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Microwave Ablation Therapy for Hepatocellular Carcinoma: The Effect of Metabolic Heat on Temperature Distribution

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ABSTRACT

Hepatocellular carcinoma is the main cause of liver cancer and one of the most occurring cancers worldwide. Microwave Ablation (MWA) is a method to destroy cancer cells by heating tumours above 50°C. Cancerous tissues can have high metabolic heat rates and affect temperature gain and distribution in thermal therapies. This research clarifies the metabolic heat effects in MWA therapy of liver cancer. Using Pennes Bioheat transfer equation with finite element numerical method, this research simulates temperature distribution with metabolic heat value ranging from 368,1 W/m3 to 29000 W/m3. The heat generated by metabolic heat is lower than the MWA heat source. However, the temperature increase should be considered as it can increase healthy surrounding tissue temperature to dangerous levels.

Keywords:

Microwave ablation; Cancer treatment; Metabolic heat; Bioheat transfer; Hepatocellular carcinoma

1. Introduction

Liver cancer has a high incidence rate and ranks sixth among the most commonly found cancers. Hepatocellular carcinoma (HCC) is the most common type and accounts for approximately 90% of liver cancer cases [1]. Hyperthermia methods, especially the application of thermal ablation to cure cancer, have been a topic of great interest in the last two decades [2] . Hyperthermia is a therapeutic procedure in which biological tissues are heated above 40°C and above 50°C for thermal ablation [2-4]. This heat is enough to destroy harmful tissues (cancer).

One of the newest thermal ablationtherapyused is microwave ablation (MWA) [5]. Microwave ablation (MWA) operates on the basic principle of dielectric heating. In its application, MWA generates an electromagnetic field around the insulated antenna. This electromagnetic field causes the rotation and vibration of dipole molecules. Polar molecules, such as water (H_2O), have dipole moments, so the water molecules continually align their poles with the alternating electromagnetic field. The electromagnetic force generated causes molecular collisions, thereby increasing the energy of the molecules in the vicinity. Ions inside body tissues also oscillate due to changes in the pole direction of the molecules influenced by the electromagnetic field (H_2O), resulting in dielectric

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heating [2] . MWA devices use two main frequencies, 915 MHz and 2450 MHz. The 2450 MHz frequency is the most commonly used, while the 915 MHz frequency can achieve deeper penetration [6,7] . MWA devices typically operate using input power ranging from 0 Watts to 150 Watts [8]. The MWA system has several components, including [9]: a microwave generator, coaxial cable, and microwave antenna. The effectiveness of MWA, also known as complete ablation, involves destroying the target tissue without leaving any residual disease tissue (cancerous tissue) [10] . MWA therapy is given by adjusting the antenna placement and the MWA device settings to ensure tissue destruction within a 10 mm tolerance around the tumour [9].

The metabolism plays a major role in controlling body temperature. Numerous factors, such as age, gender, heat conductivity, activities, body surface area, body weight, and a lot of other things, affect metabolic rate. The metabolic rate increases along with kinetic energy. As a result, body temperature increases. Hormones also increase the body's metabolic rate in other circumstances, such as illness (fever). Thermal energy, which is produced by an increased metabolism, keeps the body warm, blood circulating, breathing, and organs and cells functioning [11] . Abnormal tissues (cancer) can have a high metabolic heat rate. Healthy body tissues in a normal state have a metabolic heat rate of approximately 368.1 W/m^3. While in abnormal conditions, the metabolic heat rate can increase to 29000 W/m^3 [12].

The purpose of hyperthermia treatment is to elevate the temperature of the tumour above normal levels without causing damage due to high temperatures in the surrounding healthy body tissues. Inadequate temperature control can lead to thermal damage from excessively high temperatures in the patient's body's healthy tissues or even result in death [4,7] . Therefore, this study was conducted to understand the temperature distribution in human liver tissue during MWA procedures for HCC therapy under unsteady conditions and influenced by metabolic heat.

This study is possible by utilizing the PennesBioheat transfer equation which enables an understanding of heat transfer that occurs inside human body tissues. This also allows further use of the equation to model and understand hyperthermic phenomena in medical practices today [4,13] . Previous work such as Wahyudi *et al.*, [13] , Shrestha *et al.,* [11] and Panda and Das [12] acknowledges the use of bioheat transfer for studying thermal effects in the human body and the effects of tissue metabolic heat in tissue temperature.

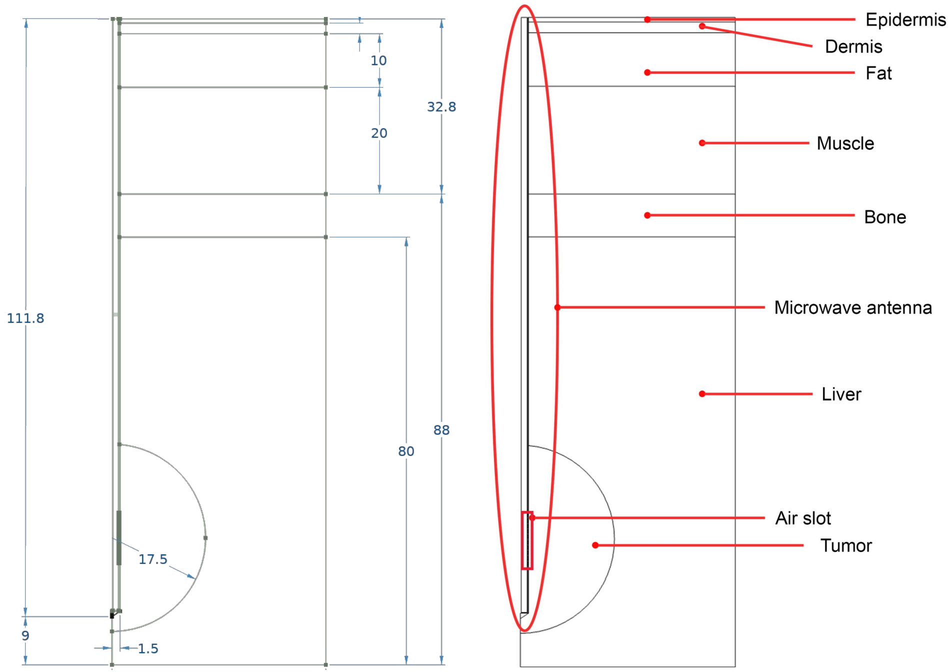
This research studies the effect of metabolic heat in MWA therapy for HCC. Six layers of tissue are considered; epidermis, dermis, fat, muscle, liver bone, and HCC tumour The heat source from the microwave antenna focused on the HCC tumour. This study aims to simulate the temperature rise caused by metabolic heat and the differences of temperature distributions to surrounding healthy tissues with increasing value of metabolic heat using the finite element numerical method with the assistance of COMSOL Multiphysics 5.6 software.

2. Methodology

The goal of this work is to model the temperature distribution inside the human body during microwave ablation (MWA) therapy using a numerical finite element technique (FEM) based on a literature review. Bioheat transfer equations and COMSOL Multiphysics 5.6 software are used to solve the FEM. This study also looks at the effect of metabolic heat on the distribution of hepatic temperature in individuals in non-steady conditions. The values of metabolic heat (368.1, 7000, 14000, and 29000 W/m^3) are used.

2.1 Determining the Geometry

The geometry used in this research follows the antenna design used in the study by Wang *et al.,* [14]. The heat source in this therapy is a microwave antenna inserted into the body and positioned at the cancer site. Geometry creation for this study was done using a 2D axisymmetric model in COMSOL Multiphysics 5.6, including six layers of body tissue with the addition of tumour tissue. The tissue geometry used in this research is shown in Figure 1.



(a) (b)

Fig. 1. 2D (a) Geometry and (b) naming of biological tissues used in simulation

2.2 Governing Equation

The Pennes' Bioheat transfer equation is used to understand the temperature distribution that occurs in the human body tissues [15], as shown in Eq. (1).

$$\rho c \frac{dT}{dt} = k\nabla^2 T + \rho_b c_b \omega_b (T_a - T) + Q_m + Q_{ext} \tag{1}$$

Where ρ is the tissue density, c is the specific heat of the tissue, k is the thermal conductivity of the tissue, ω_b is the blood perfusion rate, c_b is the specific heat of blood, ρ_b is the blood density, T_a is the blood vessel temperature, T is the observed tissue temperature, Q_m is the metabolic heat generation rate, and Q_{ext} is the external heat source. The heat generation produced by the microwave antenna can be considered an external heat source that generates heat within the tissue. The equation used to determine the amount of heat generated is Eq. (2) [15]:

$$Q_{ext} = Q_{MWA} = \frac{1}{2}\sigma\left|E^2\right| \tag{2}$$

Where σ is the electrical conductivity of tissues and E is the electric field. The value of E is solved using the electromagnetic wave equation Eq. (3) [15]:

$$\nabla \times \mu_r^{-1}(\nabla \times E) - k_0^2\left(\varepsilon_r - \frac{j\sigma}{\omega\varepsilon_0}\right)E = 0 \quad (3)$$

Where μ_r is the value of relative permeability, k_0 is the constant of electromagnetic waves in vacuum, ε_r is the relative permittivity, ω is the angular frequency and ε_0 is the electromagnetic permittivity in vacuum which has a value of 8.85 x 10^{-12} F/m.

2.3 Research Parameters

This research will focus on understanding the temperature distribution inside the human body during MWA therapy with a frequency of 2,45 GHz, input power of 10 Watts, and therapy duration of 10 minutes. The core body temperature is considered to be 37°C, and the value of blood perfusion is assumed to be constant at 0.0002 /s. The parameters used in this research include the thermal and physical properties, as well as the tissue electrical properties of the human body as shown in Table 1 and Table 2 respectively.

Table 1
Tissue thermal and physical properties

Tissue	Thickness [m] [16]	Density [ρ][16-18]	Thermal Conductivity [k] [16-18]	Specific Heat [C_p][16-18]
Epidermis	0,0008	1200	0,24	3598
Dermis	0,002	1200	0,45	3300
Fat	≈0,010	911	0,21	2348
Muscle	≈0,020	1090	0,49	3421
Bone	≈0,008	1908	0,32	1313
Tumour	-	1040	0,57	3960
Liver	-	1079	0,52	3540
Blood	-	1060	0,5	3600

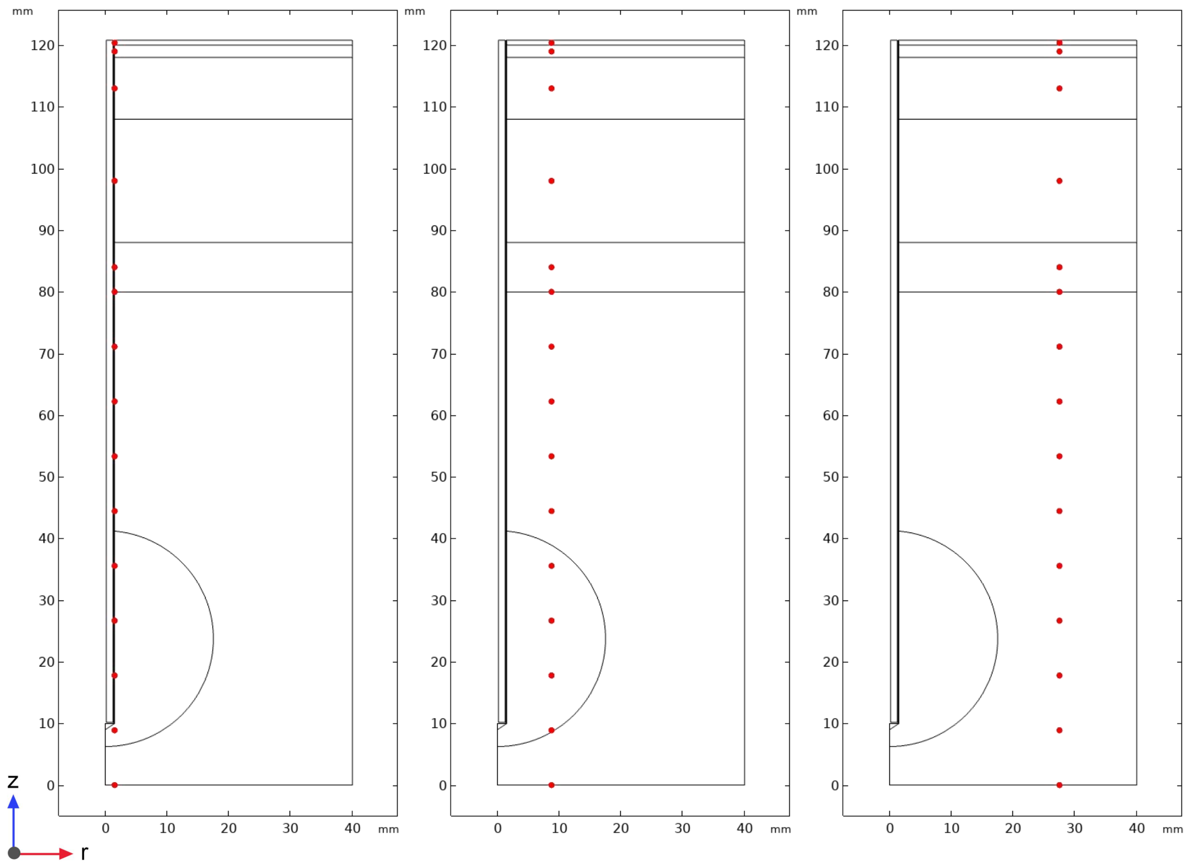
Themicrowave antenna's electrical properties are stated in Table 2.

Table 2
Tissue and antenna electrical properties

Tissue	Relative Permittivity [ε_r] [15,18-21]	Relative Permeability [μ_r] [15,19]	Electrical Conductivity [σ][15,18,20,21]
Epidermis	38	1	1,46
Dermis	38	1	1,46
Fat	12	1	0,82
Muscle	49,6	1	2,56
Bone	4,8	1	0,21
Liver	44,3	1	1,8
Tumour	54,8	1	2
Dielectric	2,03	1	0
Catheter	2,6	1	0
Air slot	1	1	1

2.4 Data Extraction

The data analysis was conducted using 2D axisymmetric geometry with cylindrical coordinates, namely, coordinates r and z. Temperature data is collected every 1 minute (total duration of 10 minutes) from 45 points as shown in Figure 2. These points represent probes where temperature data was collected along the human body's tissues, including the tumour, liver, bone, muscle, fat, dermis, and epidermis. The probes were placed at coordinates r = 1.51mm, 8.75mm, and 27.5mm. The differences in r coordinates were intended to examine the horizontal temperature distribution. Then, they were distributed along the z-axis at 15 points to examine the vertical temperature distribution, specifically at coordinates z = 0mm, 8.89mm, 17.78mm, 26.67mm, 35.56mm, 44.44mm, 53.33mm, 62.22mm, 71.11mm, 80mm, 84mm, 98mm, 113mm, 119mm, and 120.4mm.



(a) (b) (c)

Fig. 2. Temperature probe placement for data extraction at (a) r = 1.51, (b) r = 8.75, (c) r = 27.5

3. Results

3.1 Temperature Distribution Analysis on Tissue Surrounding the Microwave Antenna

This research employed the governing equation with an unsteady state. The graph in Figure 3 shows temperature data obtained from 15 probes along the z-axis with coordinates r = 1.51. At t = 0 minutes, along the z-coordinate, the initial condition was at a temperature of 37°C, and the temperature gradually increased until it reached the highest temperature when t = 10 minutes. It indicates that the duration of MWA therapy affects the achieved temperature, and the tissue's temperature increases over time [22].

The highest tissue temperature occurred at probe with coordinates z = 17.78, with a temperature of 85.801°C, and the lowest temperature occurred at coordinates z = 120.4, with a temperature of 37.058°C. It is due to the distance from the MWA heat source, which is the air slot in the microwave antenna. Consequently, the highest temperature values are achieved in tissues closest to the air slot and gradually decrease as the distance from the air slot increases [23].

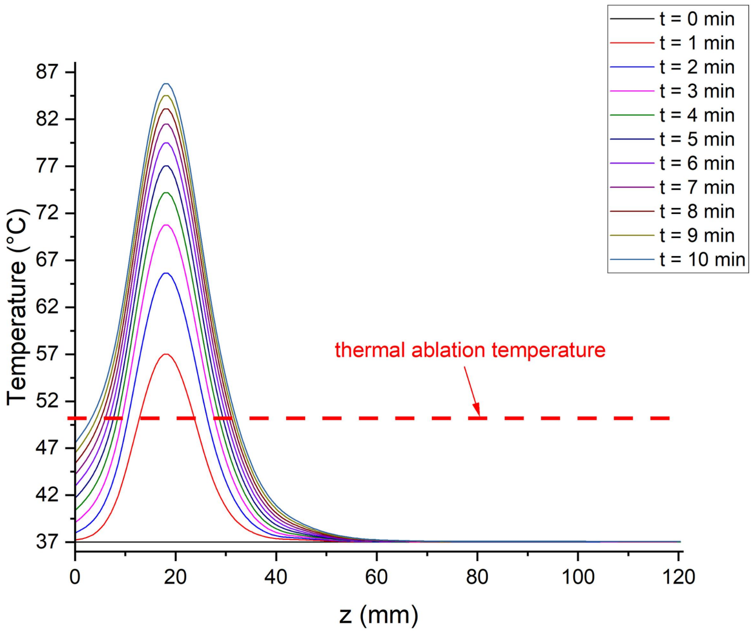


Fig. 3. Temperature distribution on microwave ablation therapy along r = 1,51 and Qm = 368,1 W/m³

3.2 Metabolic Heat Effects on Temperature Distribution

The graph in Figure 4 shows the differences in temperature distribution that occur in tissues after 10 minutes of microwave ablation therapy with variations in metabolic heat values (368.1; 7000; 14000; 29000) W/m³. The graph shows that the lowest temperature distribution is represented by 368.1 W/m3, and the largest temperature distribution is represented by a metabolic heat value of 29000 W/m3. It is in line with the current theoretical basis, which states that the quantity of heat produced by metabolism affects the amount of heat produced in biological tissues [11] . The value of metabolic heat directly influences the tissue temperature. Higher metabolic heats result in higher tissue temperature [24] . The relationship between metabolic heat and the resulting temperature is in Figure 5.

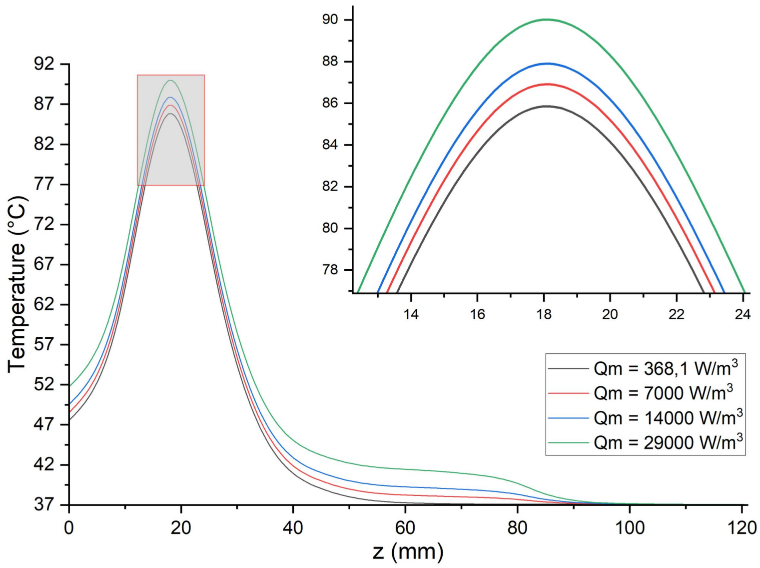


Fig. 4. Comparison of temperature distribution along r = 1.51 mm on t = 10 min with every metabolic heat value

Figure 5 depicts the graph illustrating the effects of metabolic heat on temperature gain at the probe nearest to the MWA air slot, located at coordinates r = 1.51 and z = 17.78 as tissues undergo MWA therapy. The x-axis represents the metabolic heat value, while the y-axis represents the maximum temperature gained. The graph demonstrates that temperature increases as the metabolic heat value increases. It aligns with Pennes' bioheat transfer equation used in this research, where the metabolic heat value is directly proportional to the temperature value. As shown in Figure 5, the temperature increase resulting from the difference in metabolic heat values from 368.1 W/m^3 to 29000 W/m^3 is approximately 4.162 °C. Although this number may seem small compared to the heat generated by the MWA heat source, this temperature increase can cause damaging temperatures in surrounding healthy tissues [25].

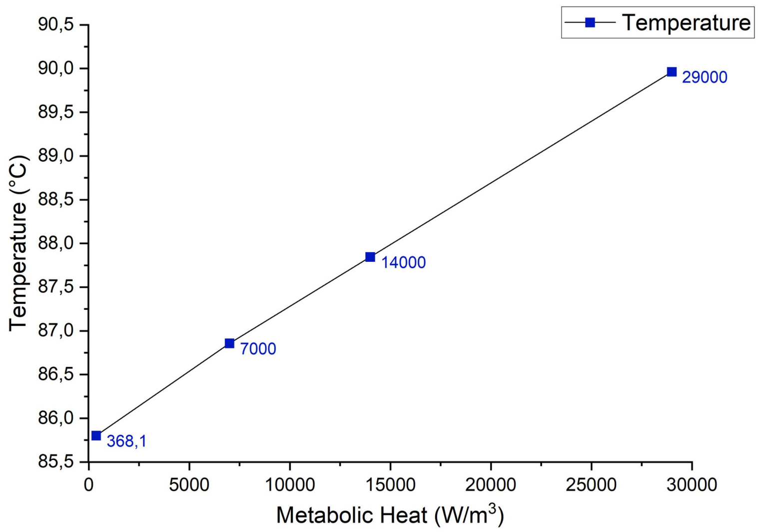
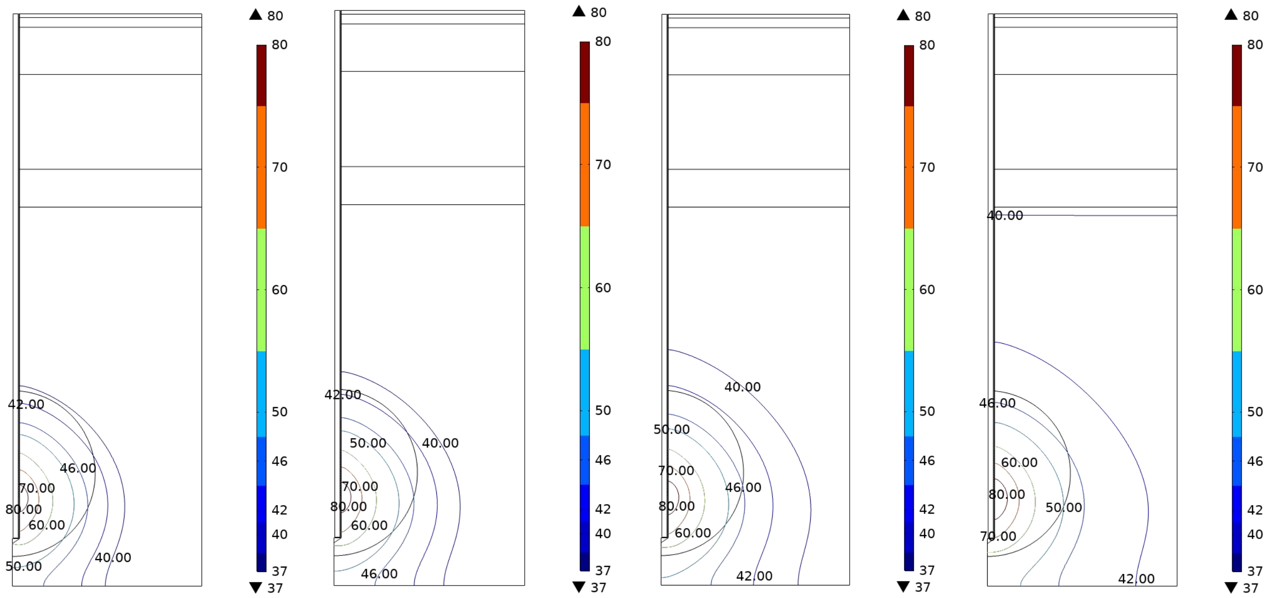


Fig. 5. Effects of metabolic heat on temperature gain on the tissues throughout the microwave ablation therapy

3.3 Contour Analysis on the Effects of Metabolic Heat

Figure 6 shows contours for metabolic heat values of 368.1 W/m^3; Qm = 7000 W/m^3; Qm = 14000 W/m^3; Qm = 29000 W/m^{3}after 10 minutes of therapy. It is evident from the temperature distribution contours that for all variations of metabolic heat values, temperatures exceed 50°C. Temperatures >50°C are the values aimed for to destroy cancer tissue [2].

Results show that metabolic heat within the tissue can increase the temperature achieved and the temperature distribution in MWA therapy. It is apparent in Figure 6 that as the metabolic heat value in tissue increases, areas of the tissue reaching hyperthermic (>42°C) and ablation temperature levels (>50°C) become much more extensive. However, the temperature generation from ablation is not evenly spread within the entire tumour region. Some parts do not reach temperatures above 50°C. Additionally, there are healthy tissues that experience temperatures above 50°C, which can cause damage. Inconsistency in temperature distribution may due to the placement of the microwave antenna in a less optimal position relative to the tumour geometry [26].



(a) (b) (c) (d)

Fig. 6. Temperaturedistributioncontouron t = 10 min withvariations; (a) Qm = 368,1 W/m^3; (b) Qm = 7000 W/m^3; (c) Qm = 14000 W/m^3; (d) Qm = 29000 W/m^3

3.4 Comparison with Previous Study

We compared the temperature distribution results obtained in this study to a previous study conducted by Radjenovi´c *et al.*, [27] . This study discussed the most optimal input power for microwave ablation therapy. Their research used the finite element numerical method with the assistance of COMSOL Multiphysics software, employing the liver and tumour geometry from the 3D-IRCADb-01 liver tumour database and applying microwave ablation power of 13 Watts. A good similarity in the temperature trend at specified points can be observed. The temperature trend observed is an increase in temperature throughout the therapy.

4. Conclusions

A study on the influence of metabolic heat in microwave ablation therapy for HCC cancer treatment was done using finite element numerical methods with the assistance of COMSOL Multiphysics simulation software. From this research, it is apparent that temperature is directly related to MWA therapy time. Therefore, the temperature achieved by the tissue will increase along with the duration of the MWA therapy. However, temperature is inversely related to distance. It can be seen by the lower temperature achieved in tissues away from the MWA antenna air slot.

Metabolic heat influences the temperature distribution inside human body tissues. An increase in metabolic heat value will directly raise the temperature in that particular tissue and effects the surrounding tissue temperature as well. Although the influence exerted by metabolic heat is relatively small compared to the primary heat source in MWA therapy, the temperature increase should be considered since it can elevate the temperature of healthy tissues to damaging levels.

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