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Effect of Frequency on Heat Spread by Interstitial Hypertemia Treatment Method for The Treatment of Sarcoma Tumors

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Abstract: Frequency is a thing to calculate a wave. In biomedical science, frequency plays an important role in delivering heat as in bioheat transfer. In bioheat transfer studies, heat transfer in the human body can be used as one way of treatment such as therapy. At high temperatures that are usually above 40°C, the cell will die and cannot develop again this is called hyperthemia therapy. This therapy is commonly used in medicine with the function to kill tumor cells. There are 3 differences in hyperthemia therapy there are external, cavity and intersitital and interstitial hyperthermia therapy has better healing ability because heat is directly delivered to the tumor tissue to minimize tissue that no tumor is exposed to therapeutic temperature (40-46°C). Then the author will conduct a study with an analysis of heat transfer carried out on five layers of the human body, namely the epidermis, dermis, fat, muscle, and bones by applying the interstitial method of hyperthermia therapy and influenced by frequencies with a value of 434; 915; 2450 MHz completed using finite element method with unsteady state conditions in two axial dimensions. This study showed that frequency affects the value of temperature distribution in the five layers of the body. The greater the frequency value given, the more easily distributed the temperature will be because the frequency will provide greater electromagnetic waves if the frequency is increased. With interstitial hyperthermia would be optimize the therapeutic temperature more stable because of the needle as the media of the heat transfer. The methods of the interstitial treatment research are insert the needle to the sarcoma hand tumor. This look very simple but need more preparation like, voltage, frequency, measure the metabolic and blood perfusion of the patient and made a analytics measure to do the treatment. The result of the research is heat that spread by interstitial hyperthermia are stable at 40-46°C which is the therapeutic temperature of tumor treatment, and the temperature will be increase with upgrade the power input of the source and the frequencies. The research has a conclusion that interstitial hyperthermia on sarcoma tumor especially on hand tumor sarcoma is effectively because the heat is spread well on the tumor at therapeutic temperature and frequencies that applied in this research is optimal for the treatment because it could keep the temperature steady on around 40-46°C.

Keywords: Bioheat transfer, frequency, interstitial hyperthermia therapy, unsteady state, finite element method, temperature distribution

1. Introduction

Bioheat transfer is the study of heat transfer in biological systems that is useful for knowing the rate of heat transfer in the human body so that it can develop new medical treatments or minimize the effects of adverse conditions [1][2]. In biomedicine, it is necessary to pay attention to factors that can affect heat transfer in the body, one of which is the frequency that can affect heat transfer can help tumor treatment through bioheat as well, the influence of variation used is electromagnetic frequencies with a specified variation are 434;915;2450 mHz. Interstitial hyperthermia is the most effective therapy because heat is emitted directly on the tumor and minimizes the effect on other normal tissues [3] and also This method, applicators were inserted into the tumor and in several cases heat therapy was combined with

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brachytherapy. This treatment is administered in at the same time as the by the post-loading method in a close connection the area to be heated. This technique was useful for tumors less than 5 cm in diameter. Several types of antennas were available, in particular microwave antennas, radiofrequency electrodes, ultrasonic transducers, sources of but also fibers. This volume target requires a distance between the applicators not exceeding 1.0 to 1.5 cm, but this is very painful. Due to their sensitivity to interference, the orientation and positioning of microwave antennas can be critical. Those systems are undergoing clinical evaluation [4][5].

Endocavitary antennae have been inserted into hollow openings such as the urethra, rectum, esophagus, cervix and vagina. the transfer of heat energy in the skin layer is a complicated thing consisting of the phenomenon of conduction, convection, and radiation. Heat conduction is usually processed simultaneously, including blood circulation, sweat, metabolic heat and sometimes heat coming out of the hair or fur on the skin [4] in bioheat transfer is at the time of application which is on average used in the healing of diseases and carried out with hyperthermia treatment, hypothermia, and crybiology [6] also On tumor healing methods for example.

With the treatment of hyperthermia and pay attention to factors that can affect the distribution of temperature. One example is interstitial microwave hyperthermia [7]. In the human body, body temperature is something that needs to be considered. The normal core body temperature is 37ºC and can range from 33.2-38.2ºC. Changes in body temperature beyond the normal range can be fatal. At a body temperature of about 42ºC can result in nerve unrest and at a body temperature of about 27ºC can result in respiratory distress but, extreme temperatures on 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 of about 40-46ºC around the cell to kill the cells, the therapy is commonly called Hyperthermia Treatment [8]. Sarcoma cancer is a disease with characteristics of uncontrolled tumor cell tissue growth. These tumors are classified in 2 types, namely tumors in bones and tumors in human soft tissues. If the tumor undergoes changes will be fatal to the body tissues where the bias becomes spread and enlarged. Tumors on the hands are very rare but when they occur, cause very serious effects [9].

The frequency will affect the electromagnetic waves flowing on the antenna and will produce electromagnetic heat waves. Electromagnetic heating is a science used as an analysis of heat transfer where electromagnetic waves are used as a source of heat. Electromagnetic heating is divided into four types according to the type of wave used, namely: joule heating, laser heating, induction heating, and microwave heating. To complete this analysis, a basic formula of calculation is needed to calculate the finite element method, namely the Pennes equation. Pennes equation is an equation used to complete the analysis related to bio-heat transfer. This equation has been used since 1948 and was further developed by researchers to analyze the phenomenon of heat transfer in human tissue layers. [10] [16]. Finite Element is one of the numerical methods that utilize matrix operations to solve physical problems. Another method is the analytical method, to do so requires a mathematical equation that is a model of physical behavior. The more complicated the physical behavior (due to the complexity of geometric shapes, the number of load interactions, constrains, material properties, etc.) the more difficult or even impossible to build a mathematical model that can represent the problem. The alternative method is to divide the case into small, simple parts where in the small part we can build a mathematical model more simply [11] [12] [13] [17].

2. Antenna Design for Interstitial Hyperthermia and Methods

This simulation goes with analytical study on electromagnetic waves and bioheat transfer with COMSOL MULTIPHYSIC on forearm skin with conductivity of different skin layers by finite element method for the temperature distribution. In this study, the study will consist of several diseases, first the authors look for related literature studies related to bioheat, electromagnetic, as well as tumor healing by the method of hyperthermia. Both authors create a geometry design of skin tissue that will be tested which is based on the literature that has been read. The third is the determination of variable values where here the author determines the value of the variable that was originally used and the variable variation. For the initial variable using a frequency of 2450 MHz while for its variation using a frequency value of 434;915;2450 MHz. the fourth is a simulation with software whas using COMSOL MULTIPHYSIC software to find the amount of distribution that occurs. Fifth is verification, the verification method here uses a comparison method between previous research and research that has been done by the author. It can also be seen from the theoretical calculations. Sixth is the analysis of research data that has been mentioned in step three, namely frequency variations where here the author compares the results of data that occurs at each frequency.

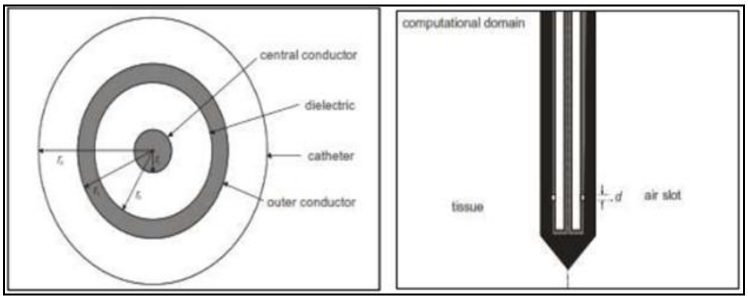

Fig. 1 - Antenna for interstitia hypertemia

3. Study Models Equations

3.1 Pennes Equation

Pennes equation is used for this model because of the simulation may effect on temperature and time on human skin. And we use one other equation that is electromagnetic waves equation for control the temperature that emmiting from antenna to the tumor in two axial dimension. Pennes Equation as shown in equation:

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

Under layer skin of forearm has a momentum and mass for the blood perfusion flow rapidly and it's need some velocity. So, equilibrium of momentum (2) and mass equilibrium (3) are used for mathematical analytics as shown in equation

$$\rho_b \left(\frac{\partial u}{\partial t} + (u \cdot \nabla)u\right) = \nabla \cdot (-p + \mu\nabla u + \mu(\nabla u)^r - \frac{2}{3}\mu(\nabla \cdot u)I) \quad (2)$$

$$\frac{\partial \rho_b}{\partial t} + \nabla \cdot (\rho_b u) = 0 \quad (3)$$

Because of the unsteady condition, the simulation have some condition:

- Initial Condition at x = 0
  T (0,0) = T_b
- Boundary Condition at x = 0; x = 30mm; 0 mm < x < 30 mm

1. T (0, t) = T_b
2. T(L,t) = T(t)
3. T(x,t) = T(t)

3.2 Electromagnetic Waves Equation

The antenna used to conduct electromagnetic waves is a symmetric coaxial antenna with cylindrical coordinates r, z, ϕ. The antenna consists of an inner conductor, a dielectric, an outside conductor, and a catheter. Electric fields and magnetic fields are defined by Maxwell-Ampere and Faraday's laws in the frequency domain [3]:

$$\nabla \times H = J + j\omega D; \quad (4)$$

$$\nabla \times E = -j\omega B \quad (5)$$

$$J = \sigma E \quad (6)$$

After applying the equation and substituting the equation we can derive the following equation describing the distribution of fields:

$$\nabla \times \left(\left(\varepsilon_r - \frac{j\sigma}{\omega \varepsilon_0} \right)^{-1} \nabla \times H \right) - \mu_r k_0^2 H = 0 \quad (7)$$

Because the magnetic field strength vector (as well as E) in the time domain is related to the complex amplitude, so the equation in domain complex is:

$$\nabla \times [\hat{\varepsilon}_r^{-1} \nabla \times \hat{H}] - \mu_r k_0^2 \hat{H} = 0 \quad (8)$$

In the presented model transverse magnetic waves (TM) are used and there is no variation in electromagnetic field in the direction of the azimuth. The magnetic field H has only components and the electric field E propagates on the r-z plane. Therefore, it can be written as:ϕ

$$\hat{H}(r,t) = H_\phi(r,z) e_\phi e^{j\omega t} \quad (9)$$

$$\hat{E}(r,t) = [E_r(r,z) e_r + E_z(r,z) e_z] e^{j\omega t} \quad (10)$$

The external boundary of the computing domain, which does not represent a physical boundary (except the boundary on the z symmetry axis where E φ(r) = 0) has what is called a matching boundary condition. They make boundaries completely non-reflective and take shape.

$$\sqrt{\varepsilon - j\frac{\sigma}{\omega}} \mathrm{n} \times E - \sqrt{\mu} H_\phi = -2\sqrt{\mu} H_{\phi 0} \quad (11)$$

4. Tissue and Electrical Properties

Based on literature studies and bioheat research. The properties data have been obtained. Properties of forearm tissue properties as shown.

Table 1 - Forearm tissue properties

Tissue properties	ρ (kg/m^3)	Thickness	C_p (J/KgK)	K (W/mK)
Epidermis	1200	0.0002	3598	0.24
Dermis	1200	0.002	3300	0.45
Fat	937	≈0.010	3258	0.21
Muscle	1000	≈0.020	4000	0.5
Bone	1920	≈0.008	1440	0.44
Tumour	1079	-	3540	0.52
Blood	1000	-	4200	0.64

Table 2 - Antenna geometry properties

Antenna Geometry Properties	Value
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
Tumour mayor axis (a)	10 mm
Tumour minor axis (b)	15 mm

Table 3 - Electrical properties

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

5. Result and Discussion

5.1 Analysis of Temperature Distribution in Five Forearm Layers with Unsteady Conditions and Two Axial Dimensions

In the results of this graph will be displayed a graph of the temperature distribution at r = 1 mm on 11 nodes scattered over the body. Tumor tissue is present in the layer between the bones and fat. Defining the results of research charts as in Figure 4. From the results of the above temperature distribution can be seen in figure 2.a. frequency of 434 MHz, the temperature always increases with time. The starting point of the temperature spread is found to be a temperature of 37^{O}C, and at the time of t = 600s each point has a temperature variation which at this frequency has a large temperature of 38^{o}C in conditions z length when 36 mm. And the lowest is 37^{o}C at the time of z length of 24 mm. in figure 2.b. displayed the temperature distribution at a frequency of 2450 MHz which has the highest temperature of 42^{o}C with a condition of z length of 8 mm. and the lowest condition of the temperature distribution at 38oC with a position of z length of 40 mm. From the three images above have the same upward tendency this is due to the theoretical basis in the Pennes Equation, the value of temperature is directly proportional to the magnitude of time. Therefore, the time of application of interstitial hyperthermia therapy will be greater the temperature. With the use of incoming power that is only 1 Watt causes heating to take a long time [3]. in figure 2.c. is shown a graph at a frequency of 915 MHz. in this condition the temperature distribution increased from before. The size of the temperature distribution is present at the time of z = 36 mm with a large temperature of 40.5^{o}C and the lowest temperature condition is 30.5^{o}C in the condition of Length z = 24 mm.

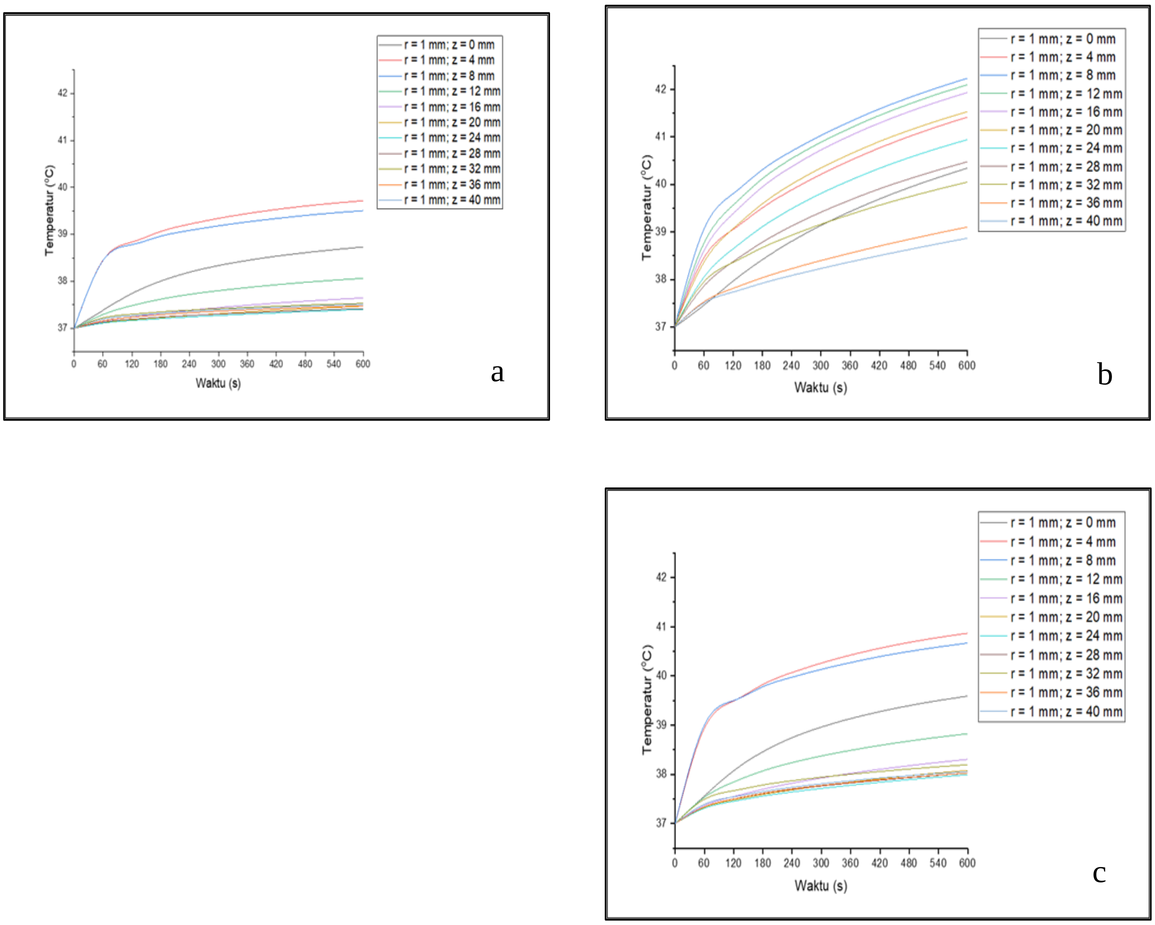

Fig. 2 - Temperature distribution between time (a) at 434 MHz; (b) at 2450 MHz; (c) at 915 MHz

5.2 Analysis of Temperature Distribution Against Distance and Air Slot with Unsteady and Axial Two-Dimensional Conditions

The air slot is part of the antenna that serves as the output of the heat distribution. What was in the analysis of the distribution of temperature to the distance from the heat source is something that must be analyzed. Antenna air slot is one part of the antenna that must be analyzed so that body tissue that does not have a tumor is not exposed to heat from the antenna and maintained at normal temperatures. In this study, there are 3 parts that will be analyzed, namely the tumor part, the edge of the tumor, and the outside of the tumor, which is the muscle part to find out the effect of air slot on the lining of the hand when distributing temperature.

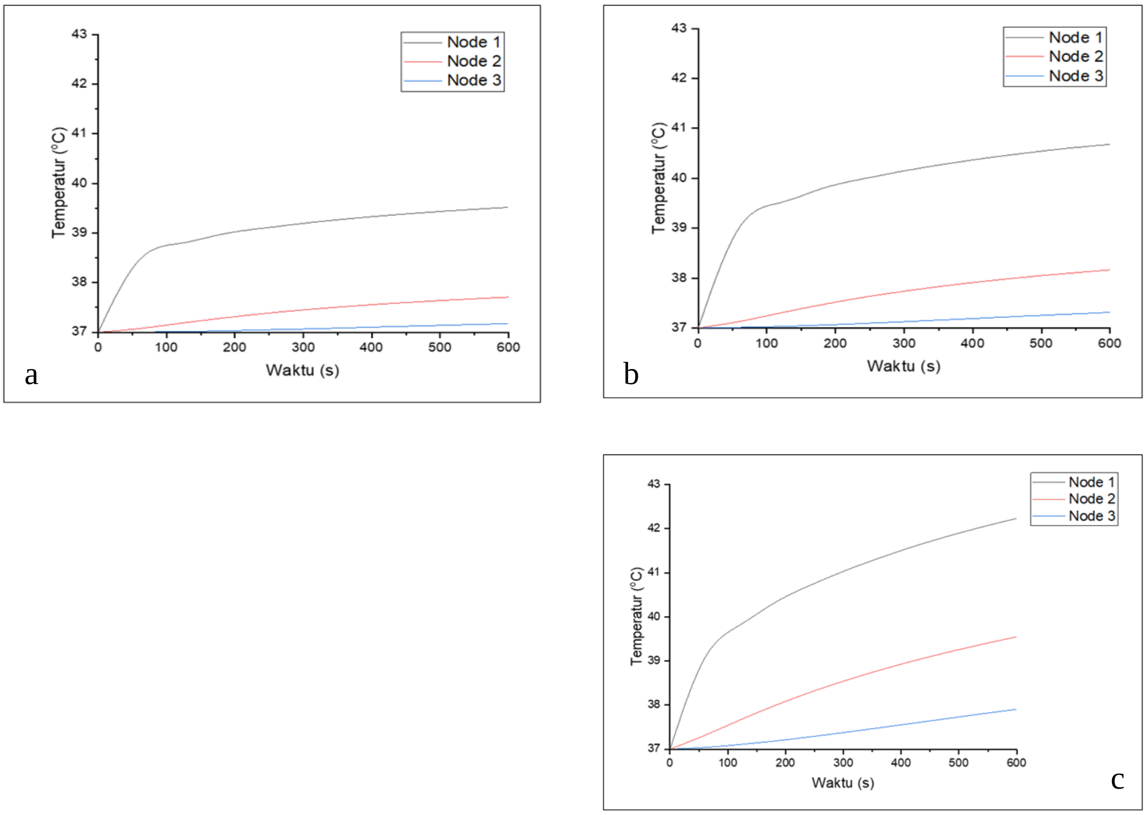

Fig. 3 - Temperature distribution at air slot (a) at 434 MHz; (b) at 915 MHz; (c) at 2450 MHz

From figure 3.a. it can be seen that it is a graph related to temperature distribution in 3 conditions, namely in the codification inside the tumor, outside the tumor, and the edges of the tumor. The results of the temperature distribution obtained are seen that at a frequency of 434 MHz gives a high temperature to node 1 y which gives a higher heat of 39.5°C because it is in the tumor while for the tumor there is in node 2 with a heat of 37.5°C and followed by a decrease in temperature in node 3 with a heat of about 37°C. Figure 3.b. shows a frequency of 915 MHz which gives the highest heat at 40.5oC at node 1 and followed by node 2 at temperature. 38°C and node 3 at 37°C.

And in figure 3.c. shows the graph at a frequency of 2450 MHz with heat on node 1 of 42°C followed by node 2 of 39°C and at node 3 at a temperature of 37.5°C. It can be underestimated that the highest temperature is always at point one, then point two, and the lowest is point three. This indicates that the tumor tissue undergoes a therapeutic temperature (40-46°C) that will be used to kill tissue cells. The fat layer does not experience therapeutic temperature so it will not damage the tissue. However, at point two the tissue does not experience therapeutic temperature, this can be adjusted by adjusting the Power Input. From the results of the temperature distribution, it can also be seen that the temperature increasing in node one, has a significant increase in the time of 0-600 seconds. This suggests that the use of interstitial hyperthermia therapy with the parameters used in this study can be easily controlled. Because if the increase is too significant, other tissues around the tumor can at any time experience therapeutic temperatures and make the cells in the tissue die [14].

5.3 Analysis of Temperature Distribution in Five Forearm Tissues with Variations in Blood Perfusion at Δt = 600s

Frequency plays an important role, where the magnitude of the frequency will affect the value of the temperature distribution. In this study, the variation in the frequency value used was 434; 915; and 2450 MHz with 11 scattered nodes. The distance of each node from the antenna airslot used is at r = 1 mm. The time used to analyze the temperature distribution is 600 seconds. Here is a graph that can be presented from the study. From these results, temperature distribution data was obtained in human body tissues with variations in frequency values from the highest in each network at r = 1mm is 2450; 915; 434 MHz. The results of this study show that the smaller the frequency value, the lower the temperature value obtained. This is because the frequency serves to drain waves from the power source into the antenna which gives the effect of electromagnetic wave heat. From electromagnetic heat waves it will produce the distribution of heat into the tumor and with the influence of time (unsteady state) will give the effect of the higher the heat that will be generated according to the input power to be used [15].

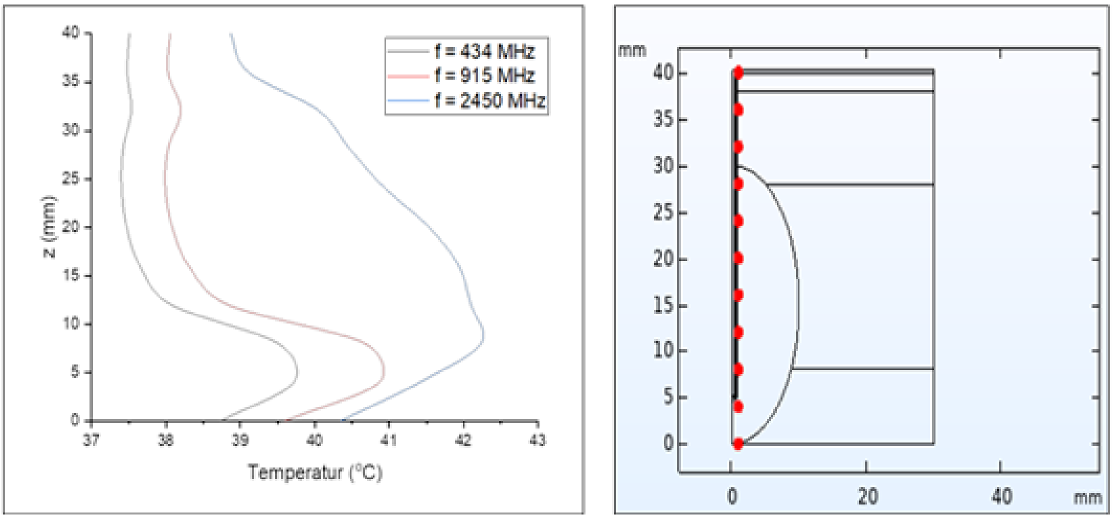

Fig. 4 - Temperature distribution on 5 layers' forearm at 600 s

5.4 Analysis of Comparison Between Frequency Variations with Radius Position Differences

In this analysis will be compared to the frequency variation used there are 3 types, namely 434; 915; and 2450 MHz. which uses 3 radius(r) spreads that are 1; 8; and 16 mm with a length (z) of 8 mm. Then there is a difference in temperature distribution that occurs between each frequency. As can be seen in the following chart.

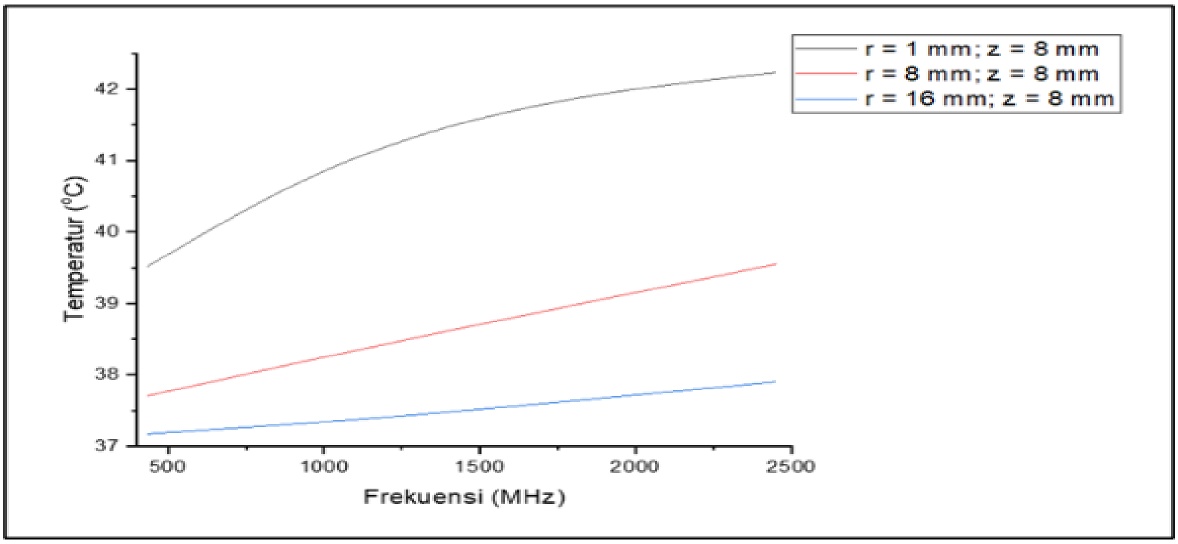

Fig. 5 - Temperature distribution on 3 frequency variation with different radius

From this graph it is explained that the temperature distribution at r = 1 mm can provide higher heat than r = 8 mm and r = 16 mm. and the highest temperature is found at 42ºC which is found at a frequency of 2450 MHz. Condition r = 1 mm is a condition where the radius is in the tumor. The results of this simulation prove that the greater the frequency used, the greater the heat that will be generated. Certain parameters such as electrical permittivity and thermal conductivity are connected to the frequency and type of the human body layer including the hand layer.

5.5 Analysis of The Contours of Temperature Distribution in Two Axial Dimensions with Frequency Variation

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 the image where the 3D temperature distribution can be seen at Δt = 600s with a frequency variation of 434; 915; 2450 mHz. Each image has a difference where at a frequency of 434 mHz has a small heat distribution coverage which does not hit the entire tumor area just like 915 mHz which only increased slightly from before. For a frequency of 2450 mHz temperature about the entire tumor. But from the picture it can be seen that no tissue died due to exposure to therapeutic heat. However, there are areas of the tumor that do not reach therapeutic temperatures. This can be achieved by increasing the power input so that the temperature is distributed and about the tumor [3]. Figure 6.a shows the temperature distribution at a frequency of 434 MHz with a contour where it can be seen that the therapeutic temperature spread is at the time the antenna emits heat as figure 6.a. But for the spread of the temperature itself is not good because the power used is less, which is only 1W and the frequency used is too low. In figure 6.b. shows the temperature distribution in the contour shape at a frequency of 915 MHz. It can also be seen that the temperature distribution has begun to improve after increasing the frequency but for the spread of contours is still not good because the frequency used is still less large. At figure 6.c. shows contours at a frequency of 2450 MHz which has a good temperature distribution where the therapeutic temperature only hits the tumor part and does not come out of the tumor. Here it is proven that the spread of temperature is good only that the power used is still less large to be given a more temperature distribution [3].

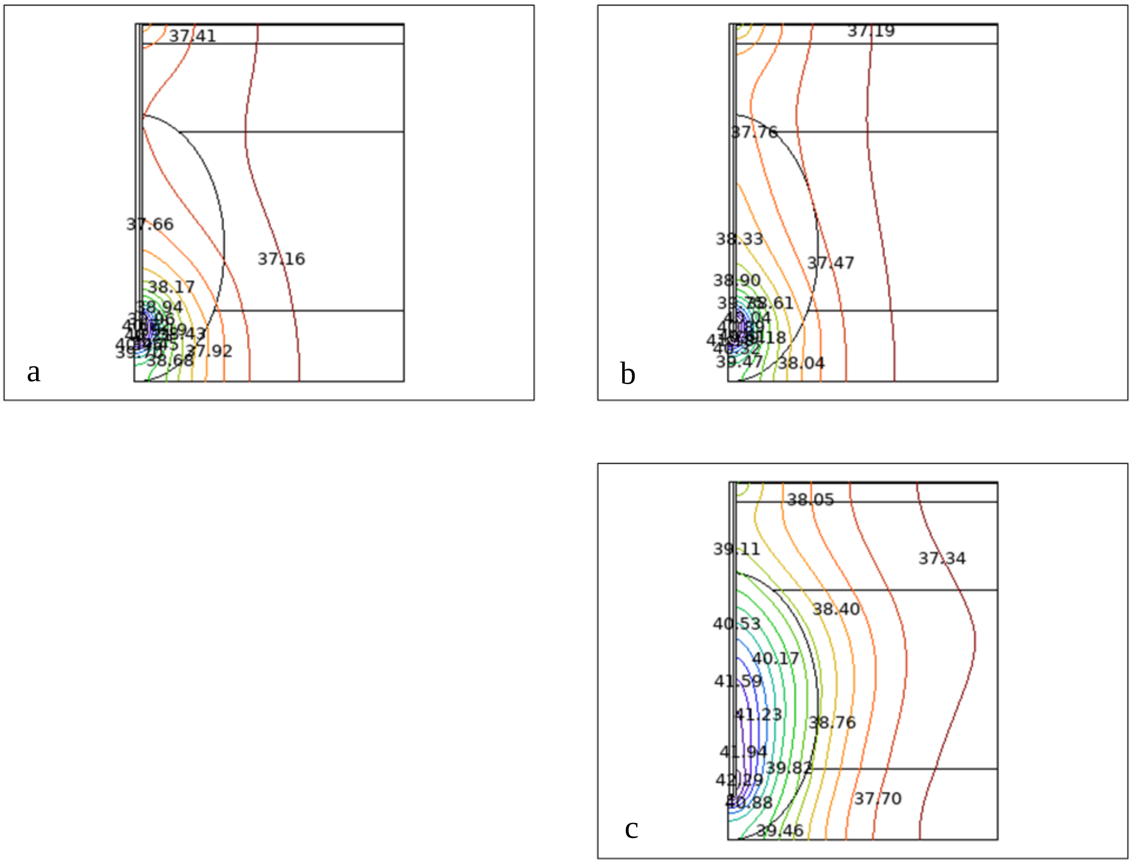

Fig. 6 - Temperature distribution with contour view

6. Conclusion

The conclusion obtained from this study is that the temperature distribution data in the interstitial application of hyperthermia therapy will always increase with time, this analysis follows the theory of the equation pennes the value of temperature directly proportional to the magnitude of time. At the temperature increase of the 0th to 600th second, the increase is seen significantly. This proves the research in accordance with the basis of the theory of pennes equations. The temperature at the frequency variation of 2450 mHz has the highest temperature value at each point, then the temperature value from the highest is followed by the frequency variation of 915 mHz and 434 mHz. This is found because the frequency serves to provide waves to the antenna, then with the higher the frequency value, the greater the electromagnetic wave that will eventually appear hot. At the temperature distribution in each frequency variation, the therapeutic temperature (40-46^{o}C) is only in the tumor tissue.

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