COMPARISON BETWEEN A-MODE AND B-MODE ULTRASOUND IN LOCAL HYPERTHERMIA MONITORING

MAIZATUL NADWA BINTI CHE AZIZ

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Dedicated, in thankful appreciation for support, encouragement and understandings to my beloved mother, father, sisters, brothers and supporters.

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ABSTRACT

Hyperthermia therapy is one of the therapy methods used for cancer treatment. It has shown to be an effective way of treating the cancerous tissue when compared to surgery, chemotherapy and radiation. However, real time monitoring method is capable in delivering a consistent heat and preventing any damages to the nearby tissue. Ultrasound is among the widely used technique in clinical setting. A-Mode ultrasound involves one-dimensional (1D) signal processing which enables a quantitative measurement on different types of breast tissues to be conducted faster as it has relatively simple signal processing requirement. On the other hand, B-Mode ultrasound offers good spatial resolution for thermal monitoring. Therefore, the aim of this study is to investigate and to compare the most optimum A-Mode and B-Mode ultrasound parameters to monitor hyperthermia in normal and pathological breast tissue. A series of experiment was conducted on 40 female Sprague Dawley rats. The pathological and normal rats were dissected and exposed to hyperthermia at variation temperature of 37°C (body temperature) and 40°C, 45°C, 50°C and 55°C for hyperthermia temperatures. A-Mode and B-Mode of 7.5 Mhz and 6Mhz was used simultaneously during the experiment for collecting acoustic information and scanning purposes before and after the hyperthermia exposure. Result obtained shows that, for normal tissue condition of both A-Mode and B-Mode, the attenuation calculation to mean of pixel intensity found to be (3.59±0.04)dB and 187.68 at temperature value of 50 °C. Meanwhile, in pathological tissue condition, the attenuation value with respect to pixel intensity was obtained by (3.36±0.26)dB at temperature value of 45°C and 199.26 was achieved at temperature value of 40°C. For backscatter coefficient to variance analysis, the result found that, in both A-Mode and B-Mode normal tissue condition, at temperature value of 40°C, (1.81±0.25) of backscatter coefficient was obtained while at 45°C, the variance value of 3298.94 was achieved. In pathological tissue, the temperature value of 40°C and 55°C was the most pronounce temperature dependent of (1.45±0.28) for backscatter coefficient with respect to 3275.35 of variance analysis. The result obtained from artificial neural network have shown that, 91.67% to 87.5% of testing to validation percentage accuracy of A-Mode was achieved, while in B-Mode, 88.89% and 81.25% of testing and validation data was obtained. Therefore, it is shown that, the use of A-Mode with comparison to B-Mode ultrasound can be used as another potential approach since its attenuation to pixel intensity and backscatter coefficient with respect to variance of A-Mode and B-Mode is very sensitive to the tissue structure in monitoring hyperthermia therapy with respect to the changes of temperature.

ABSTRAK

Terapi hipertermia merupakan salah satu kaedah terapi untuk rawatan kanser. Ia telah terbukti untuk dijadikan salah satu cara yang berkesan untuk merawat tisu kanser berbanding pembedahan, kemoterapi dan radiasi. Hipertermia memerlukan kaedah pemantauan masa yang nyata bagi meningkatkan keupayaan penghantaran haba yang tetap dan mencegah sebarang kecederaan terhadap tisu yang berdekatan. Ultra bunyi adalah teknik yang digunakan secara meluas dalam bidang klinikal. Ultra bunyi A-Mod melibatkan pemprosesan isyarat satu dimensi (1D) yang membolehkan ukuran kuantitatif dapat dijalankan dengan lebih cepat terhadap pelbagai jenis tisu payudara kerana ia mempunyai keperluan pemprosesan isyarat yang agak mudah. Malah, ultra bunyi B-Mod menawarkan resolusi spatial yang baik untuk memantau haba. Tujuan kajian ini adalah untuk menyiasat dan membandingkan parameter yang paling sesuai bagi ultra bunyi A-Mod dan ultra bunyi B-Mod dalam pemantauan hipertermia terhadap tisu payudara yang normal dan patologi. Satu siri eksperimen telah dijalankan terhadap 40 ekor tikus betina jenis Spague Dawley. Tikus patologi dan normal telah dibedah dan terdedah kepada hipertermia kepada pelbagai suhu dimana 37ºC (suhu badan) dan 40ºC, 45ºC, 50ºC dan 55ºC merupakan suhu hipertermia. Sebanyak 7.5Mhz dan 6Mhz frekuensi A-Mod dan B-Mod telah digunakan serentak semasa eksperimen dijalankan bagi tujuan mengumpul dan mengimbas maklumat akustik sebelum dan selepas pemantauan terapi hipertermia. Haisl kajian menunjukkan, untuk tisu normal kedua-dua A-Mod dan B-Mod, pengiraan pengecilan terhadap keamatan piksel didapati (3.59±0.04)dB dan 187.68 pada suhu 50 ºC. Untuk tisu patologi, nilai pengecilan terhadap keamatan piksel telah diperolehi sebanyak (3.36±0.26)dB pada suhu 45ºC dan 199.26 dicapai pada suhu 40 ºC. Untuk penyerakan pekali terhadap varian analisis, keputusan mendapati, untuk kedua-dua ultra bunyi bagi keadaan tisu normal, pada suhu 40ºC, sebanyak (1.81±0.25) penyerakan pekali telah diperolehi dan pada suhu 45ºC, varian sebanyak 3298.94 telah dicapai. Bagi tisu patologi, suhu 40ºC dan 55ºC telah dipilih sebagai suhu paling optimum dengan perolehan penyerakan pekali sebanyak(1.45±0.28) terhadap analisis varian sebanyak 3275.35. Peratusan rangkaian neural A-Mod dan B-Mod menunjukkan, sebanyak 91.67 % dan 87.5%, 88.89% dan 81.25% daripada data percubaan dan data validasi dicapai. Ini menunjukkan, kegunaan ultra bunyi A-Mod dengan perbandingan B-Mod berpotensi dan sangat sensitif terhadap struktur tisu dalam memantau terapi hipertermia dengan perubahan suhu yang pelbagai.

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MRI	-	Magnetic Resonance Imaging
RFA	-	Radio Frequency Ablation
LA	-	Laser Ablation
MWA	-	Microwave Ablation
HIFU	-	High Intensity Focused Ultrasound
H&E	-	Hematoxylin and Eosin
PRFS	-	Proton Resonance Frequency Shift
ARFI	-	Acoustic Radiation Force Impulse
SSI	-	Supersonic Shear Imaging
ANN	-	Artificial Neural Network
SVM	-	Support Vector Machine
BN	-	Bayesian Network
st-SVM	-	Standard Support Vector Machine
PSVM	-	Proximal Support Vector Machine
NSVM	-	Newton Support Vector Machine
LPSM	-	Lagrangian Support Vector Machine
SSVM	-	Smooth Support Vector Machine
ERM	-	Empirical Risk Minimization
CAD	-	Computer-aided Diagnosis
CSV	-	Comma Separate Value
MLP	-	Multilayer Perceptron
DMBA	-	7,12-Dimethylbenz anthracene
JPEG	-	Joint Photography Experts Group
FFT	-	Fast Fourier Transform
BSC	-	Backscatter Coefficient
MSE	-	Mean Squared Error

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Randomized trials on the benefits of hyperthermia therapy have been demonstrated over the past 20 years [1]. Hyperthermia is a cancer therapy that elevates the tumor to cytotoxic temperatures from 41°C to 45°C to boost in their control of temperature [2, 3]. Hyperthermia has proven to be potential in order to replace the current clinical treatment including radiotherapy and chemotherapy [2, 3, 4-8]. It has been applied in several diseases including breast cancer [5], glioblastoma [9], neck and head cancer [10], hepatocellular carcinoma [11] and lung cancer [12]. However, different type of thermal therapy with high temperature value have also been searched and investigated [13-17].

In 2012, The International Agency for Research in Cancer (GLOBOCAN) reported 5,410 new breast cancer cases in Malaysia, in which 50% of Malaysian women were diagnosed with breast cancer at an early age while 20% of women in developed countries were diagnosed before the age of 50 [18, 19]. Some tumors are very aggressive, grow much faster, and require immediate treatment. The detection of breast masses of breast abnormalities at the earliest stage significantly improved the survival rate of patients as demonstrated by group of investigators [20, 21].

Hence, early treatment of breast cancer is very important at this time to get rid of the cancer and perhaps save lives.

The application of hyperthermia therapy is now growing rapidly in medical field especially for treatment of benign and malignant solid tumors [22] as an innovative and less invasive therapy method. Hyperthermia therapy is one of the cancer treatments that also include surgery, chemotherapy, radiation therapy and immunotherapy [23]. It involves the changes and increase in body temperature over the threshold temperature of an organism [23]. In other words, hyperthermia is a process of delivering heat to cancerous tissue until its durable temperature has been exceeded by expose to heating ablation, including water bath and coagulation of microwave. The treatment could be done successfully if the temperature value of targeted tissues is controlled and monitored within a suitable range [24]. Hyperthermia treatment makes use of artificial heat, usually in the range of 40°C to 60°C, from external sources to destroy cancerous cells or to prevent their further growth [25]. Also, as reported by previous study, the temperature range of hyperthermia therapy is from 40 to 48°C and is maintained at the treated site for a period of one hour or more [26-29]. In some cases, hyperthermia therapy is used as adjuvant therapy [26] with other therapy methods such as radiation to increase the tumor regression rate rather than radiation alone [30].

The lack of precise information available in guiding therapy has been reported to be a major limitation in thermal therapies [2,3,7,31-35]. In order to achieve the goals and competency of current and forthcoming heating devices and systems, the temperature distribution is routinely measured invasively. To meet the distributions of temperature satisfaction for the purpose of assessing thermal dosage appropriately, the limited number of measurement distribution could be avoided [7,32]. Multiple heating devices has boosted the demand for controlling measurement of temperature values that has potential to provide the feedback related to distribution of temperature in details. Thus, it improves the capability and consistency in delivering the heat source by achieving desired temperature value [36-40].

Hyperthermia monitoring with the guidance of Magnetic Resonance Imaging (MRI) is the current gold standard in clinical setting and it is based on the concept of shift of proton resonance frequency. Its function is primarily for surgeons to perform a real-time progression assessment of in-vivo tissue necrosis [41,42]. Although MRI has shown to be capable in visualizing very clear and anatomically correct images, it is found that its performance degrades during hyperthermia treatment due to small temperature interval changes [43]. In contrast to ultrasound system, investigation into clinical trials in hyperthermia therapy using A-Mode has not yet been tested in clinical setting although it is an attractive modality with a simple signal processing approach for data acquisition. Previous study has been focused only on applying heat to study properties of tissue. Hence a comparison between A-Mode and B-Mode ultrasound performance is not reported. However, B-Mode ultrasound is more widely accepted in clinical environment for hyperthermia therapy as compared to A-Mode. Notably, it is sensitive to temperature change, requires simple signal processing and provides good spatial resolution [44]. Additionally B-Mode ultrasound is widely used and capable to evaluate the different kind of tumors and frequently applied in guiding the biopsies especially for breast, liver, thyroid, ovarian, kidney, prostate and uterine [45,46]. Technically, the monitoring approaches of B-Mode are based on variation in acoustic speed, [47-49], energy of backscattered pulsed ultrasound and acoustic nonlinear parameter imaging [49-51]. Although B-Mode system is widely accepted among clinicians, the presence of motion artefacts and degradation of image contrast is the biggest challenge and limitation experienced by B-Mode in hyperthermia therapy, which affects the performance of treatment as a whole.

Therefore, this research was conducted to further search and analyse the potential and its effectiveness of A-Mode ultrasound in monitoring hyperthermia in comparison to B-Mode ultrasound system. Both of this ultrasound system is relevant to be use in this study specifically to monitor temperature during hyperthermia monitoring because this technique is relatively inexpensive, portable and can be easily employed in almost any current heating monitoring system with little concern about system compatibility.

Ultrasound is an attractive medical device compared with the other medical imaging modality, as it offers at low cost, non-ionizing, portable, easy to access and yet compatible [41]. This study will help to improve the overall hyperthermia therapy reliability to be accepted in clinical practice while assisting physicians and medical practitioners in monitoring hyperthermia treatment efficiently with minimal intervention.

1.2 Problem Statement

MRI is the current gold standard in hyperthermia monitoring. It is based on the quantification of shifts in the proton resonance frequency. However, this modality becomes more complex during hyperthermia monitoring and the cost itself is expensive in clinical applications [52,53]. Due to the requirement of significant facilities and capital investment with advancement of complexity heating devices, it limits the current usage though it appear to have spatial resolution satisfaction [54]. In addition, MRI requires capital investment and labour-intensive [43]. Ultrasound is a widely used modality in hyperthermia monitoring, as it is non-ionizing and has capability in giving real-time image acquisition for rapid monitoring of physiological changes and temperature values [55,56]. However, A-Mode ultrasound is not yet tested in clinical setting for hyperthermia therapy monitoring though it has simple requirement for signal processing. Additionally, B-Mode ultrasound is available at low cost, accessible, portable and compatible with other medical imaging modality [57].

Despite the wide acceptance in using B-Mode ultrasound for hyperthermia monitoring, this modality itself experiences certain limitations including insufficient image contrast and motion artefacts [58-63]. To resolve this problem, further investigation on the effectiveness of using A-Mode ultrasound performance in monitoring hyperthermia therapy in comparison to B-Mode ultrasound system was conducted.

In this study, a set of preclinical ex-vivo studies are carried out on both normal and pathological tissues that are harvested from animal models in order to observe the relationship between ultrasonic parameters of A-Mode signals and B-Mode images with the microstructural changes occurring in normal and pathological tissue samples. The subjects were dissected and exposed to hyperthermia at various temperatures of 37°C (body temperature) and 40°C, 45°C, 50°C and 55°C for hyperthermia temperatures. This indicates the progression of tissue necrosis during hyperthermia treatment. Additionally, a classification study is also conducted to compare the performance accuracy of A-Mode with the widely used B-Mode ultrasound technique via ANN in Matlab offline environment in which hyperthermia treatment method has recently displayed the potential to be promising as an adjuvant breast cancer treatment method in clinical setting.

1.3 Research Objectives

The main objective of this research is to investigate the accuracy of A-Mode ultrasound as a hyperthermia monitoring method in comparison to B-Mode ultrasound. Specifically, this study aims are as follows:

i. To identify the A-Mode and B-Mode ultrasound parameters that are sensitive to changes in temperature and tissue structure
ii. To compare the performance of A-Mode and B-Mode ultrasound in monitoring tissue denaturation process in hyperthermia treatment using ANN

1.4 Scope of Research

This research has been carried out to study the feasibility of A-Mode ultrasound and to compare its performance in B-Mode ultrasound as a monitoring method in hyperthermia therapy with variation of temperature value from 37 ^{o}C - 55^{o}C. Specifically, the scope of this study is to identify the main parameter of A-Mode and B-Mode ultrasound that are sensitive to tissue denaturation during hyperthermia.

It involves the measurement of the attenuation and backscatter coefficients for A-Mode and determination of pixel value and standard deviation for B-Mode. The performance percentage of A-Mode and B-Mode ultrasound in monitoring tissue denaturation process in hyperthermia treatment using ANN will then be compared. For this purpose, a series of experiments was conducted on 40 female Sprague Dawley rats in which 30 pathological rats were used as pathological study and 10 healthy rats were used for control group purposes in order to assess the potentiality and the effectiveness on the overall system. The experimental outcomes are fed to signal and image processing for performance measurements and the water bath method is used to mimic the real hyperthermia procedure.

1.5 Significance of Study

In this study, three main purposes that have been addressed. First, this study is conducted to identify the A-Mode and B-Mode parameters that are sensitive to changes in temperature and tissue structure and second, to compare the performance of A-Mode and B-Mode in monitoring tissue denaturation process in hyperthermia treatment using ANN. To date, MRI is the current gold standard in hyperthermia therapy.

Due to the requirement of significant facilities and capital investment with advancement of complexity heating devices, it limits the current usage though it appear to have spatial resolution satisfaction [54]. A-Mode ultrasound is no longer tested for hyperthermia therapy monitoring, although it provides simple signal processing; however, B-Mode ultrasound is widely used for hyperthermia therapy in clinical setting. While it has been widely accepted in clinical environment, B-Mode ultrasound has certain limitations, especially in terms of contrast and motion artefacts of image itself. Hence, further investigation on the effectiveness of using A-Mode ultrasound performance in monitoring hyperthermia therapy in comparison to B-Mode ultrasound system was conducted as solution to this issue.

The signal energy of breast tissue was monitored using A-mode and B-mode scanner before and after heating exposure of the breast at different temperature values of 37ºC as body temperature and followed by 40ºC, 45ºC, 50ºC and 55ºC, as monitoring temperatures respectively. The success of this study will help to provide a simple and safe method in monitoring local hyperthermia therapy using A-Mode ultrasound.

1.6 Thesis Structure Organization

The outline of this thesis is comprised of five chapters. Chapter 1 discusses the introduction to several primary point of view including research overview, research objectives, problem statement, scope of work, significance of study and as well as thesis outline. Brief reviews and discussions relevant to this study was delivered in chapter 2, especially in breast cancer treatment, hyperthermia therapy and ultrasonic parameter in hyperthermia monitoring. Next, methodological approach that was enrolled in study is explained in detail which includes the modelling processing and designation of system, experimental procedure and ultrasonic data analysis of signal and image processing via Matlab. Results and discussions are presented and discussed in chapter 4. Finally, summary of all the findings was delivered in chapter 5 with several recommendations that possible could be done in future work.

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