Analysis on the Healthy Pixels in the Region of Tumor and the Untreated Tumor Pixels in the Boundary during High Intensity Focused Ultrasound Interventions.

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Abstract: - Magnetic resonance based High Intensity Focused Ultrasound Interventions is a leading non-invasive heat treatment for the ablation of the tumor. A new pixel based heat prediction method is proposed in this research paper. MATLAB tool is used for the pixel wise heat prediction in an abdominal CT image with metastatic tumor in the liver which has spread from colon. The simulation result of the proposed method has increased the heat to be applied to the tumor tissue, thereby decreasing the time taken to apply the heat. The number of healthy pixels that will be damaged by using the proposed heat prediction algorithm and the untreated tumor pixels in the boundary of the tumor region is analyzed in this paper.

Keywords: - Bio-heat transfer equation, Region of Interest (ROI), HIFU, Thermal dose, lesion, metastatic liver.

1 Introduction

Cancer is a leading cause of death worldwide, accounting for 8.2 million deaths in 2012. One of the most common cause of cancer death is liver cancer and about 7, 45, 000 people die every year due to this [1]. High Intensity Focused Ultrasound (HIFU) is a non-invasive method that uses non-ionizing radiation for treating tumor affected tissues [2]. Ultrasound beam is focused on a tissue chosen for ablation and it is guided and controlled using Magnetic Resonance (MR) based thermal imaging. This is known as Magnetic Resonance guided focused ultrasound (MRgFUS) technique [3]. The input at the transducer face is very low in the range of 20 to 40 Watts/cm^2 and it is translated to very high intensity of 1600 to 2000 Watts/cm^2 at the focal point. Due to the significant energy deposition at the focus, temperature within the tissue rises to more than 55^0c and completely destroys the tumor tissue [4]. The temperature and the thermal dose fields are calculated using Pennes Bio-Heat Transfer Equation (PBHTE)[5]. Accuracy in thermal dose depends on the results from the Computer aided diagnosis. An accurate dose prevents damage to the nearby organ or tissue.

Thermal ablation is related to exposure time. Thermal models are used to predict the temperature elevation in the tissue. Pennes Bio-Heat transfer Equation (PBHTE) is the basic and often used thermal model for temperature prediction during HIFU interventions. The prediction is done based on applied acoustic pressure, absorption rate, heat diffusion coefficient and perfusion value [6]. After the treatment the damaged tissue is known as the lesion. The amount of damage caused in the tissue is measured using Cumulative Equivalent Minutes (CEM) [7]. Cell killing is proportional to the temperature and length of exposure. The lesion size can be controlled by the amount of heat applied to the tumor tissue, the transducer parameters (acoustic intensity, pulse duration and frequency) and tissue parameters (attenuation coefficient and perfusion rate). Transducer parameters play a major role in deciding the lesion size than the tissue parameters [8].

In this research paper a CT image of metastasis in liver tumor is analyzed. Any abnormal cell that cluster together to form a mass or lump and disturbs the normal functionality of the particular organ in the human body is a tumor. Liver tumor is the abnormal growth in the liver [9]. Any tumor can be classified as primary or secondary tumor. 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.

In the input image taken for analysis the tumor is a secondary tumor as it has originated from colon. Ablation through HIFU destroys the structure of the tumor cell and therefore the further multiplication of the tumor cell is reduced. After HIFU treatment the healthy cells supports in transforming the ablated cell in to a healthy tissue. The image in Fig 1 shows a model of tumor cells surrounded by healthy cells.

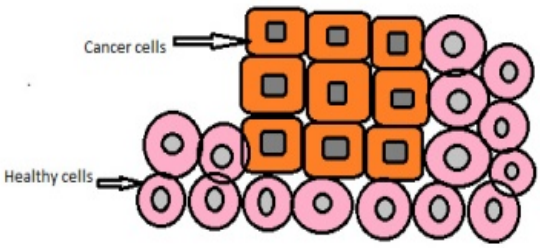

Fig 1: A model arrangement of cancer cells surrounded by healthy cells.

2. Problem Formulation

2.1. Heat prediction models

The heat transfer in the tissue and the temperature rise is modeled based on Pennes Bio-Heat Transfer Equation (PBHTE) [10]. Thus the temperature and thermal dose to be applied to the region of interest are calculated. The physical phenomena of the living tissues are studied by the Bio-Heat Transfer Equations (BHTE). The tradition and the basic one is the Pennes bio-heat transfer equation. Other thermal models of bio-heat transfer are the extended and modified versions of the original work of Pennes. The Pennes bio-heat transfer equation for blood perfused tissues is written as,

$$(\rho C_\rho)_t \frac{\partial T_t}{\partial t} = \nabla.(K_t \nabla T_t) + q_p + q_m \qquad (1)$$

where q_p, q_m = 700 W/m^3, ρ_t, $(C_\rho)_t$, T_t, K_t, t are the heat convention, metabolic heat transfer, tissue density, specific heat of tissue, temperature of tissue, thermal conductivity and time respectively. The advantage of PBHTE is that it predicts temperature fields and it is used in hyperthermia modeling. The limitation of PBHTE is that it does not consider the effect of the direction of blood flow. The limitation of PBHTE is overcome by Wulff continuum model and Klinger continuum model [11,12]. Wulff's equation is given as,

$$(\rho C_\rho)_t \frac{\partial T_t}{\partial t} = \nabla.(k_t \nabla T_t) - \rho_b V_h C_b \nabla T_b - \nabla H_b \nabla \phi \qquad (2)$$

where V_h, H_b, ρ_b, C_b and T_t are local mean blood velocity, specific enthalpy of blood, density of blood, specific heat of blood and tissue temperature respectively. The disadvantage of this method is that the local blood mass flux is hard to determine. The disadvantage of Pennes bio-heat model is that it neglects 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 written as,

$$(\rho C_\rho)_t \frac{\partial T_t}{\partial t} + (\rho C)_b V_0 \nabla T_t = k \nabla^2 T_t + q_m \qquad (3)$$

Where k_t, T_t, q_m and V_0 are the thermal conductivity, tissue temperature (convective heat caused by blood flow inside the tissue), metabolic heat transfer and the non-uniform velocity field respectively. The blood and the tissue parameters [13,14] and their values are discussed by comparing the Pennes BHTE, Wulff and Klinger and then the proposed model of heat equation is formed.

3. Problem Solution

3.1. The proposed equation

The blood perfusion rate (ω_b) and the dynamic viscosity of blood (μ) values are added in the calculation of thermal dose for the proposed model. In the existing algorithm the effect of blood flow within the tissue is neglected and so in the proposed algorithm the perfusion rate and viscosity terms are taken into consideration. Equation of the proposed algorithm is,

$$(\rho C)_t \frac{\partial T_t}{\partial t} = k_t \nabla^2 T_t - (\rho C)_b V \nabla T_t - (\rho C)_b \omega_b \nabla T_t - (\rho C)_b \mu \nabla T_t + q_m \qquad (4)$$

Where V= 10.5 m/s is the average blood velocity, ω_b = 0.5 kg/m^3.s is the perfusion rate of the blood flow and μ= 0.004 kg/m.s is the viscosity of blood.

3.2. Healthy and tumor pixels in the boundary of Region of Interest (ROI).

The tumor region is extracted from an input abdominal CT image shown in Fig 2. The tumor region (i.e.) the Region of Interest (ROI) with the

background is plotted in Fig 3. The most basic morphological operations used are dilation and erosion. For Dilation, the value of the output pixel is the maximum value of all the pixels in the input pixel's neighborhood. In a binary image, if any of

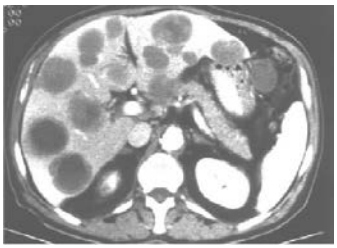

Fig 2. An abdominal CT image of a metastatic tumor in liver.

the pixels is set to the value 1, the output pixel is set to 1, and for erosion, the value of the output pixel is the minimum value of all the pixels in the input pixel's neighborhood [15].

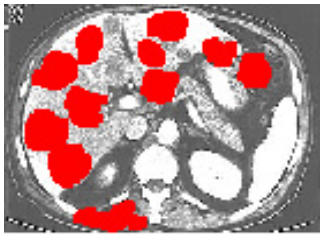

Fig 3. ROI identification from the input image after segmenting the tumor affected region in the liver.

The surrounding pixels of the ROI are known as the boundary of ROI. The boundary has mixed intensity values of healthy and tumor infected pixels as known in Fig 4.

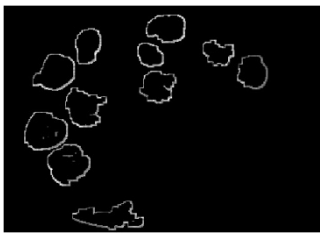

Fig 4. The boundary of the ROI

As per the proposed algorithm, the predicted heat is applied to every pixel in the Region of Interest. The proposed heat prediction method has shown approximately 10^0c rise than the PBHTE model. As the heat predicted has increased the time for treatment of HIFU has decreased. The temperature values are predicted for all pixel intensities in the input image. The input image is plotted as grey scale intensities in a mesh of size 350 x 250.

3.2.1. Healthy pixels in the region of tumor

In Fig 5, a portion of tumor of size 31 x 29 from the total 350 x 250 mesh is taken into consideration for further analysis. The region of tumor is surrounded by the boundary pixels. The boundary pixels are highlighted with yellow color. There are totally 115 pixels in the boundary and 632 pixels in the ROI. Seventy healthy pixels in the intensity range of 200 to 255 lies in the tumor affected region where HIFU treatment is planned. Therefore 11.07% of healthy pixels are in the ROI. But as the heat is predicted pixel wise the healthy pixels get a very low heat to be applied. This does not damage the healthy pixels. A list of heat predicted by both the PBHTE model and the proposed model for healthy pixel is given in Table 1. For the maximum pixel intensity value the heat predicted by the proposed algorithm is 36.7359^0c. This value is approximately equal to the normal body temperature 37^0c. Healthy pixels are not damaged as the temperature has not crossed the thermotolerence range of 55^0c, above which ablation occurs. PBHTE model has predicted 39.5334^0c temperature which is 3^0c greater than the proposed model. This equals at the pixel intensity 222 and again the heat predicted by the proposed model has increased for the pixel intensity 202.

Table 1. Healthy pixel intensities and their corresponding heat prediction by PBHTE and proposed method.

Sl.No	Pixel intensity (Cd)	Predicted temperature (°c)	
		PBHTE	Proposed
1	192	41.0405	45.0048
2	202	40.6761	43.2152
3	222	40.1031	40.2828
4	244	39.6998	37.78
5	246	39.6676	37.5812
6	255	39.5334	36.7359

3.2.2. Tumor pixels in the boundary of ROI

In the lesion taken in analyzing the pixels there are totally 115 pixels in the boundary of ROI. Out of the 115 pixels in the boundary, only 3 pixels are there in the intensity range 100 to 152 which needed heat to be applied. Therefore 2.6% of tumor pixels are there in the boundary.

In Table 2, a set of 20 pixels and their heat predicted are listed. The base heat prediction model PBHTE has shown temperature values in the thermotolerence range. Tissue removal occurs between the temperatures 55^0c to 85^0c. By the proposed heat prediction model, the predicted

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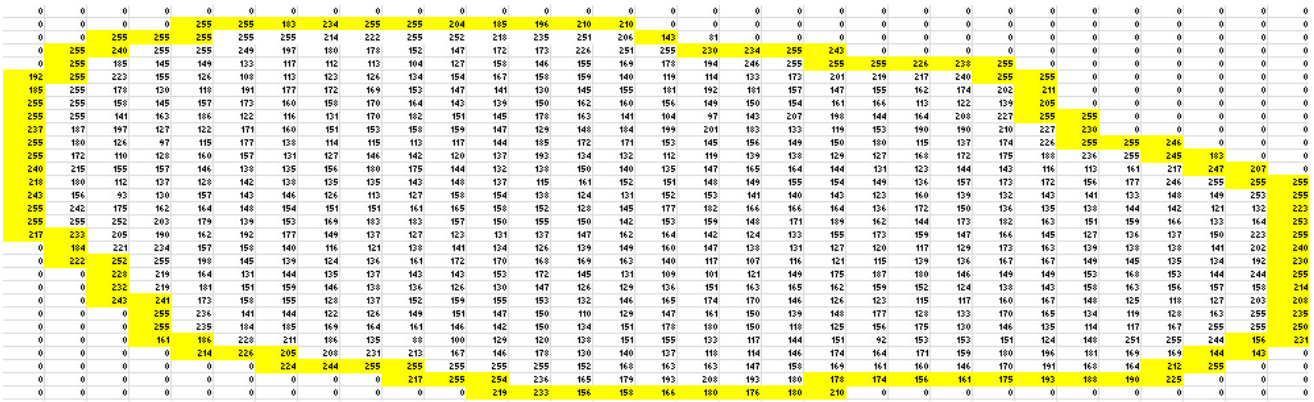

Fig 5. A Portion of tumor of size 27 x 29 taken from the input image of size 350 x 250. Yellow color represents the boundary of the tumor.

Table 2. Boundary based tumor pixels and their predicted temperature values of PBHTE and proposed heat prediction algorithm.

Sl.No	Pixel intensity (Cd)	Predicted temperature (°c)	
		PBHTE	Proposed
1	100	64.336	94.469
2	113	53.706	79.327
3	114	53.175	78.329
4	117	51.739	75.6736
5	121	50.13	72.4575
6	127	48.216	68.225
7	128	47.944	67.5799
8	132	46.96	65.1501
9	133	46.738	64.578
10	134	46.525	64.0189
11	135	46.319	63.4727
12	141	45.237	60.4409
13	144	44.778	59.0673
14	145	44.635	58.6285
15	146	44.497	58.1981
16	147	44.363	57.777
17	148	44.234	57.3651
18	149	44.109	56.9608
19	150	43.988	56.5647
20	152	43.757	55.7955

values are in the range of tissue ablation (i.e.) 55.79^0c to 94.46^0c. The pixels which have intensity less than 100 have the predicted temperature greater than 85^0c. After this maximum temperature the heat applied saturates for pixels less than 100. The above results of the predicted temperature were obtained only by MATLAB simulation and were not experimentally taken inside the tumor.

4. Discussion

When comparing the results of the proposed research paper with relevant papers,

The base temperature is taken as 37.6^0c by taking the standard value as absorption coefficient for human tissue. Also the temperature at the highly focused region is 65^0c in average and in the off focus regions the temperature is 42^0c [16]. In the proposed research paper the base temperature of human tissue is taken as 37^0c for simulation. And the predicted heat has reached 64.49^0c in an average at the highly focused region. In the region of non interest the temperature is 40.1^0c in an average. A MRI parameter, Magnetization transfer ratio (MTR) is used to identify the HIFU treated and non-treated tumor tissue. Also the temperature has raised up to 66^0c [17]. The region after applying heat is segmented as above 50^0c, 55^0c, 60^0c. The absolute highest temperature measured for a single pixel was 97.8°C [18]. In the proposed paper the highest temperature measured for a single pixel was 94.46^0c.

4. Conclusion

The proposed heat prediction method predicts heat pixel wise to be applied to the tumor. From the analysis made in the input image, the total number of pixel in the boundary of ROI is 1862. Out of this 289 pixels are tumorous. Therefore 15.52% of the pixels in the boundary are tumorous. In the region of interest there are totally 13073 pixels out of which 795 are healthy. Therefore 6.08% of healthy pixels are along with tumor pixels in the ROI. Another advantage of the proposed heat model is that the heat predicted for the healthiest pixel with intensity 255 is 36.73^0c. This equals the normal body heat.

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