbol{\nabla}\phi \quad (3)$$

Where V_h and H_b are local mean blood velocity and specific enthalpy of blood respectively. The disadvantage of this method is that the local blood mass flux is hard to determine. The disadvantage of Penne's bio heat model is that it neglected the effect of blood flow within the tissue, to overcome this, in Klinger continuum model the convective heat caused by blood flow in the tissue was considered. Heat source and velocity of blood flow inside tissue was considered and the modified penne's model equation is as,

$$(\rho\, C_\rho)_t \frac{\partial \mathbf{Tt}}{\partial \mathbf{t}} + (\rho\, C)_b V_0 \boldsymbol{\nabla} \mathbf{T}_t = k\, \boldsymbol{\nabla}^2 T_t + q_m \quad (4)$$

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. The blood and tissue parameters are listed with their values as discussed elsewhere [12,13],

Nomenclature:

Parameters	*Abbreviations*	*Values(units)*
K_b	Thermal conductivity of blood	K_b = 0.5W/ m/K
K_t	Thermal conductivity of tissue	K_b = 0.5W/ m/K

q_p	Heat convection	
q_m	Metabolic heat source	$q_m = 700$ W/m^3
T_t	Tissue temperature	(celcius)
w_b	Volumetric rate of blood perfusion in tissue per unit volume	$w_b = 0.5$ kg/m^3/s
ρ_b	Blood density	$\rho_b = 1050$ kg m^{-3}
C_b	Specific heat of blood	$C_b = 3770$ J/kg/^{o}c
H_b	Specific enthalpy of blood	$H_b = 13.7$ wm^{2o}c
W_{b1}	Blood perfusion rate	$W_{b1} = 0.00125$ kg/m^3/s
μ	Viscosity of blood	$\mu = 0.004$ kg/m/s
V_h	Local mean blood velocity	$V_h = 10.5$ m/s
Subscripts		
b	Blood	
t	Tissue	

Comparing the Pennes BHTE, Wulff and Klinger the proposed model of heat equation is formed. The blood perfusion rate(W_{b1}) and the dynamic viscosity of blood(μ) values are considered in the calculation of thermal dose for the proposed model .

$$(\rho C)_t \frac{\partial Tt}{\partial t} = K_t \nabla^2 T_t - (\rho C)_b V \nabla T_t - (\rho C)_b (w_b + \mu) \nabla T_t + q_m \quad (5)$$

4. Result and discussion

A cancer affected liver image is taken for analysis, the pixel values are analyzed for two set of pixel intensities set A and set B and the results are plottedin Table 3 and 4. Both set of values are taken from the total pixel intensities of the gray scale input image. They are two sets of 3 x 3 values taken for analysis. Set A pixel intensities are in the range 114 to 196. The proposed model has reduced the over prediction of temperature for the intensity value 114. So when the over prediction is corrected , the unwanted heat applied to the tissue is avoided. For the next intensity value 126, both the models predict the same temperature value. This temperature value is taken as breakpoint. Below this breakpoint value the temperature predicted is increasing, due to considering the parameters blood perfusion (W_{b1}) and blood viscosity (μ). And above the breakpoint temperature the temperature predicted has reduced.

Table 3. Set A- Elevation in temperature values for PBHTE vs Proposed heat model.

Pixel Intensity (Candela)	Elevation in temperature	
	PBHTE	Proposed heat model
114	84.70195	81.99984
126	78.13434	78.51421
127	77.34939	78.52047
146	69.18063	74.24557
148	68.39726	73.85524
148	68.39726	73.85524
149	68.00544	73.88179
176	60.17813	69.56939
196	55.85021	67.62164

The graph for Table 3 is shown in the Fig 4. Fig 4 shows the close relationship between the PBHTE and the proposed heat prediction model. At a certain point the graph meets and then diverts. Tissue boiling is avoided as the proposed heat prediction model has not predicted heat above 85^{0}c.

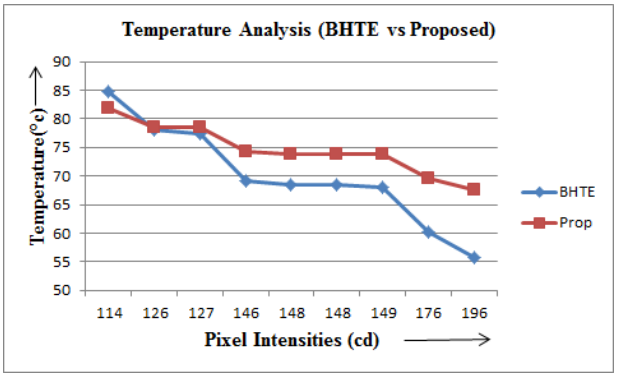

Fig 4: Temperature analysis for PBHTE and Proposed method SET A values.

Elevation in temperature values are plotted for PBHTE vs Proposed heat model for values Set B in Table 4.

Table 4. Set B- Elevation in temperature values for PBHTE vs Proposed heat model.

Pixel Intensity (Candela)	Elevation in temperature	
	PBHTE	Proposed heat model
107	89.32471	84.3177
108	88.94889	83.92999
110	87.40564	83.1576
111	86.6317	83.16753
114	84.70195	81.99984
116	83.54884	81.2749
117	82.7696	81.23283
122	80.06692	79.68127
122	80.06692	79.68127

Set B pixel intenities are in the range from 107 to 122. The temperature prediction for the proposed heat model has shown decresing values than the PBHTE model. The graph for table 4 is plotted in Fig 5.

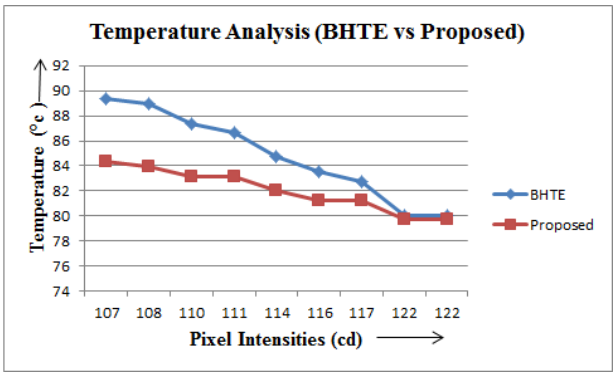

Fig 5: Temperature analysis for PBHTE and Proposed method SET B values.

Table 5: Combined temperature values for SET A & B.

Intensity	BHTE	Proposed
107	89.32471	84.3177
108	88.94889	83.92999
110	87.40564	83.1576
111	86.6317	83.16753
114	84.70195	81.99984
116	83.54884	81.2749
117	82.7696	81.23283
122	80.06692	79.68127
126	78.13434	78.51421
127	77.34939	78.52047
146	69.18063	74.24557
148	68.39726	73.85524
149	68.00544	73.88179
176	60.17813	69.56939
196	55.85021	67.62164

Dose value is decreased avoiding over dosage

Similar response

Dose value increases due to increased accuracy

By combining both SET A and SET B values and eliminating the repeated values the Table 5 is obtained. The range of pixel intensities from 107 to 122 has predicted decreased temperature values avoiding overdosage when compared with PBHE model. Pixel intensity 126 has shown similar response for both the heat models PBHTE and proposed.

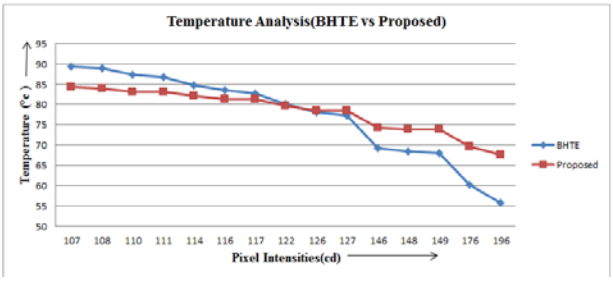

Fig 6: Combined temperature analysis for SET A & B.

Remaining pixel intensities in the range 127 to 196 has shown increased heat prediction taking into consideration the convectional heat carried away by the blood vessels passing through the liver. The graph for Table 5 is plotted in Fig 6.

In the above figure the temperature values are plotted for the intensity values of 3*3 lesion area chosen. In the graph the three points are noticed. First one is that the over prediction in the first value is corrected in the proposed method. Second the next value is overlapping means there is equal prediction. This point can be considered as the breakpoint. Then from the breakpoint value the graph is increasing. The increased values of temperature denote the improving accuracy. The number of iterations the temperature has to be applied to the focal point depends upon the depth of the tumor. The tumor is focused such that it is 8 cm from the transducer. Analysis of temperature rise with respect to time is done for the pixel value 156. Number of sonication considered is 10, and from the results obtained it is found that the present approach has decreased the number of iterations of dose. Thus the exposure time of a patient to the radiations is reduced.

5. Conclusion

The new prediction algorithm has reduced the over prediction of the temperature values and also improved the prediction of tissue temperature in the necessary pixels where the acoustic streaming due

to larger blood vessels flowing through the liver is considered. As temperature greater than 85degree Celsius causes tissue boiling and may lead to severe damage to the nearby region or pixels, the proposed heat prediction model has shown the maximum heat predicted for highly infected tissue intensity 107 as 84.3177^0c. Further this method can be improved by increasing the acuuracy of tumor area prediction. In this research paper threshold based segmntation is used and in future other efficient segmentation techniques like active contours can be used for better segmentation.

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