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Non-Invasive Heat-Induced Numerous Tissue Ablation Using High Intensity Focused Ultrasound Technique

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***Abstract*— In biomedical sector, High Intensity Focused Ultrasound (HIFU) is a non-invasive treatment that employs quasi acoustic waves to raise the temperature. According to its high efficiency and cheap cost, it has been the main focus of this research. The key stages of this tumor ablation include mechanical and thermal effects. Multiple tissue ablations were analyzed using HIFU simulation to optimize intensity, power, focal length, and lens radius of curvature to maximize tumor ablation while minimizing collateral harm to healthy tissue in the surrounding area. This model analysis incorporates clinical applications in order to determine the most optimum parameters. To accomplish this study, numerous types of human soft and hard tissue were considered. At a specific acoustic power and exposure time, the optimal frequency (1.6 MHz to 3.5 MHz) and power (120 W to 140 W) for each tissue were determined for effective tissue ablation. This study conducted all calculations by changing the lens focal length from 55 mm to 65 mm. The results of this procedure usually require a few weeks to safely and efficiently remove the tumor. Due to this optimum outcome, it indicates that the HIFU tumor ablation procedure has a high probability of success in the medical sector.**

***Index Terms*—Ablation of cancer tissue, bioeffects, healthcare, high intensity focused ultrasound (HIFU), thermal coagulation.**

I. INTRODUCTION

Biomedical engineering is the design of technological knowledge and system architecture for drug and diagnosis with the aim of boosting health care for people who need it [1]. Doctors have been able to treat cancer patients with this medication. It ranks second in the world's major causes of death. However, survival rates for several forms of cancer are increasing as a result of developments in cancer screening, therapy and prevention. It is a disease that causes uncontrolled cell division almost everywhere in the body. When this urbanization process happens in solid tissue, such as organs, muscles or marrow, it is considered as a tumor. Tumors aren't always cancerous. Extracellular matrix and a variety of tissue types make these unusual structures. Tumor signs and symptoms change based on which part of the body is afflicted. It can manifest itself in a variety of different manners. If anyone experiences unexplained bleeding or bruising, skin changes, dry cough or difficulty breathing, weight loss, fatigue or other symptoms that do not improve after a few weeks, have just seen a doctor so that issues can be diagnosed and treated as soon as possible. Tumors are classified into two categories (Benign tumor and Cancerous tumor). Benign tumors may grow to be very massive, but they do not spread or infect surrounding tissues or other organs of the body. It is possible for cancerous tumors to spread into nearby tissue, glands and other vital organs. HIFU is a nonsurgical thermal ablation approach used to treat benign and malignant substantial tumors. HIFU has healed numerous patients with endometrial cancer, pancreatic cancer, liver cancer, breast cancer, colon cancer and bone tumors throughout the last generation. Since its inception in the 1940s as a method of thermal tissue elimination that was feasible, HIFU has gained popularity due to recent improvements. For the capacity to penetrate deeper tissues, HIFU is superior to pre-existing skin tightening treatments nowadays. Throughout this process, HIFU radiation creates micro coagulation zones that extend from the deep dermis to the superficial musculoaponeurotic system. In comparison to traditional methods of cancer therapy such as surgical intervention and chemotherapy, HIFU has the feature of being quasi and having fewer post-treatment difficulties. Invasive operations have traditionally been used only to treat cancerous cells, but it is painful, pricey, time demanding and loaded with risks and hazards. It's also challenging to manage tissue-damaging consequences.

Based on the GLOBOCAN 2020 cancers occurrence and death estimates from the International Agency for Research on Cancers, nearly 19.3 million latest cancer cases would be recorded worldwide. Approximately 10.0 million people died from cancer (9.9 million assuming nonmelanoma skin cancer is excluded) [2]. It is anticipated that there will be 1,898,162 new cancer cases and 608,572 deaths in 2021 [3]. The pandemic of COVID-19 has made it harder to diagnose and cure cancer. In an attempt to enhance patient satisfaction, studies on the efficacy and safety of non-invasive treatments such as HIFU have been conducted (Endonasal therapy, laparoscopic treatment, lumpectomy and immunotherapy have all been tested) [4-7]. The main concepts of HIFU ablation are coagulative thermal necrosis caused by ultrasonic energy absorption in tissue phantom during transmission and generated

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cavitation destruction [8,9]. Consequently, this treatment has been researched for a number of health conditions, including metastatic tumors and uterine fibroids [10-12], and several other types of cancers, including the liver [13-15], kidney, prostate [16,17], breast [18,19]. HIFU uses an external energy source, which reduces the risk of spreading or tumor seeding compared to invasive medical procedures that may increase tumor growth [20,21]. In HIFU, ultrasonic waves are produced at a higher intensity and in a highly focused configuration, which is typically harmless [22,23]. It utilizes several ultrasonic beams to concentrate on the specific tissue location inside the body organ that needs therapy, similar to how a magnifying glass focuses light on a target. The ultrasound's highly concentrated energy increases the temperature of the tissue, and the heat ablates the targeted tissue area. A layer of tissue cannot be affected by the ultrasonic beams until they reach their final target. The therapeutic tumor ablation using HIFU has received FDA (Food and Drug Administration) approval in the US [24]. During HIFU, an ultrasound probe is placed into a patient's target area while they are anesthetized. The probe is positioned up to the level of the patient's body. An imaging transducer in the probe's center scans the patient's target zone to generate a three-dimensional digital map of the whole spot as well as the area to be treated. Doctors then analyze and arrange the specific treatment plan on the computer. Focused ultrasonic waves are applied to the target and ablate the specific tissue that was identified in the treatment plan. The operation is continued until all of the infected tissue has been ablated from the body. Ultrasound or MRI evaluates the therapeutic efficacy just after the procedure. The benefits of HIFU are not immediately clear. It might take up to 6 or 8 weeks for the results of HIFU to manifest completely. For one to two hours after HIFU therapy, patients will need to rest and recuperate at the clinic before being released [25].

In this paper, two types of tissues were used: soft and hard. It's not easy to determine an optimum intensity for use on various tissues. Numerous studies have been done on intensity, but all of them have been performed on a single phantom tissue [26,27]. An extensive examination of a diverse range of tissues has not been performed yet. This study aimed to improve tumor ablation while minimizing collateral damage to healthy tissue by modulating the transducer's intensity. To achieve the best possible outcomes, this study explores numerous tissue intensities at different frequencies, temperature, focal length, lens radius of curvature, power, and many other variables. According to clinical experience, this paper examines the outcomes of HIFU ablation for the most appropriate tumors, then summarizes the requirements for a satisfying treatment. Furthermore, the present issues in HIFU for engineers and doctors are highlighted.

II. METHODOLOGY

A transducer is an electronic device that converts physical parameters into electrical equivalent. The three most common HIFU devices used in healthcare are extracorporeal, transrectal and interstitial. Extracorporeal transducers are utilized to targeted tissues that are visible via an acoustic window on the patient's skin. Here, an extracorporeal HIFU device is being used. In each transducer, the sensing element and the traducing element are the two most significant components to consider. The detecting component is the analytical reveal that receives and transfers the input to physical reactions. In this instance, a piezoelectric transducer is used. A piezoelectric transducer is a kind of sensor whose principal function is to convert mechanical energy to electrical power. The output or input signal can be in the form of voltage, current or frequency. According to the piezoelectric effect, when mechanical stress or forces are applied to a quartz crystal, electrical charges are generated on the crystal surface. The voltage will develop as the stress level rises. A concave self-focusing transducer instead a spherical bowl's or a plain transducer's surface fronted with a properly configured acoustic lens can focus a high-intensity beam. The tumor must be at least 10 mm in diameter to be detected and treated with HIFU. The HIFU focus should be scanned throughout the area in order to treat the targeted tissue. Mechanically moving or alternatively adjusted with a fixed target HIFU transducer was the most frequently used technique in the initial generation of HIFU systems due to its ease of controlling regardless of software configuration. The use of a phased array permits for more quick and efficient control of the HIFU focus across tissue, as well as increased focal geometry flexibility. Extracorporeal devices often have a large lens aperture, a wide focal length and operated at maximum power. Broad aperture sources offer the convenience of scattering incident power across a broad area of skin, decreasing acoustic reflections. Extracorporeal HIFU is mainly used to treat lesions in the breast, abdomen, brain or limbs. During HIFU treatment, coupling water is normally circulated and cooled to minimize thermal destruction to the connective tissue caused by the temperature rise on the transducer's surface and maintain the transducer's operational stability. Owing to excessive acoustic intensities and tissue absorption coefficients, a large portion of the absorbed acoustic power is converted into heat energy [28].

The temperature rise is calculated using a simulation named the "Pennes bioheat transfer" [29].

$$\rho^{C_P}\frac{\partial T}{\rho\partial t} = \nabla.(k\nabla T) - \rho_b C_b w_b (T - T_b) + Q + Q_{met} \quad (1)$$

Where, T is the temperature, C_P is the specific heat, ρ is the density, ρ_b is the density of blood, k is the thermal conductivity, C_b is the specific heat of blood, w_b is the blood perfusion rate, T_b is the blood temperature, Q is the source of heat and Q_{met} is the metabolic heat source. As a result of these properties, the perfusion rate of healthy tissue is $w_{b(tissue)} = 1 \times 10^{-4}$ and the perfusion of blood rate of tumor tissue is $w_{b(tumor)} = 1 \times 10^{-2}$. It is the heat that comes from the metabolism of muscles. The rate of metabolic heat generation in fit tissue is $Q_{met\ (tissue)} = 400\ \frac{W}{m^3}$. Tumor tissue reflects the amount of heat produced by tumor tissue's metabolism is $Q_{met(tumor)} = 40000\ \frac{W}{m^3}$. Muscles need a steady supply of adenosine triphosphate (ATP) to work properly. ATP comes from the oxidation of metabolites in the mitochondria, which is a process that needs oxygen. The heat source term was calculated in the following manner:

$$Q = \frac{\sigma}{\rho_0 C^4{}_0}[(\frac{\sigma_\rho}{\sigma_t})^2] \tag{2}$$

By numerical integration, Q was time-averaged over an acoustic period being used in the “Pennes bioheat transfer” equation. To concentrate an ultrasonic signal, a phase difference or a focusing lens are usually used. In this concept, the signal is emitted by an ultrasonic transducer with a concave lens that is spherically focused. Higher-order harmonics may be created since the intensity of the signal at the supplier point is adequate. This signal's time to reach the focal point is calculated as follows:

$$t_f = \frac{d_{water}}{c_{water}} + \frac{d_{tissue}}{c_{tissue}} \tag{3}$$

Where, c is the sound speed and d is the the distance traveled in the relevant materials.

Intensity is the amount of power a wave has per unit of area.

$$I = \frac{P}{4\pi r^2} \tag{4}$$

Where, P is power and r is the radius.

Relative Pressure is usually assessed in force per unit surface area,

$$P = F / A \tag{5}$$

Where, F is force and A is the surface area.

For a sphere, the radius is the measure from its center to any point on its circumference. In geometry, the radius of curvature is defined as the diameter of a circle that lies on the curve at a specific point.

$$R = 1/K \tag{6}$$

Where, K is the curvature.

III. DEVICE STRUCTURE AND DESIGN

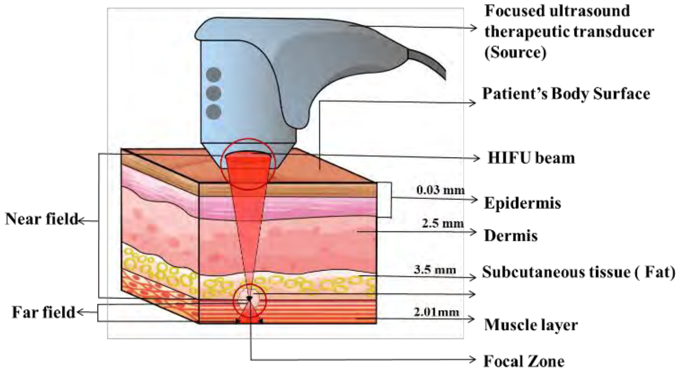


Figure 1: High-intensity focused ultrasound probe aimed toward the tumor.

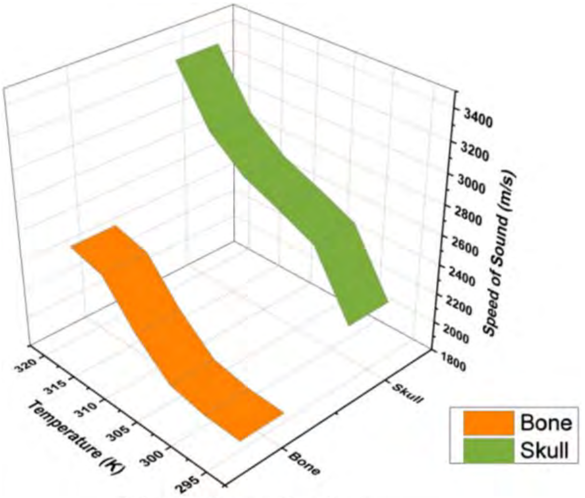
A temperature control system may be used for heating tissues that is not included inside the focused area to the required temperatures outside of the focal region. Thermal inputs are given to the tissue boundary with the aim of maintaining a heat reflection-free environment. The temperature rises swiftly as a result of the heat. The intensity of the transducer should be adjusted to enhance tumor ablation. The ultrasonic beams generated by the transducer (source) employed in HIFU tumor ablation are concentrated on a specific focal zone, as shown in Figure 1. The acoustic energy increases in the direction of the central focus. Additionally, the anatomical depth of the skin layers and the muscle tissue appears in Figure 1. The sound field of a transducer is divided into two zones, which are referred to as the near field and the far field [30]. The target section is capable of receiving the vast majority of heat produced in the near field. Consequently, no heat can be generated in the far field that might make significant damage towards the tissues in the surrounding area.

Various types of soft and hard tissues have been examined in this model. The brain, heart, kidneys and liver are all included in soft tissue. Hard tissue contains both bone and skull tissue. The density of water varies depending upon the tissue type [31]. According to this concept, the absorption coefficients of water and tissue phantoms change in response to frequency variations. Calculating the oval wavelength of various tissues has been done and the findings have been utilized for other equations to be calculated. The appropriate tissue height and width have been computed as well. The following findings have been retrieved using these parameters and they can be viewed in the section on outcomes.

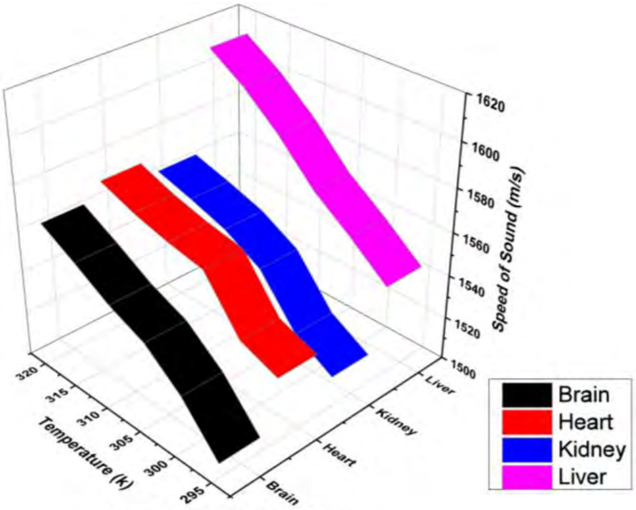
IV. RESULTS AND DISCUSSIONS

Tissues were examined for tumor ablation at varied frequencies over time. The frequency of each tissue was determined by reviewing several research and publications [32-35]. Using the results of previous studies, define the optimum frequencies for every human tissue. Relying on that information, brain and kidney tissue require 1.6 MHz, skull tissue requires 2.25 MHz, heart tissue requires 3.4 MHz, and both liver and bone tissue require 3.5 MHz. During this experiment, the temperature was obtained between 295.15 and 320.15 Kelvin. The speed of sound and how far a sound wave travels per unit of time as it passes through a medium (Tissue) would be discussed here. When it comes to the human body, these factors are not consistent. The waves propagated in a straight line from the transducer head to the targeted tissue center creating a clear channel between both. For each tissue in this situation, a fixed piezoelectric transducer was applied.

Figure 2 illustrates the propagation speed of hard and soft tissue phantoms, operating at temperatures between 295.15 to



(a) Hard Tissue Phantom

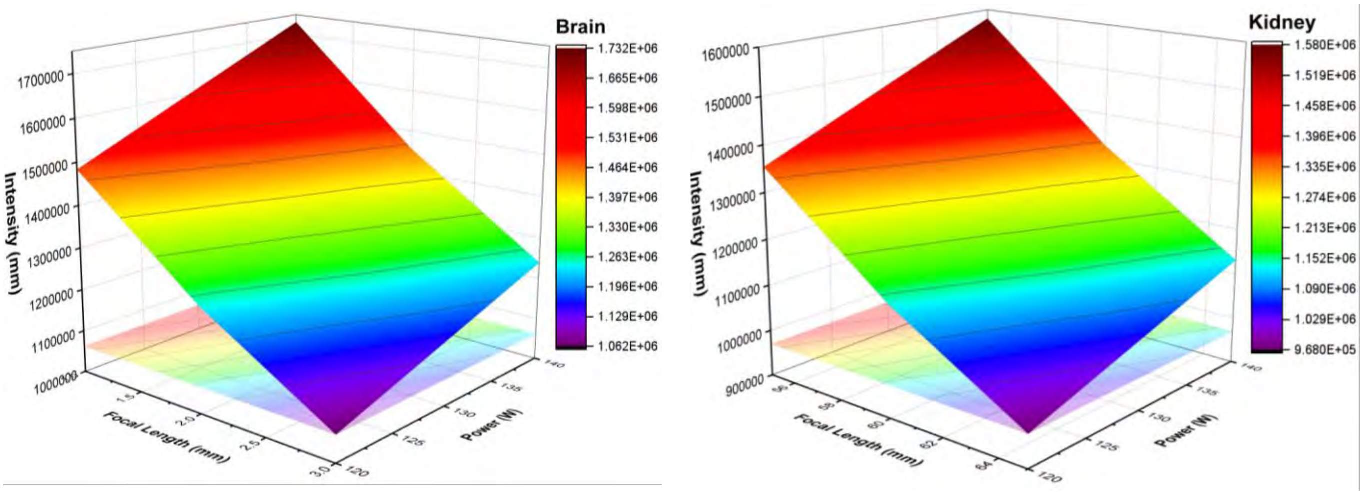


(b) Soft Tissue Phantom

Figure 2. Predictive evaluation of the propagation speed of soft and hard tissues at predefined optimal frequencies for each tissue in a range of temperatures between 295.15 to 320.15 kelvin.

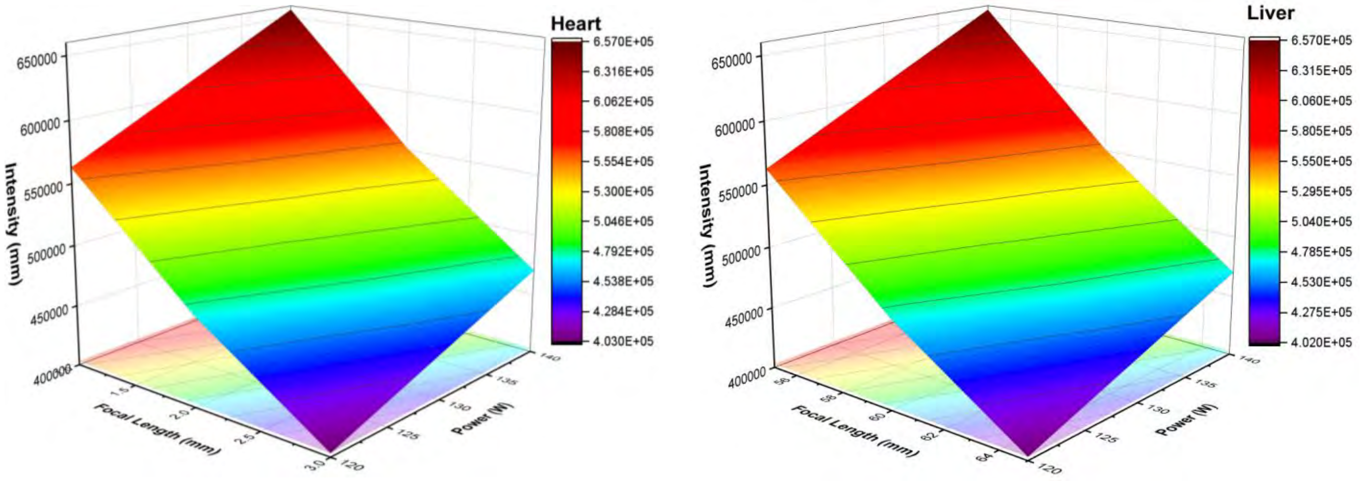
320.15 kelvin, employing a 1.6 MHz to 3.5 MHz transducer. The speed of sound through the atmosphere is influenced by its temperature. The speed of sound rises with increasing temperature. Figure 2 clearly illustrates a linear pattern of the speed of sound that varies between 1600 and 3400 meters per second. Hard tissues heat up immediately, whereas soft tissues heat up gradually, as seen in this graph. If the tissue phantom is thicker, the wave will move faster. In this place, sound speed is higher in hard tissues than in soft tissues, because hard tissues are thicker compared to soft tissues. The speed of sound changes with temperature. A closer investigation found that, the temperature fluctuates a lot. This experiment must begin at a certain temperature. It was calculated using the average temperature of a human body. Fever or any illness that causes the usual temperature of the human body to be changed is a significant challenge for healthcare professionals. Moreover, it needs to be noticed that the speed of sound varies with body temperature, and the calculations will be affected correspondingly. Continuous temperature change also has a negative impact on the total acoustic pressure of each tissue. As a consequence, the temperature for each tissue has been set at 310.15 kelvin. In this study, each tissue had a source pressure amplitude of 2.25 MPa. Source pressure amplitude is stated as the maximum displacement or distance shifted by a point on a harmonic oscillator or wave calculated from its equilibrium position. In HIFU, power is the amount of energy an acoustic wave can produce and transfer per unit of time. Since the area of the transducer head remains constant, adjusting the power rating is equivalent to changing the intensity level. Focusing on finding which power level is optimal for soft and hard tissue ablation.

From figure 3, it is clear that increases in power are accompanied by increases in intensity. We have performed primary simulations and obtained optimal values ranging from 120 W to 140 W for various tissues. This power range is appropriate for ablating tumors in a variety of tissues; hence we limit our analysis to 120 to 140 Watt. On different tissues, the HIFU intensity is varied three times: first with 120 W, then with 130 W and finally with 140 W. Each tissue's ideal temperature is set at 310.15 degrees Kelvin. In this case, predefined frequencies are used. It is noticeable that they are increasing in a linear way. As a consequence of minimal power absorption, brain and kidney tissue intensities increase more rapidly. than heart, liver, bone and skull tissue. The absorption coefficient is affected by the frequency. Instead, focus length grows with increasing power but intensity decreases with increasing focal length, as seen in these graphs. Based on the situation the intensity of the HIFU beam is inversely related to the focal length's square value. On the basis of the tumor ablation in each tissue sample, the focal lengths have been adjusted from 55 mm to 65 mm. Power levels of 120-140 W are optimum for this focal length range. When the focal length is extended, insufficient beams were absorbed, which causes inadequate heat generation and unsatisfactory tumor ablation. Due to this, we use a shorter focal length so that more HIFU beams can be absorbed. Tissue ablation rises in direct proportion to the increase of power. There is some debate regarding whether the power level is sufficient. When the power exceeds the safe limit, the procedure becomes dangerous and when it falls underneath the safe limit, tissue ablation may become difficult. In order to attain the safe limit of tissue ablation, each tissue must have an optimal power output. As a result, we fixed the optimal power for the brain and kidney at 120 W, the heart and liver at 130 W and the bone and skull at 140 W. Since power can be concentrated in a tiny space, the highest intensity is seen at the focal zone of each tissue being targeted. Depending on the tissue's anatomy, the focal lengths of different tissues fluctuate. This analysis also includes the ideal height of each tissue. Tissue heights are 480 mm for the bone, 93 mm for the brain, 120 mm for the heart, 140 mm for kidney, 70 mm for liver and 176 mm for skull respectively [36-38].



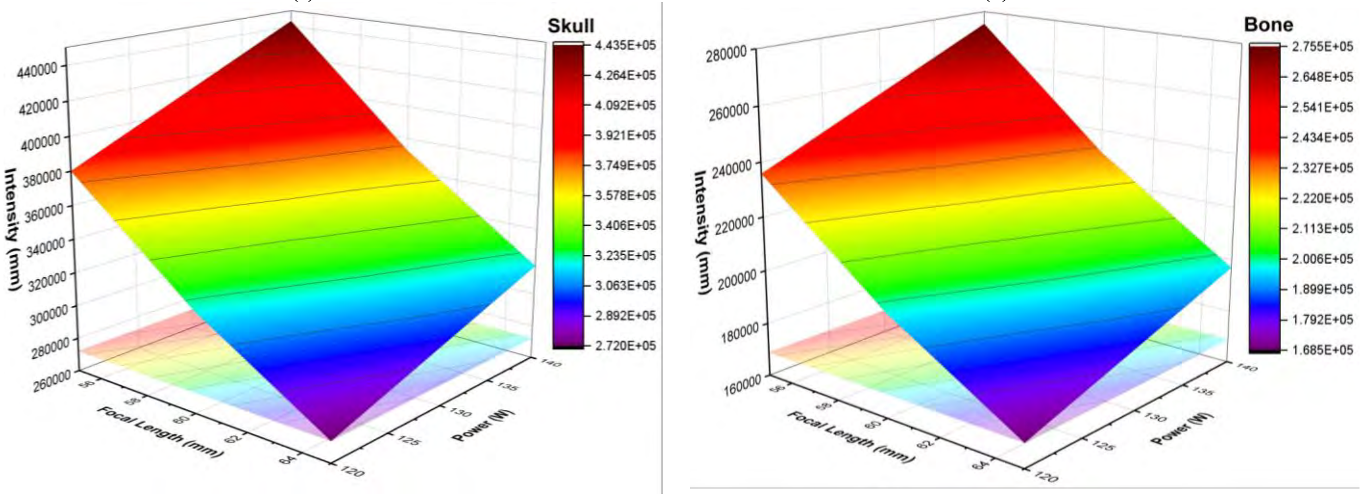
(a) Brain

(b) Kidney



(c) Heart

(d) Liver



(e) Skull

(f) Bone

Figure 3. HIFU Intensity on Different Tissues at 310.15-degree K and Optimum Frequencies against Power in 10 W Intervals from 120 W to 140 W. The focal length was extended from 55 to 65 mm.

Figure 4 shows the best positive pressure readings obtained from soft and hard tissues using relative pressure probes. We got these values from Equation 5. A force collector and a transmission device that provides an electrical signal via a dependent resistive, capacitive or inductive approach are included in the relative pressure probe constructions. In this experiment, a fixed piezoelectric transducer was employed.. As previously indicated, the optimum temperature for every tissue is 310.15-degree K. For all tissues, the focal lengths range from 55 mm to 65 mm. The graph shows that as the focal length

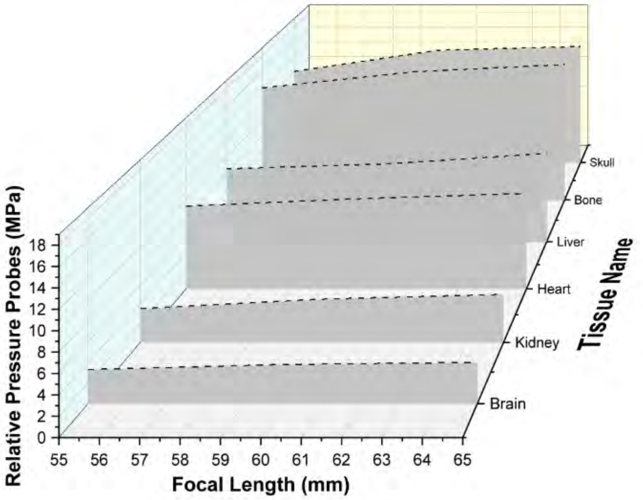


Figure 4. Relative Pressure Probes with Positive Pressure Values vs Different Focal Length Depending on the Anatomy of Each Tissue at Predetermined Optimal Power, Temperature and Frequency.

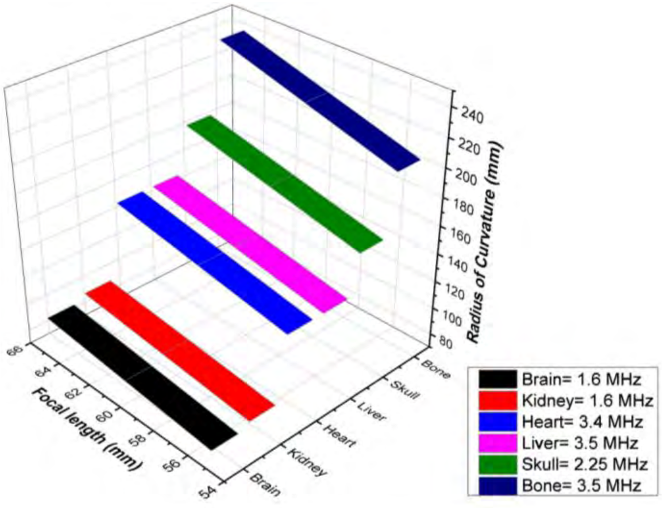
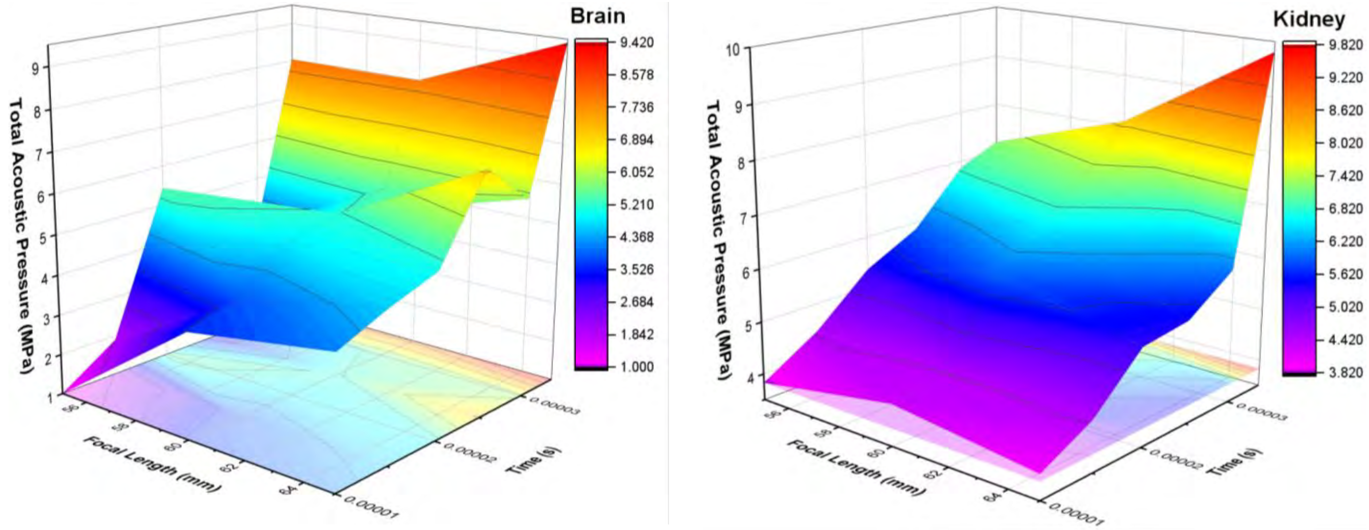


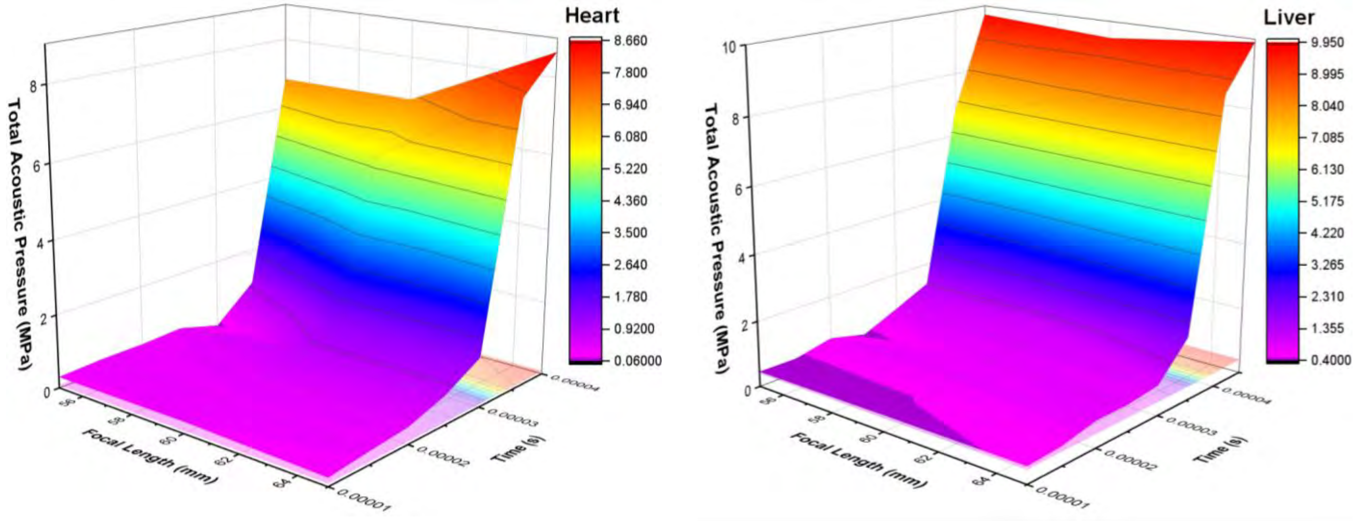
Figure 5. The Radius of Curvature of Diverse Tissues was Analyzed Using Various Focal Lengths at 310.15-degree K.

increases, the positive pressure value of the pressure probes also increases. However, this rise is only in miniscule quantities. The positive pressure exerted by hard tissues (bone and skull) is greater than that exerted by soft tissues (brain, heart, kidney and liver). When a person has a tumor, it can arise anywhere in the body. According to where the tumor is, the focal length should be adjusted. The focal length cannot be fixed because of this. In order to properly locate the tumor, the transducer's radius of curvature must be changed. This method may be used to identify the tumor and then use heat to ablate it. The wavelengths of tissues must be computed to get the radius of curvature. Each tissue's wavelength is determined by observing its velocity. The curvature radius is proportional to the focal length. Figure 5 illustrates the optimal lens curvatures for each tissue for focal lengths between 50 and 65 mm. Here, the focal length rises as the radius of curvature increases and reduces as the radius of curvature drops. Using equation 6, the optimal radius of curvature was calculated while keeping the frequency, temperature and power constant. As hard tissue is significantly thicker than soft tissue, the radius of curvature of bone and skull tissue is larger than that of soft tissue. The absorbent layer's thickness is adjusted between 4 and 12 mm for a variety of tissues [39,40]. Nevertheless, the absorption capacity of bone and skull tissues is lower so that they are thicker than other tissues. The acoustic pressure was measured as the distance between the fluid pressure and the ambient temperature pressure caused by an HIFU beam. Water is considered as "fluid" in this circumstance. The temperature of the surrounding environment is 310.15-degree K. As seen in Figures 6, the overall acoustic pressure rises as time continues. For this test, focal lengths of 55, 60, and 65 mm are chosen. The graphs also show the change in acoustic pressure as the focal length increases. Pre-set frequencies and powers are used in this

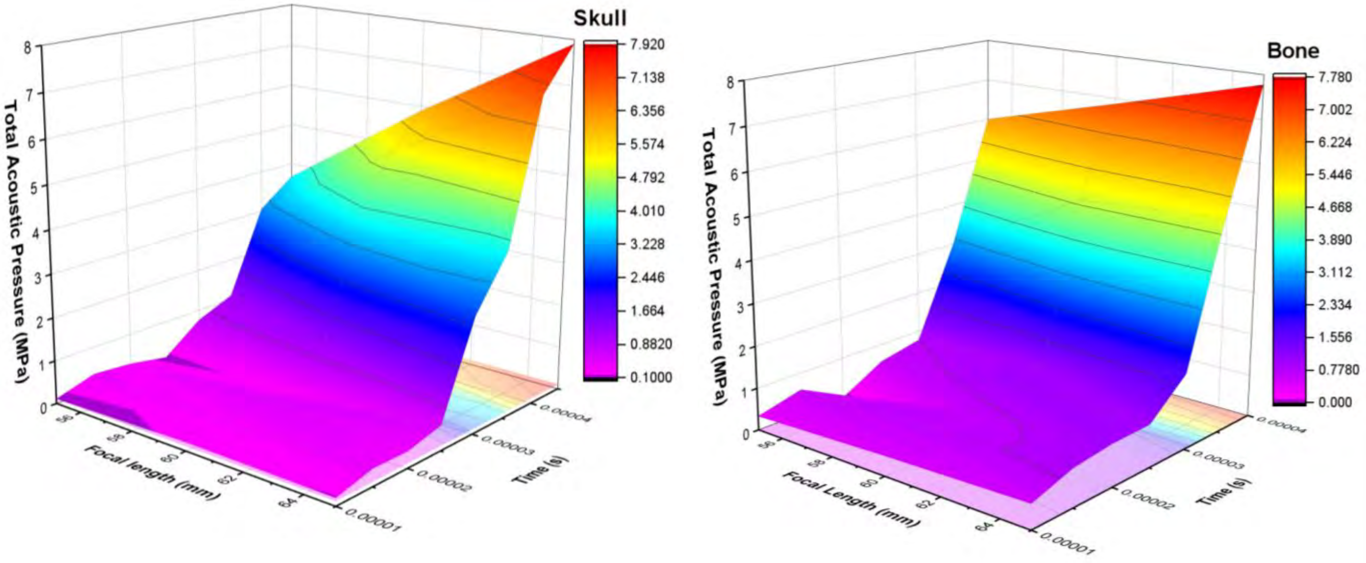


(a) Brain

(b) Kidney



(c) Heart **(d) Liver**



(e) Skull **(f) Bone**

Figure 6. The Relationship Between Time and Total Acoustic Pressure in Various Tissues at 310.15-degree K and optimum Frequencies.

analysis. The optimum temperature for this circumstance is 310.15 degrees K, although if there is a substantial variation, the overall acoustic pressure does not change significantly. It is important to know that when the amplitude of the wave is small, acoustic pressure and tissues velocity are directly proportional. The acoustic impedance can be determined by analyzing the speed of sound and tissue density. Acoustic impedances for the brain, heart, kidney, liver, bone and skull are 1.64325 MPa, 1.796796 MPa, 1.78278 MPa, 1.865538 MPa, 8.82 MPa and 6.41088 MPa, respectively. The F-stop must be calculated in order to pinpoint the position of the tumor. It controls the percentage of the visual field that is focused above and behind the targeted tissue. We can let in more ultrasound beams by setting the F-stop value lower and less ultrasound beams by setting the value higher. Variations in the F-stop occur when the focal length and aperture diameter are both changed. Aperture measurements at different F-stops require dividing the focal length by the corresponding fraction. A larger aperture will keep less of the area in focus, while a narrower aperture will bring more of the area into clear perspective. The tumor will be easier to ablate from a closer distance as the F-stop value increases.

If we wanted to conduct additional research, we would apply this HIFU tumor ablation technique to rats or rabbits. After applying this technique to these species, if the results are optimal, we will test this approach on humans and observe the outcomes. Furthermore, we anticipate useful outcomes from this medical trial.

V. CONCLUSION

HIFU is a non-invasive way for ablating targeted tissue and allowing cancer patients to get professional medical care without causing injury to surrounding organs. Nowadays, HIFU has attained a prominent position in the process of fabricating transducers as well as therapeutic guiding systems for use in medical interventions. It is a process that enables a fixed ultrasonic transducer with a focusing lens to increase the intensity of the transmitted signal within a predefined focal zone of interest. Numerous types of cancer, such as the brain, heart, skull, liver, kidney and bone have demonstrated favorable results after HIFU tumor ablation surgery. For each type of tissue, the optimal height, width, sound speed, and wavelength were calculated to determine its intensity and focal length. As observed in the figures, focus length increases with increasing power, while intensity decreases with increasing focal length. Since the tumor might be anywhere in the body, it is necessary to choose the optimum focal length. By maintaining the frequency, temperature and power; the optimum radius of curvature was computed. As the radius of curvature rises, the overall acoustic pressure and focal length also increase. When compared to other forms of surgery, this technique is less costly and requires less recovery time. The ongoing expansion and application of HIFU therapy in the medical industry are highly anticipated.

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