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Effect of Blood Perfusion on Temperature Distribution in the Multilayer of the Human Body with Interstitial Hyperthermia Treatment for Tumour Therapy

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ABSTRACT

Blood perfusion is defined as the volume of blood flowing through units of tissue volume per second. In thermoregulation, blood perfusion is a factor that affects heat transfer in the body, the greater the rate of blood perfusion will complicate the distribution of temperature throughout the body. In the study of bioheat transfer, heat transfer in the human body can be used as a therapy. At therapeutic temperatures (above 40°C), cells will die and stop their growth or commonly called hyperthermia therapy. It can allow thermonecrosis in body tissues and can be useful for tumour tissue. Of the various types of hyperthermia therapy, interstitial hyperthermia therapy is considered more effective because heat is directly delivered to tumour tissue to minimize other tissues exposed to therapeutic temperatures. Currently, there are no studies that study the effect of blood perfusion on the treatment of interstitial hyperthermia, even though blood perfusion greatly affects the temperature distribution in the human body/ In this study, heat transfer analysis will be performed on five layers of the human body, namely the epidermis, dermis, fat, muscle, and bones with interstitial application of hyperthermia therapy and affected by blood perfusion with a value of ($8x10^{-4}$; $4x10^{-4}$; $2x10^{-4}$; $1x10^{-3}$; and $2x10^{-3}$)/s completed using finite element method with unsteady conditions in two axial dimensions. The part of the tumour studied is a tumour in the arm (forearm) in the span of 600s. This study shows that blood perfusion affects the value of temperature distribution in five layers of the body in unsteady conditions. The greater the value of blood perfusion flowing in the body, the more difficult the temperature will be to transmit because the blood distributes heat throughout the body faster, the difference between blood perfusion values is quite significant.

1. Introduction

Blood perfusion as described by Dymling *et al.*, [1] is defined as the volume of blood flowing through units of tissue volume per second. According to Ricketts *et al.*, [2], blood perfusion is a major part of thermoregulation, this is because blood perfusion is responsible for the transportation of oxygen, nutrients, and waste products. In thermoregulation of the body, it is necessary to pay

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attention to factors that can affect heat transfer in the body so that the body does not experience tissue damage. Luitel *et al*., [3] explain there are some factors that can affect thermoregulation in the body include ambient temperature, blood perfusion, tissue thermal conductivity, metabolic rate, and heat transfer coefficient. The difference in the rate of blood perfusion in each person will affect the transfer of heat in the human body. Shirkavand and Nazif [4] explain that the greater rate of blood perfusion in the human body will complicate the distribution of temperature in the human body, this is because the temperature is first distributed throughout the body by the blood so that there is a balance of temperature in the human body.

Thermoregulation in the human body is intended so that the temperature of the human body is maintained under certain circumstances. Due to the temperature of the environment that can change, there will always be heat transfer between the human body and the environment to achieve equilibrium in the human body. Abidin and Misro [5] explain that heat transfer is a study of thermal energy transport within a medium of molecular interaction, fluid motion and electromagnetic waves resulting from a spatial variation in temperature. The study that studies heat transfer in biological systems is called Bioheat Transfer. Bioheat Transfer is studied with the aim of developing new medical treatments or minimizing the effects of adverse conditions.

According to Pennes [6], bioheat transfer in human tissue includes heat transfer in the bloodstream, organ systems, and thermal response of body tissues from the influence of stimulus outside those tissues. Bioheat transfer research aims to find out thermodynamic and biological phenomena that occur in the human body. The average normal core body temperature is 37°C and can range from 33.2 - 38.2°C. According to Tansey and Johnson [7], changes in body temperature beyond the normal range can be fatal. At a body temperature of about 42°C it can result in the death of body tissues and at a body temperature of about 27°C it can result in respiratory distress. 40°C – 45°C can cause the destruction of malignant cells and thermonecrosis in tumor tissue without affecting the surrounding tissues.

Extreme temperatures in the human body itself can be utilized for medical needs. Cells that harm the human body can be turned off by raising the temperature to a therapeutic temperature or about 40 - 45°C around the cell to be turned off and stop its growth, the therapy is commonly called hyperthermia therapy. According to Siauve and Lormel [8], hyperthermia therapy can be used for treatment methods of various cancerous tissues such as breast, liver, lung, cervical, bone, head, and neck. One type of hyperthermia therapy is interstitial hyperthermia, where interstitial hyperthermia uses a coaxial antenna as a heat source to directly deliver heat to the tumor and can provide temperatures exceeding 40°C without giving excess heat to the surrounding tissue. According to Gas [9], tissues that hit therapeutic temperatures (above 40°C) are about 1-2 cm away from the antenna. This allows for the healing of tumors in the human body with a diameter not exceeding 5 cm.

There is a type of tumor called Ewing Sarcoma (ES) which is a type of tumor that has a high degree of malignancy. Ewing sarcoma tumor is the second most bone tumor with the most cases in the age range of 10-30 years. One of the locations of the ewing sarcoma tumor is in the bone in the lower arm (forearm). According to Gozal and Djakaria [10], using a combination of chemotherapy treatments, surgery, and treatment using radiotherapy or increased temperature in tumors, it can reduce the 5-year survival rate from <10% to >60% in patients with Ewing Sarkoma Tumor.

According to Haghniaz *et al*., [11], heat transfer between the environment and the body occurs in the skin layer. The skin layer itself is divided into two, namely the epidermis and dermis. The epidermis will then release heat into the environment by convection, radiation, and evaporation by sweat. In addition to the skin layer, heat transfer in the human body is generally in the fat, muscle, and bone layers. According to Barnoon and Ashkiyan [12], at a temperature of 40°C – 47°C the cell will lose its loss to divide and will begin to die. Then it should be considered so that tissues other than tumors so that at normal temperatures. Therefore, observations are needed to determine the appropriate temperature distribution at the time of interstitial application of hyperthermia therapy so as not to damage other tissues. To find out the distribution of temperature in the human body during the interstitial application of hyperthermia therapy, the Pennes equation is used which is solved by finite element method in two dimensions with an unsteady state.

The purpose of this study was to determine the distribution of temperature during the application of interstitial hyperthermia therapy in five layers of the body for tumor therapy.

2. Methodology

The method used in this study is the completion of using finite element method to determine the distribution of temperature in human body tissues that are treated interstitial hyperthermia therapy. The study also looked for the influence of blood perfusion on the distribution of temperature in human body tissues in unsteady conditions. The blood perfusion values used are ($8x10^{-4}$, $4x10^{-4}$, $2x10^{-4}$, $1x10^{-3}$, $2x10^{-3}$)/s. The study will be done with preprocessing, solver, and post processing.

2.1 Pre-processing

Pre-processing is the initial stage of the completion process in this study. In this study, heat transfer was observed in two axial and unsteady dimensions. The steps in pre-processing are:

i. Parameter determination:
There are several parameters that are set before conducting research, namely:
(a) Parameters of the physical properties of the layers of the human body on the hands
The parameters of the physical properties of the layers of the human body on the hands are shown in Table 1 [13, 14].

Table 1
Parameters of the physical properties of the layers of the human body on the hands

	Thickness, l (m)	Density, ρ (kg/m^3)	Thermal Conductivity, K (W/mK)	Specific Heat, C_p (J/KgK)
Epidermis	0,0008	1200	0,24	3598
Dermis	0,002	1200	0,45	3300
Fat	≈0,010	937	0,21	3258
Muscle	≈0,020	1000	0,5	4000
Bone	≈0,008	1920	0,44	1440
Tumor	-	1079	0.52	3540
Blood	-	1000	0,64	4200

(b) Design geometry parameters
The geometry of the design used is two axial dimensions with five layers of the human body namely the epidermis, dermis, fat, muscle, and bones with tumor tissue as the heat destination of the antenna slot as in Figure 1 with units used in millimeters. The design of the antenna slot in Figure 2. Parameters of design geometry as in Table 2 [9].

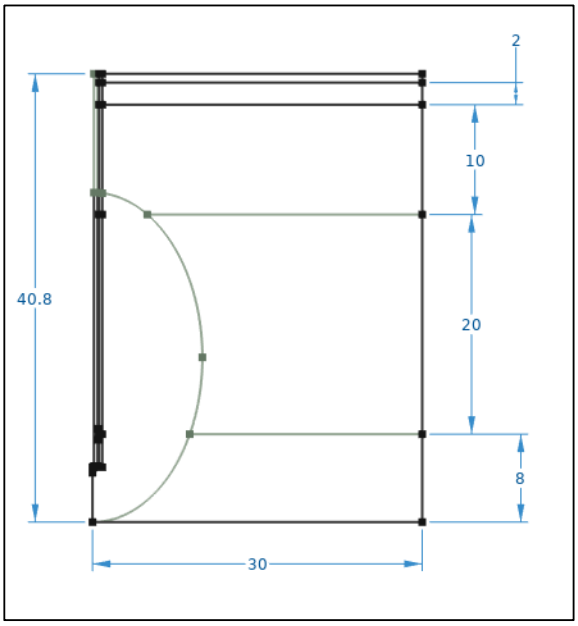


Fig. 1. Study Geometry Design

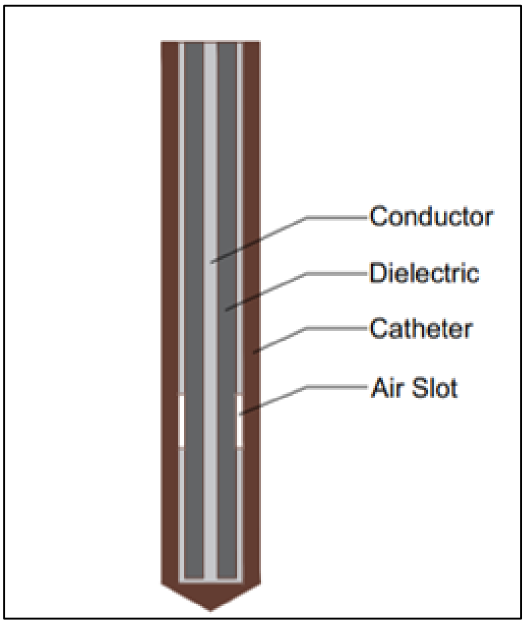


Fig. 2. Antenna Slot design

Table 2
Parameters of the physical properties of the layers of the human body on the hands

Property	Symbol	Value
Inner radius of the central conductor	r_1	0.135 mm
Inner radius of the outer conductor	r_2	0.47 mm
Outer radius of the outer conductor	r_3	0.595 mm
Radius of the catheter	r_4	0.895 mm
Size of the air slot	d	1 mm
Major axis – tumor	a	10 mm
Minor axis – tumor	b	15 mm

(c) Electrical parameters
Electrical parameters of human body tissues and antenna slots are shown in Table 3 [15].

Table 3
Parameters of the physical properties of the layers of the human body on the hands

	Relative permittivity, ε_r	Relative permeability, μ_r	Electrical conductivity, σ (S/m)
Epidermis	38	1	1.46
Dermis	38	1	1.46
Fat	10.8	1	0.27
Muscle	52.7	1	1.74
Bone	5.3	1	0.095
Dielectric	2.03	1	0
Catheter	2.06	1	0
Air slot	1	1	1

(d) Core body temperature (37°C)
(e) Power Input 1W
(f) Frequency 2.45 GHz

ii. Governing Equation

The governing equation used in this study is the Pennes Equation as shown as Eq. (1) under unsteady conditions. And the external heat source equation shown in Eq. (2).

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

$$Q_{ext} = \frac{1}{2}\sigma \hat{E}.\hat{E}^* = \frac{\sigma|\hat{E}|^2}{2} \tag{2}$$

iii. Meshing

Meshing is the process of dividing components to be analyzed into smaller elements. In this study, there were 5584 domain elements and 805 boundary elements. The meshing used in this study is shown in Figure 3.

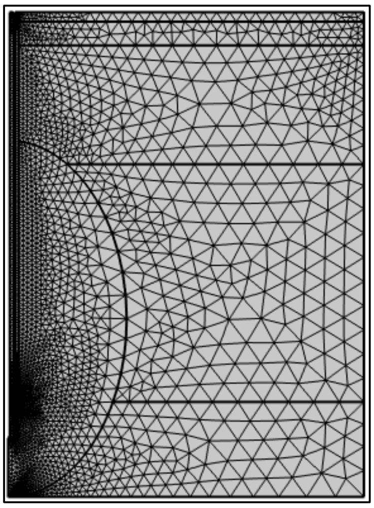


Fig. 3. Meshing

iv. Node spacing determination

Nodes are points in the research area that will be analyzed the results of the temperature distribution. In this study, the nodes will be spread along five layers of the body at r = 1mm. On the z-axis, nodes are spread along 0-0.00402 meters by searching for Δz as shown in Eq. (3).

$$\Delta z = \frac{L}{M-1} \tag{3}$$

Where z is distance between nodes on the z axis (m), L is total layer thickness (m), and M is Number of nodes. In determining the distance between 11 nodes, the equation used is as shown in Eq. (4).

$$\Delta z = \frac{L}{M-1} = \frac{0.0402\ m}{11-1} = 0.00402\ m \tag{4}$$

The distance between nodes is defined by Figure 4.

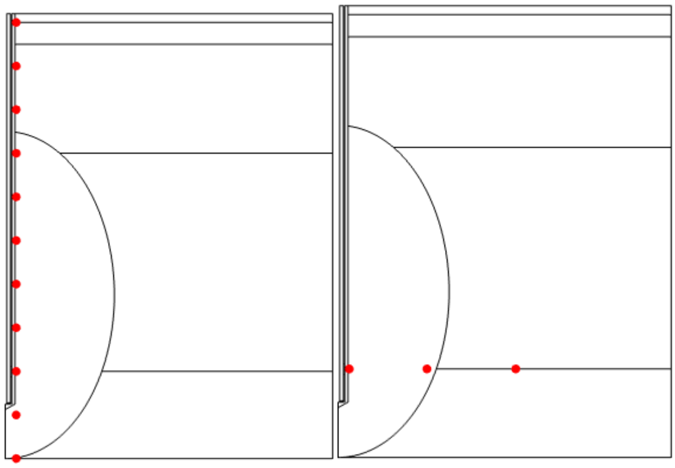


Fig. 4. Defining research nodes

2.2 Solver

The solver process in this study used Comsol Multiphysics Software to help solve Pennes equations. There are two studies used, namely frequency domains to solve electromagnetic equations and time dependent to solve bioheat transfer equations.

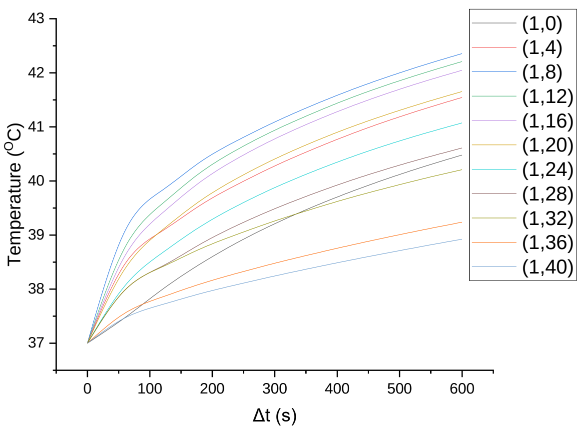
2.3 Post Processing

In the post-processing stage, there will be an analysis of the results and discussion of the research that has been done. Analysis of the results in the form of a graph of the temperature distribution of finite element method results with a variation of blood perfusion.

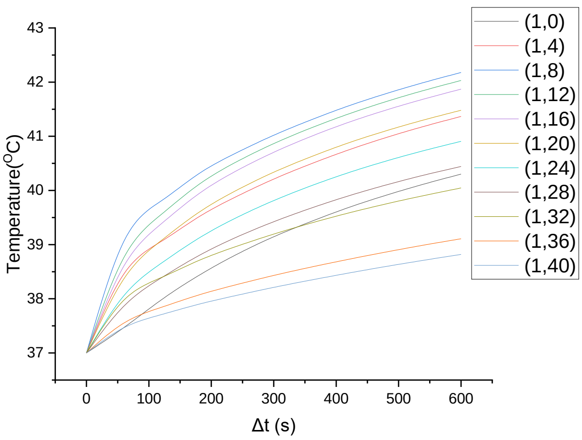
3. Result

3.1 Analysis of Temperature Distribution in Five Layers of the Body with Unsteady and Two Axial Dimensions

In Figure 5 shown a graph of temperature distribution at r = 1 mm with 11 nodes spread in the body layer from the bone to the epidermis with the placement of tumor tissue. node one to node eight are inside the tumor tissue, node 9 and 10 are on the fat tissue and node 11 are on the epidermal tissue. Defining of research nodes as in Figure 4 and solved using the Eq. (1) and Eq. (2).



(a)



(b)

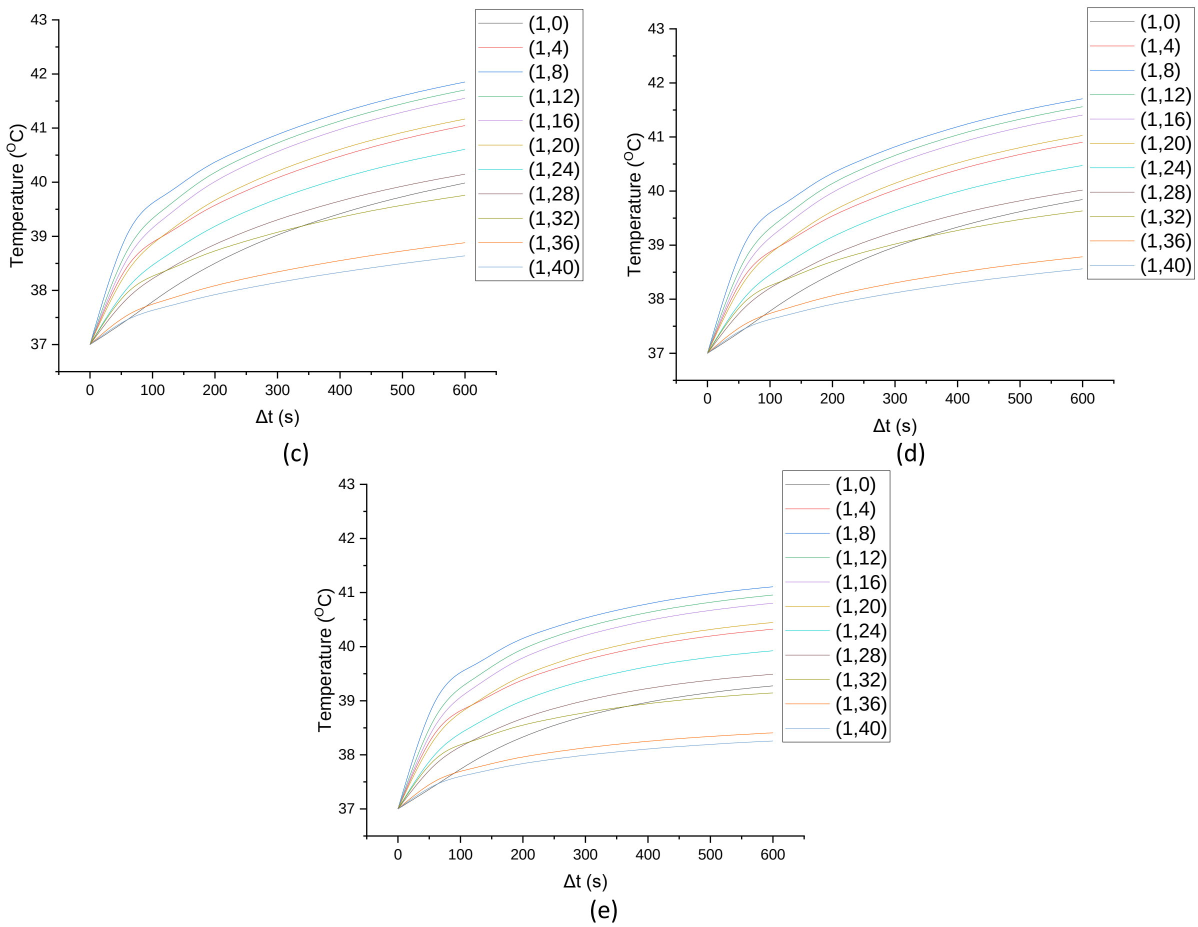


Fig. 5. Graph of temperature distribution at r = 1mm with variations in blood perfusion values, namely (a) ωb=2x10^{-4}/s, (b) ωb=4x10^{-4}/s, (c) ω =8x10^{-4}/s, (d) ω =1x10^{-3}/s (e) ωb=2x10^{-3}/s

In Figure 5, a graph of temperature distribution with variations in perfusion values is displayed, Figure 5(a) ωb = 2x10^{-4}/s, (b) ωb = 4x10^{-4}/s, (c) ωb = 8x10^{-4}/s, (d) ωb = 1x10^{-3}/s (e) ωb = 2x10^{-3}/s. In Figure 5(a), Figure 5(b), and Figure 5(c), the temperature on each node continues to increase over time. Meanwhile, in Figure 5(d) and Figure 5(e) the temperature increases to the 400th second and tends to increase slopingly from the 400th second to the 600th second. This indicates that the displacement in Figure 5(d) and Figure 5(e) of temperature equilibrium is faster to achieve compared to Figure (5a), Figure 5(b), and Figure 5(c). This happens because the greater the rate of blood flowing, the more blood will distribute the temperature throughout the body [4].

The increase in temperature with the increase in time due to the Pennes Equation used, the temperature value is directly proportional to the amount of time, therefore the longer the time of interstitial application of hyperthermia therapy, the greater the temperature value. The use of low power input (P = 1W) will take a longer duration in the application of interstitial hyperthermia, but can make it easier to control the temperature distribution in each body tissue [9].

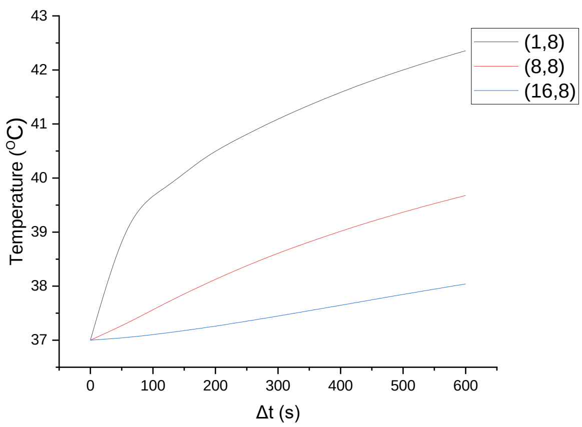
From the results of the temperature distribution above, it can also be seen that the highest temperature value is at the node (1,8) and the lowest is at the node (1,40). This is due to the influence of the node distance to the heat source, namely the microwave antenna slot. The temperature in the body tissue will be smaller with the distance from the air slot antenna, and the largest temperature value will be obtained by the network closest to the air slot antenna [9].

3.2 Analysis of The Distribution of The Norm to the Distance from The Air Slot with Unsteady Conditions and Two Axial Dimensions

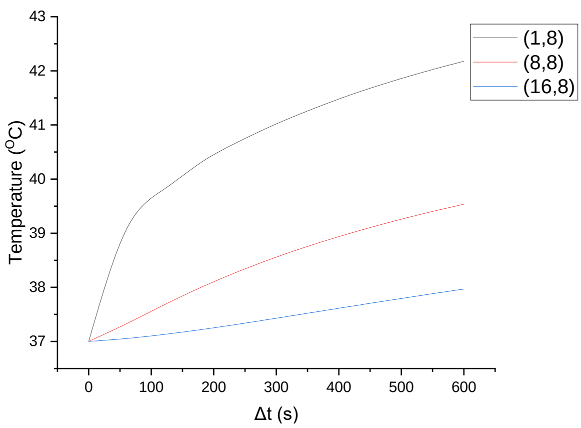
Analyzing the temperature distribution of the distance from the heat source, namely the slot air antenna, is important so that unwanted body tissues exposed to therapeutic temperatures are maintained at normal temperatures. In this study, there are three nodes that will be analyzed to find out the temperature distribution, node 1 at coordinates (1,8) and node 2 on coordinates (8,8) which are in the tumor tissue, then node 3 at coordinates (16.8) which are in muscle tissue. Figure 6 shows a graph of the temperature distribution at z= 8mm with variations in blood perfusion. graph of the temperature distribution at each node on z = 8mm with variations of blood perfusion shown in Figure 6.

From the results of the temperature distribution, it can be seen in Figure 6 that the highest temperature is always at node one, then node two, and the lowest is node three. This indicates that tumor tissue experiences a therapeutic temperature that will turn off tumor tissue cells. Fat tissue does not experience therapeutic temperatures so it will not damage the tissue. However, at node two the tissue does not experience therapeutic temperature, this can be controlled by increasing the Power Input [9].

From the results of the temperature distribution in Figure 6(a), Figure 6(b), and Figure 6(c), the temperature at node (1.8) continues to increase with increasing time. While in Figure 6(d) and Figure 6(e) the temperature increase is significant at a time of 400 seconds and will increase slowly until the 600th second. This shows that the greater the value of blood perfusion used in research, the easier equilibrium will be achieved on heat transfer in the human body [4].



(a)



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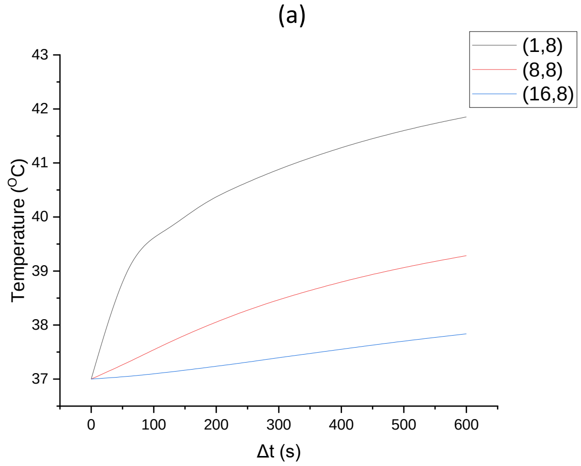
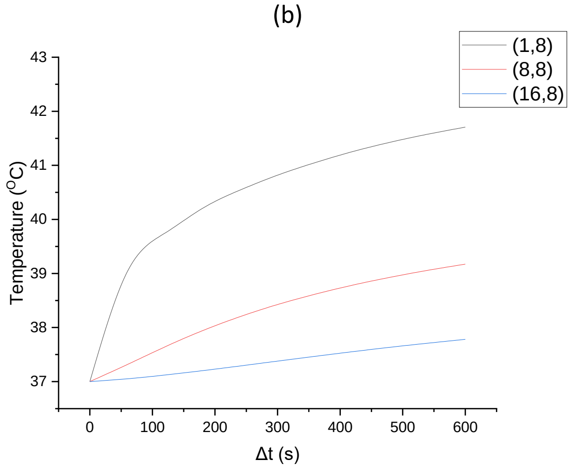
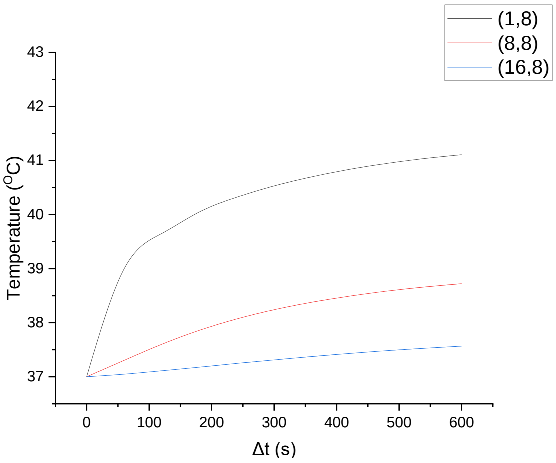


(c)



(d)



(e)

Fig. 6. Graph of the temperature distribution at each node at z = 8 mm with variations in blood perfusion values, namely; (a) ωb=2x10^{-4}/s, (b) ωb=4x10^{-4}/s, (c) ωb=8x10^{-4}/s, (d) ωb=1x10^{-3}/s (e) ωb=2x10^{-3}/s

3.3 Analysis of Temperature Distribution in Five Human Body Tissues with Variations in Blood Perfusion and Δt = 600s

Blood perfusion is a local blood flow that measures the amount of volumetric flow rate of blood per second. In the distribution of temperature in the tissues of the human body, blood perfusion plays an important role, where the amount of blood perfusion will affect the value of temperature distribution. In this study, variations in blood perfusion values used were (8x10^{-4}, 4x10^{-4}, 2x10^{-4}, 1x10^{-3}, 2x10^{-3})/s with 11 nodes spread from epidermal tissue to bone. The distance of each node from the antenna airslot used is at r = 1mm. The time used to analyze the temperature distribution is 600 seconds. Figure 7 show a graph that can be presented from the study.

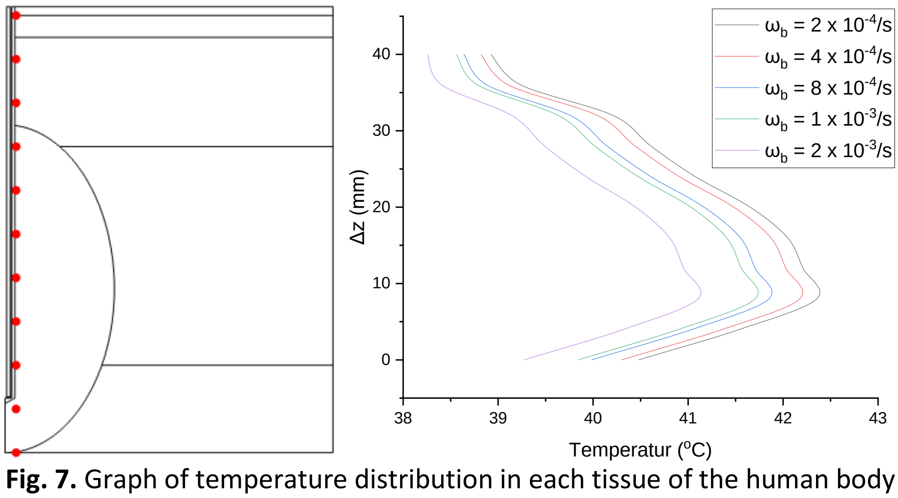


Fig. 7. Graph of temperature distribution in each tissue of the human body at r=1mm and Δt=600s

From the simulation results, temperature distribution data was obtained in human body tissues with variations in blood perfusion values from the highest in each network at r = 1 is 2x10^{-4} / s, 4 x10^{-4} / s, 8 x10^{-4} / s, 1 x10^{-3} / s, and 2 x10^{-3} / s. The results of this study showed that the smaller the value of blood perfusion, the higher the temperature value obtained. This is because blood perfusion serves to drain blood throughout the body, with the higher the value of blood perfusion, the more blood will flow in the tissues and distribute temperature throughout the body so that heat balance is created. Such blood flow prevents heat transfer to other parts of body tissues and can be used as a preventive parameter in the application of hyperthermia [4].

3.4 Analysis of The Contours of Temperature Distribution in Two Axial Dimensions with Variations of Blood Perfusion and Δt = 600s

Analysis is carried out on all body tissues with two axial dimensions applied. The result of the contours of the temperature distribution can be seen in Figure 8, the contours of the temperature distribution at Δt = 600s with variations in blood perfusion ($8x10^{-4}$, $4x10^{-4}$, $2x10^{-4}$, $1x10^{-3}$, $2x10^{-3}$)/s. of each image have similarities where the therapeutic temperature is only the farthest at r=6mm and z= 30mm. This indicates that no tissue dies due to hyperthermia because the therapeutic temperature is only in the tumor. However, there are areas of the tumor that do not reach therapeutic temperatures. This can be achieved by increasing the input power so that all tumor tissue experiences therapeutic temperature.

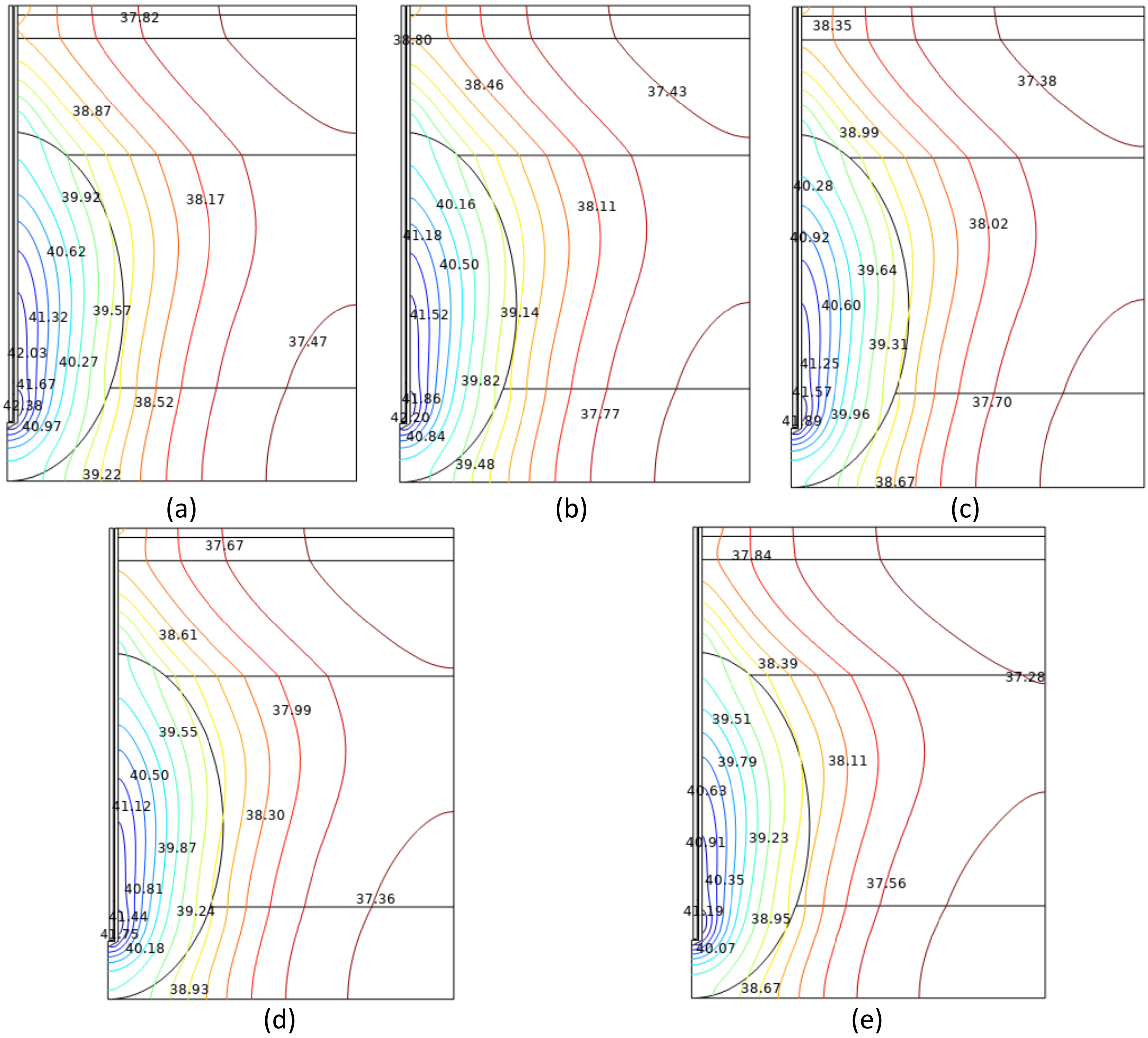


Fig. 8. Contours of temperature distribution at Δt = 600s and blood perfusion variations; $\omega b = 2x10^{-4}$/s, (b) $\omega b = 4x10^{-4}$/s, (c) $\omega b = 8x10^{-4}$/s, (d) $\omega b = 1x10^{-3}$/s (e) $\omega b = 2x10^{-3}$/s

3.5 Comparison of Temperature Distribution in Research by Piotr GAS [16]

The results of temperature distribution in this study were compared with the results of temperature distribution in a study conducted by Piotr and Schmidt with the title *"Transient Analysis of Interstitial Microwave Hyperthermia Using Multi-slotCoaxial Antenna"* in 2014 who conducted a study to determine the distribution of temperature with interstitial application hyperthermia therapy using finite element method (FEM) simulation with a frequency of 2.45 GHz and Power Input 1 W. In Piotr research, also used Pennes equations to determine the distribution of temperature in some body tissues. The study used two axial dimensions that harness heat waves generated from electromagnetic heating.

Figure 9 is a graph of the results of Piotr Gas researchers, Figure 10 is a graph of the results of this study with variations in blood perfusion 2x10^{-3}/s [16]. from both charts show the similarity of trends of temperature distribution in human body tissues in the interstitial application of hyperthermia treatment for tumor therapy. From the two charts obtained similarities where the temperature will increase with the increase in time and the increase in temperature begins to landau at a time above the 400th second.

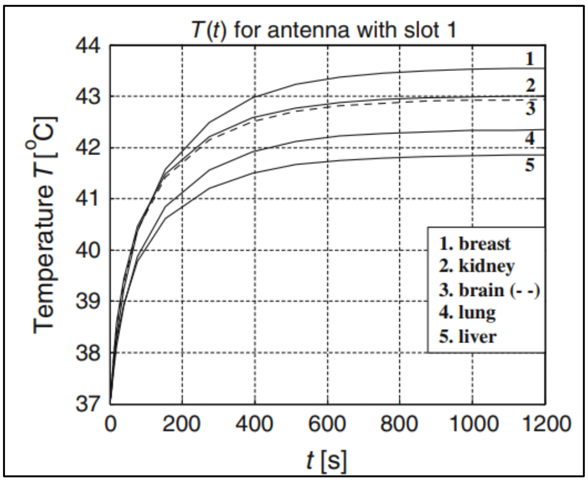


Fig. 9. Temperature distribution in Piotr Gas study with node distance from heat source 1 mm

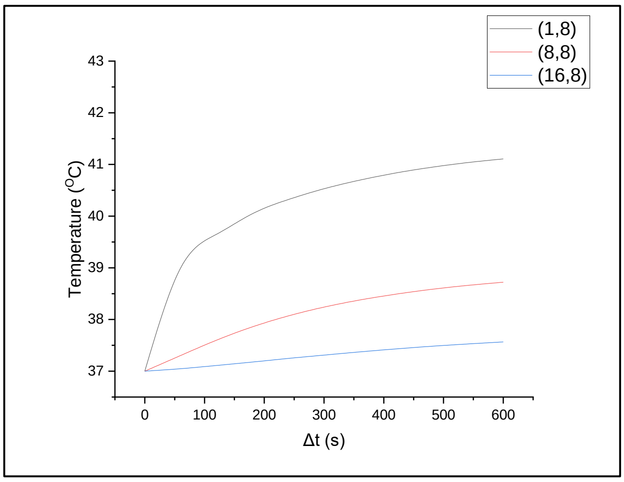


Fig. 10. Temperature distribution of research results with variations in blood perfusion 2x10^{-3}/s

Figure 9 is a graph of the results of Piotr Gas researchers, Figure 10 is a graph of the results of this study with variations in blood perfusion 2x10^{-3}/s [16]. from both charts show the similarity of trends of temperature distribution in human body tissues in the interstitial application of hyperthermia treatment for tumor therapy. From the two charts obtained similarities where the temperature will increase with the increase in time and the increase in temperature begins to landau at a time above the 400th second.

4. Conclusion

The conclusion obtained from this study is that the temperature distribution data in the interstitial application of hyperthermia therapy will always increase with the increase in time, this is because in the Pennes equation the temperature value is directly proportional to the magnitude of time. The highest temperature is at the node (1.8) where it is closest to the air slot antenna as a heat source. As the temperature increases over time, the value of the blood perfusion variation of 1x10^{-}

^{3}/s and 2x10^{-3}/s refractors will increase significantly in the 0th to 400th second, but in the 400th to 600th second the temperature rise is more sloping. This is obtained because blood perfusion serves to drain blood throughout the body, then with the higher the value of blood perfusion, the more blood flows in the tissues and distributes throughout the body so that the temperature equilibrium will be easier to reach. The temperature in the blood perfusion variation 2x10^{-4}/s has the highest temperature value at each node, then the temperature value from the highest is followed by the variation of blood perfusion 4x10^{-4}/s, 8x10^{-4}/s, 1x10^{-3}/s, and the smallest is the variation of blood perfusion 2x10^{-3} /s. it is also obtained because the more blood flows, the easier it will be to distribute the temperature throughout the human body. In the temperature distribution in each variation of blood perfusion, the therapeutic temperature is only in the tumor tissue, meaning that no other body tissue dies due to interstitial application of hyperthermia therapy. However, some areas in the tumor are still not exposed to therapeutic temperatures, this can be achieved by increasing the power input. The use of this therapy can be done repeatedly to help patients have a longer life span due to tumor cells that are stopped from development.

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