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WATER BOLUS MODIFICATION FOR REDUCING UNWANTED HOT SPOTS FOR BREAST HYPERTHERMIA CANCER PROCEDURE

Nurul Syamimi Hanim binti Noraini

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NURUL SYAMIMI HANIM BINTI NORAINI

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ABSTRACT

Hyperthermia Treatment Procedure (HTP) is a method that raises the temperature between 41^0-46^0C, which then denaturate cancer tissue into necrotic tissue. However, due to the poor penetration depth and difficulty in controlling focus position distance to the treated tissue, the HTP success rate is still low. In conjunction with that, many kinds of research are conducted in order to overcome the matters involved with penetration depth and focus position distance. HTP has fewer side effects, but since HTP utilizes high heat in its procedure towards the treated cancer tissue, it may lead to massive skin burn problems. Therefore, in this research, a modified water bolus is developed in order to provide a cooling environment during HTP execution. Nevertheless, the addition of the water bolus, it may reshape the focus position distance. Hence, a modification of water bolus is significant in ensuring not only reducing the skin burn problem, at the same time, the penetration depth and focus position distance on the treated tissue can be fully provided with a minimal area of unwanted hot spots at surrounding healthy tissue. SEMCAD X is used to model a breast phantom, which consists of breast fat and breast cancer. It is also used to model the microstrip antenna that is used as an HTP applicator and to model the water bolus. Then, the simulation to attain the Specific Absorption Rate (SAR) is also carried out by using SEMCAD X. The SAR represented the penetration depth and focus position distance on the treated tissue. Based on the simulation results, adding the rectangular water bolus with distilled has presented the best penetration depth and focus position distance towards the treated tissue. Furthermore, the unwanted hot spots in surrounding healthy tissue also have been reduced. However, there are some recommendations that need to take into account, especially in providing more investigation in terms of water bolus cover materials, other coolant fluids and water bolus hardware fabrication to further observe the impact of adding the water bolus to the treatment procedure.

ABSTRAK

Prosedur Rawatan Hyperthermia (HTP) adalah kaedah yang menaikkan suhu antara 41°-46 °C, yang kemudian menguraikan tisu barah ke dalam tisu nekrotik. Oleh kerana kedalaman penetrasi yang lemah dan sukar untuk mengawal jarak kedudukan fokus ke tisu yang dirawat, kadar keberkesanan HTP masih belum dapat dicapai sepenuhnya. Hasilnya, beberapa penyelidikan dilakukan sepanjang kajian ini untuk meningkatkan jarak kedudukan fokus dan kedalaman penetrasi. HTP mempunyai kesan sampingan yang lebih sedikit, tetapi memandangkan HTP menggunakan haba yang tinggi dalam prosedurnya ke arah tisu kanser yang dirawat, ia boleh menyebabkan masalah pembakaran kulit yang berlebihan. Oleh itu, dalam penyelidikan ini bolus air yang diubah suai dibangunkan untuk menyediakan persekitaran penyejukan semasa pelaksanaan HTP. Namun begitu, penambahan bolus air, ia mungkin membentuk semula jarak kedudukan fokus. Oleh itu, pengubahsuaian bolus air adalah penting dalam memastikan bukan sahaja mengurangkan masalah kulit terbakar, pada masa yang sama, kedalaman penembusan dan jarak kedudukan fokus pada tisu yang dirawat boleh disediakan sepenuhnya dengan kawasan minimum titik panas yang tidak diingini di sekeliling tisu yang sihat. SEMCAD X digunakan untuk memodelkan phantom payudara, yang terdiri daripada lemak payudara dan kanser payudara. Ia juga digunakan untuk memodelkan antena jalur mikro yang digunakan sebagai aplikator HTP dan untuk memodelkan bolus air. Kemudian, simulasi untuk mencapai Kadar Penyerapan Khusus (SAR) juga dijalankan dengan menggunakan SEMCAD X. SAR mewakili kedalaman penembusan dan jarak kedudukan fokus pada tisu yang dirawat. Berdasarkan keputusan simulasi, menambah bolus air segi empat tepat dengan air suling telah memberikan kedalaman penembusan terbaik dan jarak kedudukan fokus ke arah tisu yang dirawat. Tambahan pula, bintik panas yang tidak diingini dalam tisu sihat di sekeliling juga telah dikurangkan. Walau bagaimanapun, terdapat beberapa cadangan yang perlu diambil kira, terutamanya dalam menyediakan lebih banyak penyiasatan dari segi bahan penutup bolus air, cecair penyejuk lain dan fabrikasi perkakasan bolus air untuk memerhatikan lagi kesan penambahan bolus air kepada prosedur rawatan.

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LIST OF ABBREVIATIONS

CC	-	Cranio Caudal
HTP	-	Hyperthermia Treatment Procedure
ID	-	Inner Depth
MLO	-	Medio-lateral obliques
MRI	--	Magnetic Resonance Index
SAR	-	Specific Absorption Rate
SD	-	Surface Depth

LIST OF SYMBOLS

ρ	-	Density
c	-	Specific heat capacity
W	-	Width of antenna
L	-	Length of antenna
Wg	-	Width of the ground antenna
Lg	-	Length of the ground antenna
f	-	Operating frequency
C	-	Speed of light
t	-	Timetaken
V	-	Volume
T	-	Temperature
E	-	Peak electric field vector

CHAPTER 1

INTRODUCTION

1.1 Research Background

Hyperthermia is one of the treatments used in treating breast cancer. Hyperthermia is a type of treatment in which body tissue is heated to as high as 41–45°C to help damage and kill cancer cells with little or no harm to normal tissue [1]. Therefore, most healthy tissue is not damaged during hyperthermia if the temperature remains below the range temperature. But different features on different tissues can cause higher temperatures to occur in certain places, which can cause burns, blisters, discomfort, or pain [2].

A treatment of non-invasive hyperthermia treatment procedure (HTP) has three (3) main components, which are a hyperthermia applicator, a water bolus, and a treated tissue. The most used hyperthermia applicator in hyperthermia research is a microstrip antenna [3]. It can perform a very good penetration depth and focus position distance on the treated tissue.

Since the antenna is placed close to the patient, body surface heating occurs due to conductive and dielectric loss, which is unavoidable and, therefore, the body surface needs to be cooled [4]. Therefore, it is solved by the circulation of ionised/demineralised water through a plastic or silicone bag placed between the antenna applicator and the body, called the water bolus. Water bolus consists of a circulating deionised water-filled with a flexible shape at a controlled temperature, which is used for reducing the unwanted hot spots on surrounding healthy tissue [3]. Furthermore, it also provides a cooling environment to the skin during hyperthermia execution that is able to reduce the massive skin burn problem.

This research focused on water bolus modelling, and various modifications on material types and water structures, including different thicknesses, heights, and widths, are investigated. This investigation is important to carry out to ensure the reduction of unwanted hot spots on the surrounding healthy tissue is adequate in terms of penetration depth and focal position distance. Therefore, water bolus modifications are emphasised to ensure the HTP can be improved with minimal side effects during the hyperthermia execution.

1.2 Problem Statement

Breast cancer in Malaysia, as reported by the World Health Organization (WHO), will increase by (17.3%) in 2020. Breast cancer is the highest incidence among Malaysian women, with 32.9% compared to other cancer incidences [5]. Accordingly, with this increased incidence of breast cancer, this research accentuates breast cancer as a tissue to be treated.

Currently, hyperthermia treatment is considered a safer treatment for breast cancer, with three main components, which are a hyperthermia applicator, water bolus and cancer that need to be treated. The good design of the water bolus and applicator, penetration depth and focus position distance can be achieved.

However, there is an issue in hyperthermia treatment that needs to be highlighted the massive skin burn problem and health effects due to unwanted hot spots on healthy tissue. The water bolus needs to be designed to reduce the problem without affecting the required penetration depth and focus position distance on the treated tissue.

Based on previous studies, the current existing water bolus consists of the following:

i. Most of the water bolus used distilled water as a coolant liquid in water bolus
ii. Hydrogels have the potential to be used as a water bolus during hyperthermia treatment
iii. Materials to cover the water bolus were also not included in the simulation study
iv. Water bolus thickness, width, and height to obtain the required penetration depth and focus position distance on the treated tissue were not investigated thoroughly.

Hence, in this research, a modified water bolus is proposed to treat breast cancer while minimising health effects that may contribute during hyperthermia execution, such as unwanted hot spots on the surrounding healthy tissue.

1.3 Research Objectives

Concerning the stated problem statements in Section 1.2, three research objectives are listed:

i. To design a rectangular microstrip antenna applicator as a heat applicator for hyperthermia procedure
ii. To add water bolus to the treatment procedure to reduce the unwanted hot spots on surrounding healthy tissue
iii. To analyse the SAR distribution in the treated tissue while maintaining the required depth and focus position distance on the treated tissue.

1.4 Summary of the Chapter

In this chapter, a background, problem statement, research objectives, and research have been discussed. In summary, hyperthermia uses heat with a temperature around 41^oC-46^oC to help damage and kill cancer cells. The effects of high temperatures that can lead to adverse health effects can be reduced with a water bolus added into the treatment procedure. A water bolus is a cooling system to reduce unwanted hot spots and simultaneously prevent skin blisters on the patient during hyperthermia treatment. Further investigation on water bolus is carried out to observe the biological responses on the treated tissue when different water bolus sizes are applied.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter provides a review of the relevant literature and research related to hyperthermia, microstrip antenna and water bolus development for hyperthermia cancer treatment procedures. This literature review discusses four main parts; hyperthermia for cancer treatment, breast cancer, applicators, and water boluses. They are explained in Sections 2.1 to 2.3.

2.2 Breast Cancer in Malaysia

In Malaysia, the common types of cancer are breast cancer, lung cancer, and nasopharyngeal cancer. The statistics provided by World Health Organization (WHO) shows that breast cancer is the highest cancer incidence in 2020 for both sexes and all ages, as in Figure 2.1.

In addition, 8418 cases were recorded, which accounted for 17.3% in 2020 and breast cancer is the highest incidence, as shown in Figure 2.2. Breast Cancer in Young Women is caused by a variety of risk factors (BCYW). One of the issues is the younger generation of women's bad lifestyle. Breast cancer is increased by unhealthy lifestyle behaviours such as eating high-fat meals, being physically sedentary, and being obese, as well as smoking, not having children, not nursing, birth control, hormone treatment, and breast implants. [3].

In conjunction with that, this increment in breast cancer incidences, it has become a major concern that needs to be addressed, and the requirement in identifying alternative cancer procedures is substantial.

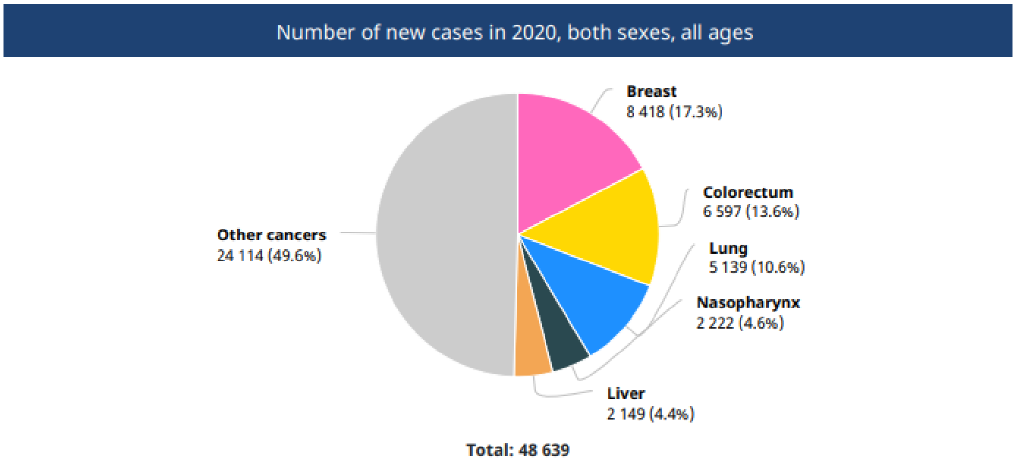

Figure 2.1: Number of new cases in 2020

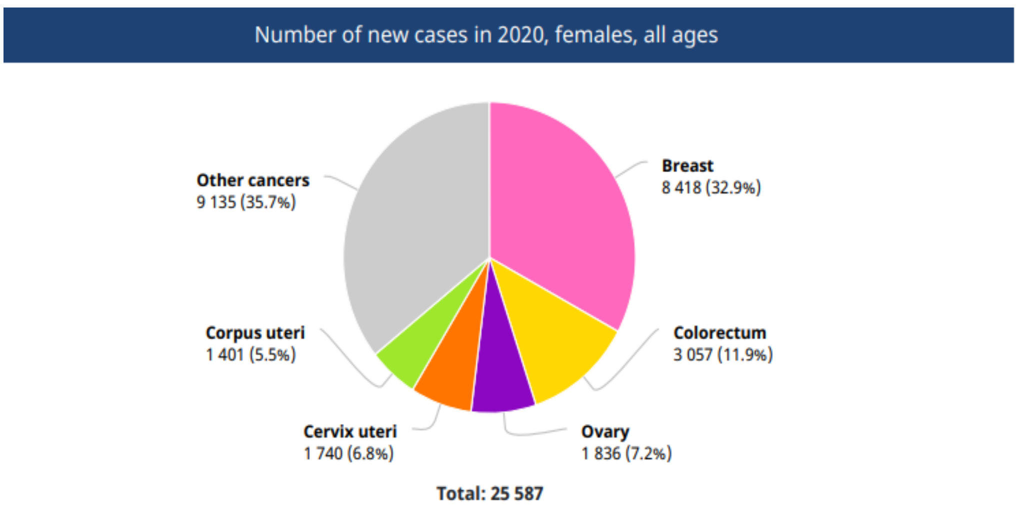

Figure 0.2: Number of new cases in 2020 for females.

2.2.1 Screening and Treatment

Currently, Mammography is the most commonly used breast cancer screening test. Women at high risk of breast cancer may benefit from magnetic resonance imaging (MRI). Certain variables influence whether a woman should be examined for breast cancer and which screening test should be used. Breast examinations, thermography, and tissue sample are other screening methods that have been or are being examined in clinical trials. Tests are used to screen for different forms of cancer in people who do not have symptoms. [4]

On the other hand, the treatment options for breast cancer are surgery, adjuvant therapy, and neoadjuvant therapy, including chemotherapy, radiotherapy, and hyperthermia.[5]. Breast cancer can be treated in several ways. It depends on the type of breast cancer and how far it has spread. Each treatment has its own advantages and disadvantages, as in Table 2.1.

Table 2.1 Different Types of Breast Cancer Treatment [5]

Therapeutic method	Surgary	Chemotherapy	Radiotherapy	HTP
Range of applicator	Early, mid-term, and large stage cancer	Mid-term, advanced and metastatic cancer stage	Mid-term, advanced, and Region-sensitive cancer stage	Early-stage, Mid term and Advanced cancer
Advantages	Mechanistic method to temporarily remove a large tumor, without chemo- and radio-resistance effects	It is a systematic therapeutic method with wide ranges of cancer-killing effects	• It can effectively terminate cancer cells using multiple beams of radiation. • Effective in killing actively dividing cells	• Normal tissues remain undamaged • Increase immune responses in the body against cancer
Disadvantages	• Hard to conduct in certain parts. • Could not kill cancer completely	• Lack of specificity which easily does harm to normal tissues. • Ineffective in chemoresistance cancer cell	•Long treatment cycle. •Many complications after radiotherapy. • Could not kill cancer completel	•The requirement to focus the microwave power at the targe

Based on Table 2.1, HTP is investigated further in this research as it can increase the immune responses in the body against cancer while decreasing the immune suppression and immune escape of cancer. Moreover, the cancerous cells will undergo apoptosis in the direct response to the HTP without affecting the healthy tissues. More advantages have been shown with hyperthermia cancer treatment procedures if compared to other conventional cancer therapies. However, there are several limitations of HTP that need to be considered. These limitation needs to be improved in order to increase the effectiveness and simultaneously increase the success rate of this treatment, especially in different stages of cancer.[5]

2.2.1 The mechanism behind hyperthermia therapy

Hyperthermia treatment raises the body temperature to ~ 107 °F and makes the increases oxygen level in red blood cells through the vessels and to the tumour, as shown in Figure 2.3 below.

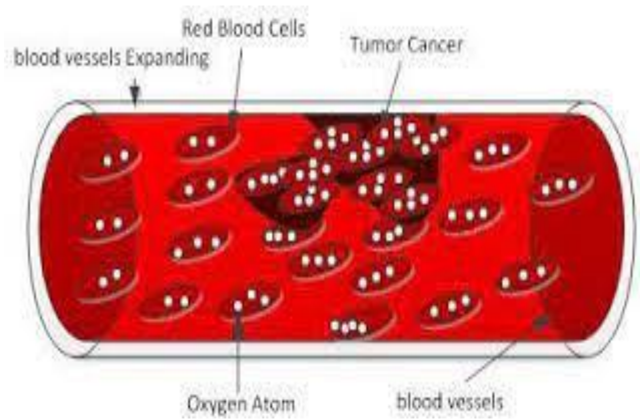

Figure 2.3: Red Blood Cells and Oxygen Transfer during Hyperthermia Therapy

Hyperthermia treatment basically objectives the blood vessels and inflate them at the same time as this treatment beams frequency makes a speciality of the most cancers area. This inflation gives more chance to the chemotherapy to attack the cancer cells, as shown in Figure 2.4 below. Alshehr, 2020, stated this therapy diminishes the cancer cells and can help to spot the cancer cells easily [8]

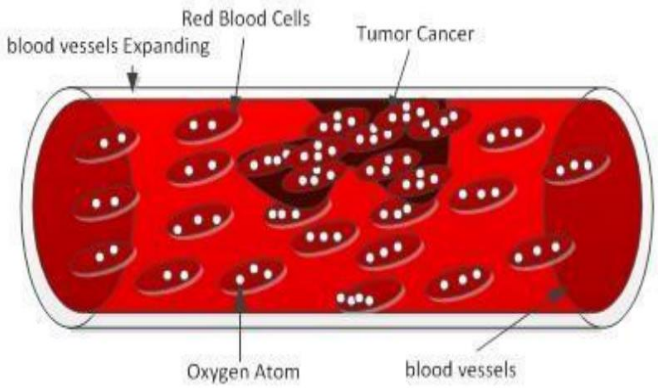

Figure 2.4: Expansion of Blood Vessels Due to Elevated Temperature

In addition, medical trials consider that radiation therapy must be given to the patients after an hour of hyperthermia therapy for an extra effective attack on the cancer cells. Further, they recommend the cancer trials that hyperthermia therapy cannot receive every single day. It needs two days as a minimum every season for the extra effective end result in an effort to avoid thermotolerance. Additionally, research shows that this therapy cannot receive every day due to the biological structure of the human body system. Similarly, the human body system is capable of creating a strong defence for its cells against heat alleviation, known as thermotolerance, where the body resists the heat and attempts to stabilise the body temperature. Tumour physiology research showed a sturdy bond between the tumour cells and the thermotolerance, and these cells can live on between 4-24 hours. Alshehr's research also proved that thermotolerance can be evolved fast and decays within the next five days. Thermotolerance can push and stress the human cells and might purpose tissue poisoning for a long time. This trouble decreased the development of the engineering revolution and increased the conflict of using hyperthermia therapy [8].

Furthermore, HTP is classified as a form of heat treatment in medical procedures. Thermal treatments are classified into three types: diathermy, hyperthermia, and thermal ablation. Table 2.2 shows a comparison of different thermal therapy.

Table 2.2 Comparison of Thermal Therapy [33]

Thermal Therapy	Characteristics
Diathermy	Diathermy is a pain-relieving therapy approach that uses electromagnetic radiation to produce heat inside the patient's body. This increased blood circulation, resulting in speedier recovery. This therapy is used to treat injuries such as sprains and strains, as well as muscle and tendon tears.
Hyperthermia	Externally exposed malignant tissues are heated to 41°C-45°C to convert them to necrotic tissues.
Thermal Ablation	Thermal ablation is a therapy that involves overheating the malignant tissue until it becomes necrotic. The temperature range used is 550C to 1000C. However, excessively heating the tissue can result in the destruction of different physiological and biological phenomena, especially in key organs such as the heart and brain..

2.2.3 Hyperthermia Therapy Challenges

The mechanism and period of heating inside the hyperthermia therapy are the poorest factors. While the hyperthermia devices address troubles, human body temperature and room temperature, they lose heat which means that the devices resist the heat and weaken their performance devices. The subsequent goals formerly and currently are to:

i. Decrease the heating time and study the efficiency of the devices after a long time of utilisation.
ii. Analyse how heat receives absorbed in the human body and the relationships between the thickness of human tissues and absorption.

iii. Study how to improve the heating mechanism through water bolus optimisation.

For this research, the improvement of the heating mechanism through water bolus optimisation is discovered by modifying the water bolus structure, especially in terms of height, width and thickness.

There are many types of hyperthermia, which are:

i. Whole-body hyperthermia
ii. Regional hyperthermia
iii. Local hyperthemia

Details on the discussion are presented in then next Section 2.2.4

2.2.4 Type of Hyperthermia

There are several methods of hyperthermia that still in analysis, which are regional, whole-body and local hyperthermia[34]. These methods are discussed in Section 2.2.4.1, 2.2.4.2. and 2.2.4.3, respectively.

2.2.4.1 Whole-body Hyperthermia

Cancer that has spread throughout the body is treated with whole-body hyperthermia treatment. In this kind of hyperthermia, patients were placed in a thermal chamber or wrapped in hot water blankets for brief periods of time, raising the temperature of the entire body to 41-46 °C. [28] . Immersed in a hot water bath and radiate with ultraviolet radiation are methods that normally used for this treatment. A circuit of blood will form an extracorporeal ring beside the body [29]. The circulating blood is crossed through a water bath or hot air for warmth and mixed into the central vein. The current volume of the blood that injected can be altered to fix and measure the anticipated body temperature. A WBH treatment session is usually operated for a few hours to reach the wanted temperature, followed by a one hour cooling period. Normal saline is injected to maintain the patient’s systolic blood pressure above 100 mmHg [29]. An example of a whole-body hyperthermia applicator is shown in Figure 2.5[30]