Application of complementary split ring resonator to focus microwave for cancer treatment using the hyperthermia method

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Abstract. The hyperthermia method for cancer treatment aims to select and eliminate cancer and normal cells by raising the temperature of the cancer cells in the 36-48°C using radiation from electromagnetic waves, while normal cells are kept at ambient temperature. This research is conducted by simulating an applicator as a complementary Split Ring Resonator (cSRR) in the radio frequency range of 434-915 MHz using Finite Element Method. The average temperature distribution of cancer cells in the shape of a ball 1 mm in diameter with a position of 5 mm from the port reaches 55.5°C. Cell size variations show a different temperature distribution, larger cell sizes (5 mm in diameter) have decreased in temperature distribution which only reached around 46.1°C. This temperature distribution is also caused by the position of the cell against the port, the cell is shifted away from the port which results in a temperature distribution of 43.3°C. So that the optimal size and position of cancer cell for this treatment is as small as and as close as the cell with port. This data shows that the cSRR applicator can be used for the hyperthermia method.

1. Introduction

Cancer (also known as malignant tumor) is a disease caused by the growth and development of cells that are abnormal, beyond normal, and very wild[1]. Cancer is caused by internal factors (genetic and immune) and external factors (lifestyle and environment). The number of cancer sufferers tends to increase from year to year. In 2018, globally there were 18,078,957 new cases with a total of 9,555,027 deaths[2].

Apart from the effects of death, cancer also has psychological and economic impacts. The psychological impact that many cancer sufferers experience is stress, despair, and an attitude of withdrawing from the environment. The psychological impact can also be caused by the large amount of medical costs borne by the patient and his family[3].

Several cancer treatments were developed such as chemotherapy, radiotherapy, cryotherapy, and hyperthermia. These treatments aim to kill cancer cells, control and stop the growth of cancer cells from spreading, or cut the symptoms caused by the cancer. Generally, the above cancer treatments cause...
various side effects. In chemotherapy treatment side effects can be fatal, such as bone marrow depression, impaired liver function, cardiotoxicity, and an increased chance of a second primary tumor caused by the antitumor drugs used[4,5]. Radiotherapy treatment using x-ray or gamma radiation to destroy the cancerous tissue has side effects such as central nervous system complications, hyposaliva, heart defects, and central nervous system complications[6].

Cancer treatment in principle aims to eliminate cancer cells from normal cells. The most effective treatment for this targeting of cells is the hyperthermia method. Hyperthermia is cancer therapy by heating the area containing cancer cells at a temperature of 40-46°C, while the surrounding normal cells are kept at room temperature[7]. Cancer cell damage is caused by disruption of the heat-shock factor (HSF) which purposed to protect cells from rising intracellular temperature. Normal cells do not have the HSF disorders. The size and distribution of the induced hyperthermia cause cell death at 45.5°C. besides that, at a temperature of 40°C the cells had the highest fluorescence intensity[8]. Hyperthermia methods that cause cell death also affect cell membrane function, increase cell permeability, and cancer cell proteins where the proteins undergo denaturation and aggregation at temperatures>39°C [9]. Hyperthermia method can be used independently for cancer therapy and can be used as a support for other cancer therapies. For example, the combination of the hyperthermia method with chemotherapy, surgery, and other methods increases the percentage of life expectancy of people with bladder tumors from 51% to 75%[10].

Hyperthermia uses electromagnetic waves to raise the temperature of cancer cells. The increase in temperature damages the protein structure and the cancer cell cycle, as well as influences the internal electric field which results in reducing of tumor size and cancer cell death[11]. Hyperthermia can be applied using an electromagnetic wave applicator that can control the focus and field distribution of cancer cells in microwaves. This method is safe and effective but still has side effects such as sunburn and heating to unwanted areas.

In this study, an electromagnetic wave applicator was used in the form of a flat metamaterial with a complementary Split Ring Resonator (cSRR) structure. The use of this applicator is because this structure has the desired magnetic susceptibility (response), high performance for the hyperthermia method, easy fabrication, produces a focused radiation pattern.

2. Research Methods
This study uses the Finite Element Method (FEM) which used by the Comsol Multiphysics 5.0 software. Comsol Multiphysics makes it possible to design products in 3D. FEM is a numerical method for obtaining solutions to differential problems, both ordinary differential equations and ordinary partial differential equations with an acceptable level of accuracy. In this study, fault tolerance is at a value of 0.01.

This research is conducted by determining the parameters used to design the simulation model. The simulation is divided into two parts, that are simulation for cSRR and simulation for cancer cells. In this study, the design by Selvaraju, et al[12] is used where the cSRR variations consisted of four variations, namely variations of one gap, two gaps, three gaps, and four gaps. These variations aim to produce resonant frequencies in the frequency range from 434 to 915 MHz. To see the shifting of resonancy in that range which already set up before, variation of the width of the gap is carried out. Furthermore, cSRR is applied in the simulation of cancer cells to see the effect of cSRR on temperature distribution in cancer cells. Variations for cancer cells consist of two variations, namely size variations from 1-5 mm, and variations in the position of the cells about the axis (i.e. y-axis and z-axis). These variations in cancer cells will produce a temperature distribution.

The cancer tissue parameters used are shown in Table 2.1 below.
Table 1. Tissue parameters for cancer simulation

| Tissue | Density (kg/m³) | Heat Capacity at constant pressure (J/(Kg.K)) | Relative Permeability | Thermal Conductivity (W/m K) | Electrical Conductivity (S/m) |
|--------|----------------|-----------------------------------------------|-----------------------|----------------------------|-------------------------------|
| Skin   | 1109           | 3391                                          | 3                     | 0.37                        | 0.333                         |
| Fat    | 911            | 2348                                          | 4                     | 0.21                        | 0.333                         |
| Muscle | 1090           | 3421                                          | 34                    | 0.49                        | 0.677                         |
| Cancer | 1020           | 3510                                          | 50                    | 0.5641                      | 5                             |

Based on those tissue parameters, the design for the Hyperthermia with cSRR in one, two, three, and four gaps has been made. As shown in Figure 1. Below.

![Figure 1. Hyperthermia simulation design](image)

In this simulation design a complementary Split Ring Resonator (cSRR) is placed at the port. After determining the model design and tissue parameters used, the simulation is then followed by Comsol Multiphysics by calculating and analyzing the model and parameters used. The simulation results will show the temperature distribution in cancer cells.

3. Result and Discussion

3.1 complementary Split Ring Resonator Variation (cSRR)

The variation in the gap width indicates a shifting in the resonant frequency towards a higher frequency. Every cSRR with contain one, two, three, and four gaps is shown the shifting of resonant frequency. But, this shifting easily can see in the cSRR which has three and four gaps only. as shown in Figure 2. below.
In the same parameter with the number of gaps varied the resonant frequency in different ranges and in cSRR with three gaps shows the resonant frequency in the two close frequency regions. Although, the second resonant frequency which produced by 0.5 mm width of 3 gaps is not in the resonant frequency range which needed, for the resonant frequency is 980 MHz.

One cSRR with different number of gaps generates resonant frequency in different range of frequency. In cSRR with one gap, the resonant frequency range is in 482-487 MHz with the value of S11 parameter in the value range from (-75.5) to (-75.8) dB. Specifically, the resonance frequency generated by the cSRR gap width of 0.5 mm is 482 MHz and the value of the S11 parameter is at a value of -75.8 dB, for cSRR with a gap width of 2.2 mm it has a resonant frequency at a value of 485 MHz and a value of S11 parameter in the -75.6 region. dB, then at the gap width of 3.5 mm the resulting resonant frequency is in the area of 487 MHz and the parameter value of S11 is in the region of -75 dB.

In two gaps of cSRR, the resonant frequency is in the range 474-476 MHz. Where the cSRR with a gap width of 0.5 mm has a resonant frequency at 474 MHz with a parameter S11 value of -76.5 dB, for a gap width of 2.2 mm the resulting resonant frequency is at a value of 476 MHz with a parameter S11 value of -76.5 dB, then for cSRR with width The 3.5 mm gap has a resonant frequency of 474 MHz with the parameter S11 in the -76.6 dB region.

As the figure shows, the shifting in the resonant frequency of the cSRR with one gap and two gaps is not very significant. The result of resonant frequency is in a narrow resonant frequency area. The difference is also not indicated by the resulting S11 Parameter value.

However, this is different from the cSRR which has three and four gaps. Where the shifting of resonant frequency can be seen clearly. In addition, cSRR with 3 gaps can produce resonant frequencies in two adjacent regions even though it is out of the required resonant frequency limit. Where the resonant frequency required for this method is 434-915 MHz.

The cSRR with three gaps has a resonant frequency in the range 556-718 MHz. As shown by the gap width of 0.5 mm which has a resonant frequency in the area of 556 MHz and a parameter S11 value of -68.8 dB, for a gap width of 2.2 mm the resonance frequency is in the 600 MHz area with the parameter.
S11 value in the -66 dB area, then for 3.5 mm gap width the resulting resonant frequency is in the area of 718 MHz with the parameter S11 value in the area of -60.3 dB.

Furthermore, cSRR with four gap gaps has a resonant frequency in the region of 723-781 MHz where the gap width of 0.5 mm produces a resonant frequency at the value of 723 MHz with the parameter S11 value in the -60.1 dB region, for cSRR with a gap width of 2.2 mm has a resonant frequency in the region. 757 MHz with a parameter S11 value in the area of -57.8 dB. Furthermore, the resonant frequency with a gap width of 3.5 mm has a resonant frequency at a value of 781 MHz and a value for S11 parameter in the area of -56.4 dB.

From the results above, it can be seen that the change in the gap determines the shift in the resonant frequency. The wider the gap, the greater the resulting resonant frequency. This variation also shows its effect on the parameter S11 value indicated by the sharpness of the resonant frequency peak.

![Figure 3. Resonant Frequency on Parameter S21](image)

This resonant frequency shift is also indicated by the parameter S21 as shown in the figure below. However, in S21 this parameter the resulting resonant frequency varies, some are in the required frequency range and some do not produce a resonant frequency in the required area. As shown by the cSRR with one and two slits. In cSRR with one resonant frequency gap generated by this gap width variation in the range 960-965 MHz, the cSRR with two resonant frequency gaps does not show the sharpness of the graph in that frequency range. Likewise, the resonant frequency shown by the parameter S11 in the image above shows that in cSRR with one and two slits, the variations do not show a wide shift in resonant frequency because the resulting graphs are still coinciding with one another.

In cSRR with three and four gaps the resulting resonant frequency gap shows a gap in the resonant frequency shift. In cSRR with three gaps the resulting resonant frequency is in the range 541-735 MHz, where the 0.5 mm gap indicates the resonant frequency at 648 MHz with the S21 parameter value in the -170 dB area, for the 2.2 mm gap the resonant frequency obtained is 735 MHz with the S21 parameter value is in the -130 dB area, then the resonant frequency generated by the cSRR with a gap width of 3.5 mm, the resonance frequency is 541 MHz with the S21 parameter value in the -185 dB area.
In cSRR with four gaps the resonant frequency gap for parameter S21 is in the range of 723-781 MHz. For the 0.5 mm gap the resulting resonant frequency is in the 723 MHz region, for the 2.2 mm gap the resonance frequency is 757 MHz, and for the 3.5 mm gap the resonant frequency is 781 MHz. All slit widths yield the S21 parameter value in the same area of 0 dB.

3.2. Variation in the size of cancer cells

In the variation in the size of the cancer tissue, a change in the temperature distribution range of cancer cells is shown. Where the smaller the size of the cancer cells, the cells can easily reach temperatures up to 55.5°C, for larger sizes the highest temperature only reaches a temperature of 46.1°C.

As shown in Figure 5, the variation in the gap in the cSRR used indicates the temperature variation achieved. In addition to the larger cell size, the decrease in temperature is also indicated by the effect of the number of gaps. cSRR with 1 gap with a cell size of 1 mm has the highest temperature of 55.5°C and the lowest temperature of 48.2°C, for cells with 2 gaps has the highest temperature of 54.9°C and the lowest temperature of 47.2°C, for cells with 3 gaps the highest temperature is 54.5°C and the lowest temperature at 46.1°C. This shows that there is a decrease in temperature as the number of gaps in the cSRR is used to simulate this cancer cell. The size of the cells also causes changes in the average value of the temperature distribution where a cell with a size of 1 mm has the highest temperature compared to the temperature in a larger cell, which is 2-5 mm in size.

3.3 Cancer Cell Distance Variation (y-axis)

Cancer cells placed in a position parallel to the port reached the highest temperature, namely 54.6°C with a wider temperature distribution surface. Meanwhile, cancer cells that are shifted in the direction of the y-axis have decreased the high temperature distribution gradually.
Figure 5. Distribution of temperature based on cell distance

As shown in Figure 6, the shift in the distance of cancer cells from the port (along the y-axis) affects the temperature distribution in cancer cells. Cancer cells with 1 cSRR gap had the highest temperature of 54.6°C and the lowest temperature was 46.6°C, in cancer cells with two cSRR slits the highest temperature was 53.6°C and the lowest temperature was 46.5°C, cancer cells with 3 cSRR slits had the highest temperature of 53.1°C and the lowest temperature was 45.6°C, and then cancer cells with 4 gaps had the highest temperature at 51.1°C and the lowest temperature at 43.3°C.

3.4 Cancer Cell Distance Variation (z-axis)
Cancer cells are shifted in the direction of the z-axis away from the port which is intended to see the effect of cell position on the temperature distribution of these cells. As Figure 4 shown, there is decreasing in temperature distribution when cancer cells are moved far from the port. As shown in Figure 7 below.

Figure 6. Temperature distribution based on cell spacing

The highest temperature distribution was obtained by cancer cells with the cell position 0 mm in the direction of the z-axis. In this position the highest distribution of cancer cells is owned by cancer cells with cSRR which has one gap, namely 54.6°C, for cSRR with two gaps cancer cells have the highest
temperature distribution of 53.6°C, for cSRR with three slits cancer cells have the highest temperature distribution of 53.1°C, and for cSRR with four cancer cell slits had the highest temperature distribution of 51.1°C.

4. Conclusion
Hyperthermia is an important cancer treatment method today. The complementary Split Ring Resonator (cSRR) can generate resonant frequencies by shifting the resonant frequency in the frequency range required in the hyperthermia method, namely 434-915 MHz. Shifting the gap width in the cSRR results in a higher shift in the resonant frequency. The application of cSRR to cancer cells can increase the temperature for the treatment of hyperthermia, reaching a temperature of around 56°C.

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