Finite Element Analysis (FEA) of Local Hyperthermia on Soft Tissue

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Abstract. Finite Element Analysis (FEA) is a method for simulating a local hyperthermia (HT) effect on the soft tissue liver by exposing it to an external heat higher than normal core body temperature. Local HT treatments are most commonly used to treat cancer tissue smaller than 3 cm in size by using radiofrequency ablation (RFA) technique. The radiofrequency probe provides an intense external heat source within the target zone with temperatures exceeding 50 °C, but its maximum temperature should not approach 100 °C. In this paper, the main idea is to study the effect of tumor diameter size on the exposure time, thermal exposure intensity and applied voltage. There are five (5) different tumor diameter tissue sizes that would be treated: 1 cm, 1.5 cm, and 2 cm of tumor tissue diameter treated with a monopolar of plain electrode, and 2 cm, 2.5 cm, and 3 cm of tumor diameter tissue treated with 4-prong retractable antennas of an electrode. The findings showed that the exposure time is influenced by the tumor diameter tissue and the voltage applied, with the bigger tumor diameter tissue necessitating the longest time exposure with a high voltage. The temperature range of 50-100 °C has been given by all of the voltage supplied. Both electrodes provide thermal damage between 6-20 minutes, which is 6 – 18.5 minutes for a plain electrode with a voltage supply of 20-35 V applied to 1cm, 1.5cm and 2 cm of tumor diameter tissue, and 10.5 – 12.5 minutes for a 4-prongs electrode with a voltage supply of 22-45 V applied to 2 cm, 2.5 cm and 3 cm of tumor tissue.

1. Introduction
Liver cancer is the world's sixth most prevalent cancer and the highest rate among Asians and Africans, primarily due to the higher incidence of infection with viral hepatitis [1]. A liver that is exposed to pathogenic or abnormal cell cancer results in failure of the organ, which may become life – threatening. It’s because the liver plays crucial roles, such as the metabolism and storing of ingested nutrients, for example, vitamin and iron; the development of clotting factors that include stopping bleeding from wounds; the production of bile that is essential to the assimilation of nutrients; and the breakdown and elimination of toxic substances such as medications and alcohols from the body [2]. People with liver disease require close examination to identify emerging liver lesions as quickly as possible in order to eliminate the cancer. Hyperthermia (HT) is a type of cancer treatment therapy, where a tumor tissue is exposed to an external heat intending to destroy cancer cells regardless the surrounding normal cell. Local hyperthermia is a type of hyperthermia that can be used to treat small regions of tumor tissue in the human body, either on the surface tissue or within the internal organ, at a temperature that is kept precise. Meanwhile, radio-frequency (RF) hyperthermia ablation technique is safer, reliable and favourable for heating tumor located in heterogeneous anatomies with various dielectric and thermal
properties of tissues than other cancer therapies, because this technique does not change the DNA of cells and RF system able to generate signal precisely targeting tumor [3].

Finite element analysis (FEA) is a numerical approach in simulating thermal effect on soft tissue in liver. In the analysis of thermal effect, three factors of interest are thermal exposure intensity, exposure time, and applied voltage on destroyed whole tumour tissue size while decreasing effect on surrounding healthy tissue. In this study, the margin of interest would be ranging from is 5-10 mm beyond the tumor boundary region, which is 5 mm free margin of nearby healthy tissue is allowed to complete damage as it ensures the entire tumor region that is close to the healthy tissue has died, while the 10mm free margin should not exceed 50 % of damage in order to reduce the harm impairing on undesired region. According to Xiaoru Wang at el.[4], the ablation volume must entirely embrace the tumour tissue while maintaining a safety margin of 5-10 mm for RFA success. They believed that properly predicting the form and size of the tissue coagulation zone during the RFA treatment has the potential to significantly increase the therapeutic impact of RFA while reducing needless destruction to the surrounding normal tissues and critical structures. The evaluation and estimation for these variables involved some equations that would be solved using COMSOL Multiphysics® 5.5, which is a FEA software to help understanding hyperthermia study with theoretical method that involving tools of electromagnetic, heat transfer and material properties of biological tissue [5]. Optimization is well suited to computational models in a low cost manner since the time, effort and expense of laboratory experiments can be reduced significantly [6]. Sheetal Jha at el., [7], who investigated the role and risk factors of cancer therapy through hyperthermia, viewed that RF ablation technique on soft tissue should be considered the variety of technical aspects including mathematical models, tissue properties, realistic human anatomy, tissue damage and thermal dose. These considering elements significantly enhance the effectiveness of medical treatment by using a virtual experiment to model and optimise the therapy with great accuracy.

2. Simulation

In this study, 3D models of spherical shape tumor with diameters of 1 cm, 1.5 cm, 2 cm, 2.5 cm, and 3 cm were exposed to RF thermal. Model with tumors diameter size less than 2 cm (1 cm, 1.5 cm, and 2 cm) would be treated with a monopolar plain electrode whereas a 4-prong retractable needle electrode for tumor with diameters of 2 cm, 2.5 cm, and 3 cm. Normal liver tissue and blood vessels have been modeled in a cylindrical shape for better visualization of the spherical surface of tumor tissue during ablation, as illustrated in Figure 1 and Figure 2. The blood vessel has a diameter of 10 mm and positioned 26 mm from the tumor center, which is a little far away for tumors less than 2 cm.

![Figure 1. The simulation model of cancer tissue treatment using a plain electrode](image1)

![Figure 2. The simulation model of cancer tissue treatment using a 4-prong retractable antenna of an electrode](image2)
2.1. Tumor Ablation Simulation Process

The flowchart in Figure 3 summarized the tumor ablation simulation process that would be conducted. The simulation is done on five (5) different tumor diameters that are less than 3 cm, ranging from 1 – 3 cm with 0.5 cm increment, the electrode potential set for the simulation will be ranged from 20 - 45 V but it also ensures the temperature exposure within the entire tumor tissue is above 50 °C, which can prevent bleeding and tumor seeding. For tumors with diameter less than 2 cm, a monopolar plain RF probe position with one cycle will be used, and for tumors bigger than 2 cm diameter, targeted heating will use the 4-prong retractable electrode. The simulation was then run to identify the ablation zone within tumor and the neighboring normal tissue that was impacted with a margin of 5 - 10 mm. The therapy simulation process is complete if the fraction damage of whole tumor tissue that has been treated yields an output of 1 indicating that the tumor tissue has been destroyed 100 %, and it also allowed total damage of approximately 5mm margin of closest normal tissue beyond tumor boundary, but it should not exceed 50 % damage into a 10 mm margin to avoid overheating. The time exposure and temperature that reach fraction damage with 1 would be recorded and compared with the surface tumor ablation in terms of temperature and fraction damage over time.

![Flowchart of Tumor Ablation Simulation Process](image-url)

Figure 3. Flow of tumor ablation simulation process
3. Result and Discussion

3.1. Plain Electrode

The plain electrode was set with a voltage in the range of 20 – 35 V for tumors less than 2 cm in diameter (1, 1.5 and 2 cm). The outcomes of this study have been summarized in the form of a table for these three different sizes of tumors, which are used for simulation of cancer therapy using plain electrodes as shown in Table 1.

Table 1. The summarize results of 1cm, 1.5cm and 2cm of tumour diameter tissue

|                | 1 cm       | 1.5 cm     | 2 cm       |
|----------------|------------|------------|------------|
| Voltage Apply  | 20V        | 28V        | 35V        |
| Time Damage    | 6 min      | 12 min     | 18.5 min   |
| Temperature within Whole Tumor Tissue at Time Damage | 56 – 99 ºC | 53 - 99 ºC | 51 - 99 ºC |
| Fraction Damage (5 mm of Margin) | 0.6 – 1.0 | 0.5 – 1.0 | 0.5 – 1.0 |
| Temperature (5mm of Margin) | 42ºC - 56 ºC | 42ºC - 53 ºC | 40ºC - 51 ºC |
| Fraction Damage (10 mm of Margin) | 0.35 – 0.5 | 0.3 – 0.5 | 0.18 – 0.4 |
| Temperature (10 mm of Margin) | 38 – 42 ºC | 38 - 42 ºC | 37 - 40 ºC |

The tumour tissue diameters of 1, 1.5, and 2 cm have been offered with temperatures over 50 ºC, which increases tumours completely impaired with severe external heat source. Excessive heat exceeding 50 ºC within the tumour tissue region is necessary in this treatment. However, it should not surpass 100 ºC. The temperature that is exposed to the neighbouring normal tissue with a 5 mm free margin should be maintained at 42 – 50 ºC, causing the normal tissue to be destructive above 50 percent during 6 - 20 minutes of thermal heat ablation modelling. The free margin region of 5 mm beyond the tumour boundary is allowed to be damaged by 99.99% because this region should be ablated to ensure that this small thickness of tumour border that is associated with normal tissue is destroyed. Meanwhile, 10 mm of free margin should be damaged below 50 % for normal tissue destruction to avoid excessive damage to undesired regions. This region should also have temperatures below 38 ºC that are close to body temperature, allowing for less overheating within this margin region.

The results of simulations of 1 cm, 1.5 cm, and 2 cm of tumour tissue would be compared with the results of prior research, as listed in Table 2, to assess the validity of this study's simulation results. Previous research should be correlated with the criteria and features of modelling geometry, such as the 1-2 cm tumour diameter size that has been evaluated using the monopolar electrode by employing the RFA technique. This study yielded almost identical results to earlier studies in terms of temperature range, voltage, and time damage. It also closed the simulation result with Sundeep Singh since this study conducted the same dimension and material of monopolar electrode as his research [8].

Table 2. Features of HT therapy that has been treated using the plain electrode with RFA technique

| Study                  | Size of Tumor            | Voltage | Time   | Temperature  | Simulation/ Experiment |
|------------------------|--------------------------|---------|--------|--------------|------------------------|
| Gurwinder Singh [9]    | Irregular shape of 1.3 cm of tumor diameter | 24V     | 10 min | 65 - 100 ºC | Simulation (COMSOL)    |
| George Zorbas [10]     | 2 cm                     | 20 V    | 12 - 15 min | 60 - 72 ºC | Simulation (Matlab)    |
| Sundeep Singh [8]      | 1 cm                     | 20 V    | 7.2 min | 50 - 100 ºC | Simulation (2D COMSOL) |
|                        | 1.5 cm                   | 25 V    | 12.9 min |              |                         |
|                        | 2 cm                     | 30 V    | 18.7 min |              |                         |
3.2. The 4-Prongs Retractable Antennas of An Electrode

The 4-prong retractable electrodes of a needle offer greater surface contact with soft tissue as compared to a plain electrode, resulting in complete thermal destruction of the target location with minor overheating at the undesired region within the range of 20 – 45 V.

| Voltage Apply   | 2 cm | 2.5 cm | 3 cm |
|-----------------|------|--------|------|
| Time Damage     | 10.5 min | 11.5 min | 12.5 min |
| Temperature within Whole Tumor Tissue at Time Damage | 43 - 65 °C | 51 - 99 °C | 52 - 100 °C |
| Fraction Damage (5 mm of Margin) | 0.9 – 1.0 | 0.5 – 1.0 | 0.4 – 1.0 |
| Temperature (5 mm of Margin) | 44 - 79 °C | 42 - 65 °C | 40 - 52°C |
| Fraction Damage (10 mm of Margin) | 0.35 – 1.0 | 0.3 – 0.5 | 0.18 – 0.4 |
| Temperature (10 mm of Margin) | 43 - 60°C | 38 - 42°C | 37.5 - 40°C |

Based on Table 3, the temperature exposed within 5 mm of a normal cell is higher than within a 2 cm tumour cell, while the temperature exposed within 10 mm of a normal cell is nearly identical, which would cause excessive damage of unwanted area by 100 % when applying voltage at 22 V, indicating that the 4 antennas with full curves are not suitable for 2 cm tumour diameter tissue even though the optimum voltage supply has been supplied. However, tumour tissue diameters of 2.5 cm and 3 cm are best suited for treatment with this type of electrode since the percentage damage within a 10mm margin is less than 50 % and the temperature is close to body temperature. As a consequence, as the ablation continues, the tissue may become dehydrated and burnt, increasing the resistance of the tissue to electrical current. Rising impedance and excessive local temperature limit RFA [11]. The damaged healthy cell is only a small region that can be repaired by regenerating new cells. As a result, the RFA approach is minimally invasive since it does not cause serious harm and it is highly effective at fully demolishing 99.9 percent of cancer tissue. In a previous study, the RFA method was suggested to be a possible first-line therapy for certain patients with small hepatocellular carcinomas or an option for those who are not suited for surgical intervention or have failed chemotherapy.

When all of the surface coordinates within the tumor reach a fraction damage of one, the temperature usually over 50 °C, indicating that it is completely burning and has met the RFA temperature condition. In this study, the 2.5 cm and 3 cm tumor tissue diameters kept their temperatures above this high heat, while keeping them below 100 °C with optimal voltages of 35 V and 40 V, respectively. Their 5 mm margin exhibited significant damage with a maximum fraction damage of 1 in certain regions, but their 10 mm margin showed less undesired cell burning with a lower 50 percent damage to healthy tissue for both tumor diameters. If the normal tissue is exposed to 40 °C for more than 12.5 minutes, the tissue damage is estimated to be 40 % for a 3 cm tumor diameter. Even while normal tissue has a higher resistance than tumor tissue, it can still cause harm at lower temperatures if exposed for an extended period of time.
Table 4. Features of HT therapy that has been treated using 4-prongs antenna of an electrode with RFA technique

| Study                      | Size of Tumor           | Type of Electrode                                                                 | Voltage/ Power          | Time   | Temperature  |
|----------------------------|-------------------------|-----------------------------------------------------------------------------------|-------------------------|--------|--------------|
| Gerald D. Dodd [12]        | 2 - 5 cm                | - Single electrode                                                               | 50 – 200 W (450-500 kHz)| 8-20 min| 50 – 100 °C  |
|                            | 2 - 3 cm                | - 4-prongs retractable needle electrodes (6 overlapping ablations)               |
|                            | More than 3 cm          | - 4-prongs retractable needle electrodes (12 overlapping ablations)              |
| Cleber da Silva [13]       | (Ablation only within liver tissue) | 4-prong ablation catheter (15 gauge) with multiple retractable electrodes | 14.5 V and 10 W (450 – 500 kHz)| 16 min| Less than 100 °C |
| Yuman Fong [14]            | 3cm of 4-prongs retractable needle electrodes: | 100 -200 W (460 – 500 kHz) | 5 min for 1 overlapping ablation | 50 – 100 °C |
|                            | Less than 3 cm          | - 1 or 2 multiple overlapping ablations                                          |
|                            | More than 3 cm          | - 12 multiple overlapping ablations                                              |

Table 4 displayed the prior research simulation results relating to RFA within soft tissue of the liver in terms of damage duration, energy sources (voltage, power, and current supply), and temperature range applied in order to compare this study simulation result. Except for Cleber da Silva [13], who studied the electrode testing of a 4-prong ablation catheter (15 gauge) with multiple retractable electrodes (Rita Medical Systems) on healthy tissue only, the majority of studies used a two compartments model, which is a model that includes tumour and healthy tissue with different tissue properties. He claims to know the ablation region exposed inside liver tissue in determining the appropriate size of tumour that is suitable for this type of electrode.

The studies that used 4-prong retractable needle electrodes mostly used multiple overlapping ablation to increase the damage at completely on 10 mm margin from tumour tissue boundary, which can completely destroy a tumour tissue exceeding 3 cm in diameter with a required margin of normal tissue. According to them, a systematic strategy is required to treat the whole lesion with at least a 10mm margin of destruction to ensure that the tumour is completely destroyed and unable to metastasize. In this study, the minimal damage is applied by only assuring a completely destructive tumour region with a little damage area on a 5 - 10 mm margin within normal tissue. In this case, the neighbouring normal tissue is not affected too much during tumour ablation since the ablation primarily occurs inside the tumour border region, as opposed to a prior research in which the ablation also included a 10 mm free margin at a temperature over 50 °C to ensure entire ablation. Thermal damage time and temperature ranges are nearly identical to earlier research. Thus, the first ablation is actually sufficient to destroy the cancer tissue.

4. Discussion
Local HT treatments are mostly used to treat cancer tissue that is less than 3 cm in size. In this study, a plain electrode is used to treat cancer cells less than 2 cm in size, while the tumour tissue diameter of 2 - 3 cm has been treated with a 4-prong retractable electrode of a needle in order to shorten the time required to kill the cancer cell while increasing the surface contact of the electrode with the tumour region. The 4-prong electrode is inconvenient for eliminating tumour tissue less than 2 cm in size.
because it causes a wider zone of overheating inside nearby normal tissue. The free-margin of 5 mm is permitted to inflict entire destruction, as the high heat delivered might destroy normal tissue that comes into contact with the target region's border. Furthermore, the free-margin of 10 mm cannot exceed temperature damage beyond 42 °C, and its temperature must be near to normal body temperature with a fraction damage of less than 0.5. HT promotes cytotoxic effects on tumour cells. Tumor cells are more sensitive to heat than normal cells, thus they would be killed following HT treatment utilising the RFA method at 50 °C within 6-20 min for tumour diameter tissue of 1-3 cm. When heated, tumour cells have a temperature that is 3–7 °C higher than nearby normal cells because of their high thermosensitivity [14]. Hence, appropriate HT will directly destroy tumour cells while causing no harm to adjacent normal cells. The voltage supply range to the 1, 1.5, and 2 cm of tumour tissue is 20 - 35 V using a plain electrode, and the temperature that has been given over 50 °C is completely destroyed inside the tumour tissue region. While the tumour tissue diameters of 2 cm, 2.5 cm, and 3 cm have been treated using a 4-prong electrode with a voltage range of 22 - 45 V. Both electrodes destroyed the cancer tissue within 6 - 20 minutes while keeping the temperature inside the tumour tissue area above 50 °C. When a 2cm tumour diameter tissue is treated using plain electrodes rather than a needle's 4-prong retractable electrode, favourable results are obtained. It is because the length of the 4-prongs of retractable electrodes is more than 2 cm of tumour tissue, resulting in direct contact with normal tissue, which can cause more damage to normal tissue than tumour tissue due to its proximity to normal tissue.

5. Conclusion and Future work
When the temperature rises beyond 50 °C, thermal coagulation and protein denaturation occurred, eventually leading to tissue necrosis. Thus, temperature exposure within tumour tissue of 50 - 100 °C has totally killed the targeted region, while minimizing damage to the adjacent normal tissue region with within 5 - 10 mm free-margin. The exposure duration is determined by the tumour diameter and the voltage used, with the larger tumour diameter tissue requiring the greatest time exposure with a high voltage. The greatest exposure period can potentially cause excessive damage to the closest tumour cell if the tissue is exposed to external high heat for longer than the optimal damage duration.

In future works, retractable electrodes with more than four prongs, such as six or eight prongs, are appropriate to maximise target tissue ablation while creating less time damage. Besides that, both simulation and real-world experiments should be carried out in order to determine the correctness of both data sets with high resemblance, suggesting that the HT therapy is successful in destroying cancer treatments with intense heat exposure.

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