A Review of Non-Invasive Ultrasonic Therapeutic for Liver Cancer Elimination

Nurain Atiqah Aqilah Zulkifli[1], Zulkarnay Zakaria[1,2], Ahmad Ikhwan Ahmad Basri[1], Siti Fatimah Abdul Halim[1], Handy Ali Munir[3], Anas Mohd Noor[1,2], Mohd Hafiz Fazalul Rahiman[3], Jaysuman Pusppanathan[4], Ahmad Nasrul Norali[1,2], Ruzairi Abdul Rahim[5]

[1]Biomedical Electronic Engineering, Faculty of Electronic Engineering Technology, Universiti Malaysia Perlis, Pauh Campus, 02600 Arau, Perlis, Malaysia.
[2]Medical Device & Life Sciences Cluster, Sports Engineering Research Centre (SERC), Universiti Malaysia Perlis, Arau 02600, Perlis, Malaysia
[3]Electrical Engineering, Faculty of Electrical Engineering Technology, Universiti Malaysia Perlis, Pauh Campus, 02600 Arau, Perlis, Malaysia.
[4]Department of Biomedical Engineering & Health Sciences, Faculty Electrical of Engineering, Universiti Teknologi Malaysia, Jalan Iman, 81310 Skudai, Johor, Malaysia
[5]Protom-I Research Group, Innovative Engineering Research Alliance, Faculty of Electrical Engineering Universiti Teknologi Malaysia, 81310 UTM, Johor Bahru, Johor, Malaysia

Corresponding author* email: zulkarnay@unimap.edu.my
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ABSTRACT

Liver cancer, a leading cause of cancer-related deaths globally, poses significant treatment challenges due to its late-stage diagnosis and complex treatment options. Non-invasive therapeutic techniques have gained attention as promising alternatives for cancer treatment, with ultrasonic therapy being one of the most innovative approaches. This study explores the potential of non-invasive ultrasonic therapeutic methods for the elimination of liver cancer cells. By utilizing high-frequency sound waves, the therapy can target and disrupt cancerous tissues with minimal damage to surrounding healthy structures. The effectiveness of ultrasonic waves in penetrating liver tissues, coupled with their ability to induce thermal effects and cavitation, makes this approach suitable for focused treatment of localized tumors. Current technologies for liver cancer treatment include surgical resection, liver transplantation, radiofrequency ablation (RFA), trans arterial chemoembolization (TACE), and systemic therapies such as targeted drugs and immunotherapy. However, these methods have limitations, including invasiveness, high recurrence rates, systemic side effects, and limited effectiveness in advanced-stage cases. Preliminary results from clinical trials indicate that non-invasive ultrasonic therapy can induce tumor regression and enhance liver function without the need for surgery or chemotherapy. This report reviews the mechanisms of action, the technological advancements in ultrasonic equipment, and the clinical outcomes to date, demonstrating the potential of this non-invasive technique as a viable therapeutic option for liver cancer treatment. Further research is needed to optimize treatment protocols and evaluate long-term efficacy and safety.

Keywords: High-Intensity Focused Ultrasound (HIFU), Liver Cancer, Non-Invasive Therapy, Tumour Ablation, Ultrasonic Treatment, Cavitation

1. Introduction

Magnetic Liver cancer, particularly hepatocellular carcinoma (HCC), is a pressing global health concern and a leading cause of cancer-related mortality [1]. Despite advances in early detection and therapeutic techniques, survival rates remain poor due to late diagnosis, complex liver anatomy, and the limitations of existing treatment options. Conventional modalities such as surgical resection, liver transplantation, chemotherapy, and radiotherapy often present significant drawbacks including invasiveness, high recurrence rates, systemic toxicity, and limited accessibility in low-resource settings [2,3].

In recent years, non-invasive therapeutic approaches have emerged as promising alternatives for cancer treatment, especially for patients who are not eligible for surgery [4]. Among these, High-Intensity Focused Ultrasound (HIFU) has gained recognition for its ability to precisely ablate tumour tissue through thermal and mechanical effects, without damaging surrounding healthy structures [5,6]. HIFU focuses ultrasonic energy on a specific region, inducing localized heating (above 60°C) that leads to coagulative necrosis of cancerous tissues. Additionally, the mechanical action—such as acoustic cavitation—enhances therapeutic efficacy by disrupting cellular membranes [7,8].

Complementary techniques such as histotripsy and sonodynamic therapy (SDT) are also gaining traction. Histotripsy uses short bursts of high-intensity ultrasound to mechanically fractionate tissues via cavitation, whereas SDT leverages ultrasound to activate son sensitizing agents, generating reactive oxygen species that induce tumour cell death [9,10]. These technologies have demonstrated significant potential in preclinical and early clinical trials.

With growing clinical evidence and technological refinement, non-invasive ultrasonic therapies are increasingly being integrated into oncology practice. For instance, the U.S. Food and Drug Administration (FDA) approved histotripsy for liver tumour treatment in 2023, highlighting the modality's clinical promise. Despite these advances, challenges persist in achieving precise energy delivery through anatomical barriers like the ribcage, managing respiratory-induced liver motion, and optimizing treatment parameters for different tumour profiles [11,12,13].

This study investigates the use of ultrasonic therapeutic systems, particularly HIFU, as a non-invasive solution for liver cancer elimination. The research aims to evaluate the mechanisms of action, simulation-based optimization using COMSOL Multiphysics, and future directions for enhancing treatment efficacy and safety. Through this work, we aim to support the broader clinical adoption of ultrasonic modalities in liver oncology, offering new hope for improved patient outcomes and reduced treatment burden.

1.1 Research Question & Objective

This study addresses the critical need for a non-invasive, precise, and effective therapeutic solution for liver cancer, particularly in cases where conventional treatments such as surgery, chemotherapy, or radiotherapy are not viable. The central research question explores whether an ultrasonic transducer system can be designed and optimized to deliver focused ultrasound energy at tissue depths between 4 and 16 cm, enabling efficient tumour ablation while preserving surrounding healthy structures. To answer this question, the study aims to develop a computational model of a high-intensity focused ultrasound (HIFU) transducer and simulate its performance under varying conditions. Specifically, the objectives are to assess the model's ability to deliver enough thermal energy and acoustic pressure at targeted depths, and to evaluate how different ultrasonic frequencies influence the effectiveness of tumour cell elimination. The outcomes are expected to contribute toward optimizing HIFU protocols for liver cancer therapy and advancing the development of safe, non-invasive cancer treatments.

2. History of HIFU

The initial findings regarding the biological impacts of high-energy ultrasound waves were documented by Wood and Loomis in 1927, with further foundational studies conducted by Lynn et al. in 1942 [14]. The clinical application of HIFU began in the 8 1950s when it was tested for treating Parkinson's disease and other neurological disorders by the Fry brothers, William and Frank [6]. Figure 1 shows the evolution of HIFU as from 1993 up until 2016.

However, these procedures required opening the skull through a craniotomy, making them highly invasive and leading to the discontinuation of this HIFU application. Research into the technology resumed in the 1990s, yielding varying degrees of success.

Figure 1. Evolution of HIFU technology over the decades [14]

In recent years, China has emerged as a frontrunner in the clinical use of HIFU, with thousands of patients treated over the last two decades for issues like uterine fibroids and benign prostate hypertrophy. In the UK, team in Surrey have been at the forefront of HIFU research, and in 2002, a specialized HIFU unit was established. This unit has conducted multiple trials on a range of different clinical uses for HIFU [15].

3. Current Therapeutic Approaches

Liver cancer treatments are broadly categorized into surgical, locoregional, and systemic approaches. Each of these methods has its unique role, indications, and limitations, which are critical to understanding the significance of emerging therapies like HIFU[16,17,18].

3.1 Surgical Treatments

Surgical resection and liver transplantation remain the gold standards for treating earlystage liver cancer. Resection involves removing the tumor along with a portion of healthy liver tissue, provided the liver's functionality is sufficient. Liver transplantation offers the advantage of eradicating the cancer while addressing underlying liver disease, such as cirrhosis [19,20]. However, these options are often limited by strict eligibility criteria, including tumor size, number, and liver function. Postoperative complications, including liver failure and infections, also pose significant challenges [21]. Figure 2 shows the surgical resection of liver cancer.

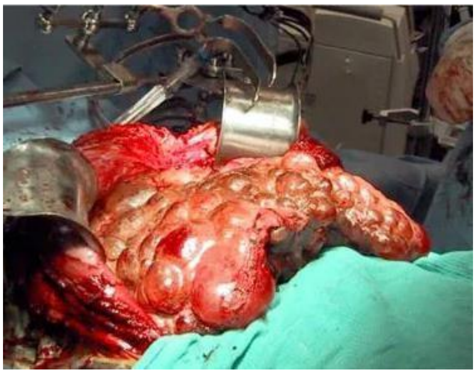

Figure 2. Surgical resection of liver cancer [11]

3.2 Locoregional Therapies

Locoregional treatments are minimally invasive methods aimed at targeting liver tumours directly. Key approaches include:

3.2.1 Radiofrequency Ablation (RFA) and Microwave Ablation (MWA)

These techniques use heat to destroy tumour cells. RFA employs high-frequency electrical currents, while MWA utilizes electromagnetic waves. Both methods are effective for small tumours (typically <3-5 cm) but may be less successful for larger or poorly accessible lesions.

3.2.2 Trans arterial Chemoembolization (TACE)

This involves the injection of chemotherapy drugs directly into the liver's blood supply, followed by the embolization of the artery to restrict blood flow to the tumour. TACE is widely used for intermediate-stage liver cancer but is associated with high recurrence rates and risks of ischemic complications.

3.2.3 Selective Internal Radiation Therapy (SIRT)

Also known as radioembolization, this technique delivers radioactive microspheres to the tumour, offering a targeted radiotherapeutic approach. SIRT is particularly useful for patients with portal vein thrombosis but requires careful management of radiation-related side effects [20].

3.3 Systemic Therapies

Systemic treatments are primarily utilized for advanced or metastatic liver cancer. The most commonly used systemic therapies include:

3.3.1 Targeted Therapy

Tyrosine kinase inhibitors (TKIs) such as sorafenib and lenvatinib inhibit tumour growth by targeting angiogenesis and other pathways. While effective in prolonging survival, these drugs are often accompanied by adverse effects, including hypertension, fatigue, and diarrhea.

3.3.2 Immunotherapy

Immune checkpoint inhibitors, such as nivolumab and pembrolizumab, have shown promising results by enhancing the immune system's ability to recognize and destroy cancer cells. However, these therapies can lead to immune-related adverse events, including colitis and pneumonitis.

3.3.3 Combination Therapies

Combining targeted therapy with immunotherapy is an emerging approach that aims to maximize therapeutic efficacy. Clinical trials are ongoing to evaluate the safety and effectiveness of these combinations [13]. Figure 3 shows the one of the processes of systemic therapy by injecting AAV vector.

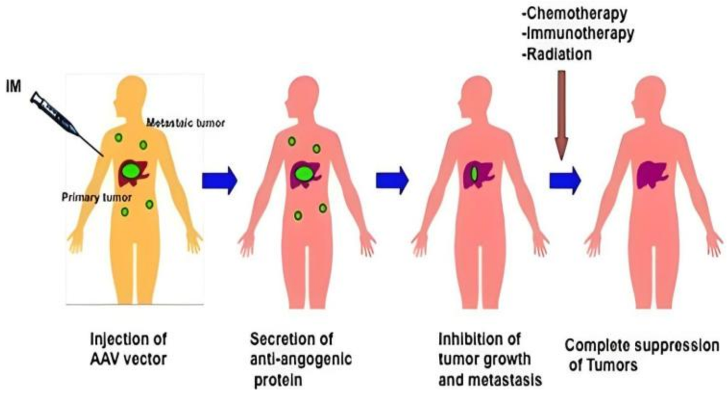

Figure 3. Process of systemic therapy [14]

3.3.4 Palliative Care and Supportive Treatments

For patients in advanced stages or those unfit for aggressive therapies, palliative care focuses on symptom management and improving quality of life. Techniques such as percutaneous ethanol injection (PEI) and palliative radiation therapy can help control pain and other symptoms associated with liver cancer [11].

4. Limitations of Current Approaches

Despite their effectiveness, conventional therapies face several limitations, including high recurrence rates, significant side effects, and limited accessibility in resourceconstrained settings. These challenges underscore the need for innovative approaches like HIFU that offer a more targeted, non-invasive, and patient-friendly treatment option.

4.1 Comparative Analysis with Other Modalities

HIFU provides distinct advantages over other liver cancer treatments. Unlike RFA and MWA, HIFU's non-invasive nature eliminates the need for percutaneous probes, reducing the risk of complications such as haemorrhage and infection. In comparison to TACE, HIFU avoids embolic complications and offers better preservation of vascular integrity. Table 1 summarizes key comparisons:

Table 1. Comparative analysis of HIFU and conventional liver cancer therapies.

Feature	HIFU	RFA/MWA	TACE	Systemic Therapy
Invasiveness	Non-invasive	Minimally invasive	Minimally invasive	Non-invasive
Tumor Size	<5 cm (optimal)	<2-5 cm	Any size	Any size
Complication Risk	Low	Moderate	Moderate	High
Recurrence Rate	Low	Moderate	High	High
Systemic Side Effect	None	None	Minimal	Significant

5. High-Intensity Focused Ultrasound (HIFU)

HIFU is a non-invasive medical procedure that uses focused ultrasound waves to generate heat and destroy targeted tissues, such as tumors, without the need for surgery. It is commonly used in cancer treatment, particularly for prostate cancer and certain liver tumors, as well as in cosmetic and therapeutic applications. HIFU offers benefits like minimal recovery time, reduced risk of infection, and precise targeting of affected areas while sparing surrounding healthy tissue.

6. Mechanisms of HIFU

HIFU employs focused ultrasonic waves to induce localized thermal and mechanical effects. The thermal effect causes coagulative necrosis of cancerous tissues, while the mechanical effect, driven by acoustic cavitation, disrupts cell membranes and enhances treatment efficacy. This dual mechanism allows for precise targeting of tumors while 14 sparing adjacent healthy tissues [16]. Figure 4 illustrates the thermal and mechanical effect of HIFU on cancer tissues.

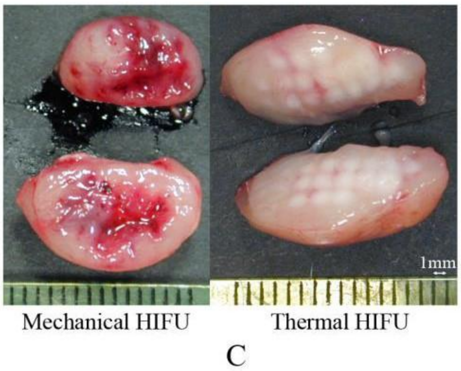

Figure 4. Diagram illustrating the thermal and mechanical effects of HIFU on tumor tissues. [16]

This image compares the effects of Thermal HIFU and Mechanical HIFU through temperature analysis, acoustic power measurement, and tissue response. In Graph A, the temperature changes over time during HIFU treatment. Thermal HIFU (solid circles) causes a rapid temperature rise, peaking above 70°C before gradually decreasing, whereas Mechanical HIFU (open circles) results in a lower overall temperature increase, staying below 60°C. Graph B presents the acoustic power spectrum, showing that 15 Mechanical HIFU has a stronger peak at around 3 MHz, suggesting more mechanical energy transmission, while Thermal HIFU absorbs more energy as heat. Image C displays the physical effects on tissue, where Mechanical HIFU leads to severe hemorrhagic damage due to mechanical disruption, whereas Thermal HIFU results in coagulative necrosis with a more uniform, pale appearance due to heat-induced denaturation. These differences indicate that Thermal HIFU is more effective for precise tissue coagulation, while Mechanical HIFU causes more structural disruption, making the choice between them application-dependent.

7. Applications of HIFU

HIFU (High-Intensity Focused Ultrasound) is used in medical treatments for non-invasive tumor ablation, including prostate cancer, liver cancer, and uterine fibroids. It is also applied in cosmetic procedures for skin tightening and wrinkle reduction. Additionally, HIFU is used in neurology to treat conditions like essential tremors and Parkinson's disease by targeting specific brain areas without surgery. Its ability to precisely target tissues while minimizing damage to surrounding areas makes it a valuable tool in modern medicine.

7.1 Pancreas and Breast Cancer

Pancreatic cancer often carries a poor prognosis, with surgery offering the best chance for a cure. However, only about 15–20% of patients qualify for surgical treatment. In Oxford, a multi-center clinical trial is investigating the use of HIFU for individuals with pancreatic cancer. The study includes patients who are ineligible for surgery but show no signs of metastasis. Participants first receive chemotherapy for three months, followed by HIFU therapy, and are monitored for two years. Thus far, several patients have 16 undergone the treatment successfully, with no significant side effects reported. This suggests that HIFU could be a promising option. Similarly, HIFU therapy trials are being conducted for breast cancer, which is particularly well-suited for this approach due to the superficial location of the breast and the absence of nearby sensitive or gas-filled structures. HIFU has already been established as a treatment for breast cancer in China, and a trial has recently been approved in Oxford.

7.2 Drug Delivery Enhanced by Ultrasound

Ultrasound waves can facilitate the delivery of drugs and genes into living cells through a process called sonoporation, in which ultrasound temporarily perforates the plasma membrane [15,16]. A clinical study explored this concept in patients with liver tumors that were unsuitable for surgical removal or ablation. The study involved 10 participants who received a single dose of doxorubicin encapsulated in a thermosensitive liposomal carrier. High-Intensity Focused Ultrasound (HIFU) was then applied to the tumors, generating heat that triggered the controlled release of the drug. Biopsies taken before and after HIFU treatment showed an average 3.7-fold increase in drug concentrations within the tumors [17].

7.3 Liver

A study conducted in Oxford examined the safety and feasibility of HIFU for treating liver and kidney tumors in a Western population [10]. The trial included 30 participants, 22 of whom had liver tumors. Each patient underwent a single HIFU session under general anesthesia. Of the 30 patients, 27 were evaluated for treatment response via MRI scans 12 days after the procedure. Evidence of tumor ablation was observed in 25 cases (93%). The accuracy of the treatment was also assessed by determining whether the ablation zones were confined to the tumor area or affected surrounding tissues. Treatment accuracy was rated as "good" in 21 patients, indicating precise targeting. Post-treatment monitoring revealed mild discomfort at the treatment site in 80% of cases, which was the only significant clinical symptom reported. Skin toxicity occurred in eight patients (27%), with seven cases involving small, non-clinically significant blisters or tracks that resolved without intervention.

A more recent study by Yang et al. further explored HIFU as a treatment for colorectal liver metastases (CRLM), particularly those considered "difficult" and unsuitable for surgical resection or radiological ablation [18]. This phase 1 clinical trial enrolled 13 patients aged 20–80, utilizing ultrasound-guided HIFU to ablate liver tumors. While hepatectomy offers a 5-year survival rate of 50% for CRLM, approximately 80% of CRLM patients present with unresectable tumors at diagnosis, with an average survival of less than one year [19]. The trial's findings were promising, showing minimal adverse events, with pain and fatigue being the most common. After a median follow-up of 25 months, the two-year overall survival rate was 77.8%, and the median overall survival duration was 25 months. These results indicate that HIFU is a safe and effective treatment option for patients with 18 complex CRLM cases and should be considered for those ineligibles for alternative therapies.

8. Recent Studies on HIFU Efficacy

Currently, numerous HIFU devices are available for different purposes, catering to both extracorporeal and intracavitary uses [20,21,22], with the latter primarily focusing on prostate cancer through systems like Ablatherm® (EDAP-Technomed, Lyon, France) and Sonablate®500 (Focus Surgery, Indianapolis, IN, USA) [17,23] like in Figure 5.

Figure 5. Two commercially transrectal HIFU devices: Ablatherm® (EDAP-Technomed, Lyon, France) and Sonablate® [23]

Traditionally, HIFU treatments relied on either magnetic resonance imaging (MRI) or ultrasound imaging, although advancements have enabled the fusion of these two imaging techniques [24]. Ultrasound-guided HIFU merges the diagnostic and therapeutic applications of ultrasound, effectively facilitating real-time imaging by positioning a diagnostic transducer close to the treatment transducer. In the context of ultrasound-guided HIFU, successful ablation is indicated by changes in grayscale and bright echoes in the targeted region, which arise from the formation of bubbles generated by water boiling in the tissues. Compared to MRI-guided HIFU, ultrasound-guided HIFU is more affordable, compact, and widely accessible; however, the latter lacks the 'real-time' imaging capabilities of MRI, which, while costlier, offers clearer three-dimensional images that are easier to interpret, along with the ability to generate temperature maps for the targeted areas.

9. Challenges and Innovations in HIFU Technology

HIFU technology faces challenges such as limited penetration depth, long treatment times, and difficulty in monitoring tissue changes in real time. Heating effects can also be unpredictable, and precise targeting is crucial to avoid damaging healthy tissues [25,26,27]. However, innovations like advanced imaging techniques (MRI and ultrasound guidance), improved transducer designs, and AI-based treatment planning are helping to enhance accuracy, efficiency, and safety. Researchers are also exploring combining HIFU with drug delivery and immunotherapy to improve cancer treatment outcomes. These advancements continue to make HIFU more effective and widely applicable in medicine.

9.1 Technical Challenges

The clinical application of HIFU for liver tumor treatment faces several significant hurdles that impact its effectiveness. One of the key challenges is acoustic attenuation, which refers to the reduction in the strength of ultrasonic waves as they pass through various tissues. The ribcage, located between the ultrasound transducer and the liver, can obstruct wave propagation, significantly weakening the focus and precision of the 20-ultrasound energy. Additionally, the anatomical position of the liver adds to the difficulty, as the liver's location deep within the body makes it more challenging to deliver the ultrasound waves accurately to the targeted tumor.

Another substantial challenge is respiratory motion. As the liver is situated within the diaphragm's movement range, its position shifts with each breath. This motion can cause misalignment of the ultrasound beam, making it difficult to maintain a consistent and precise focus on the tumor. Furthermore, the heat dissipation effect is another hurdle in the application of HIFU. The liver, being highly vascular with rich blood perfusion, tends to dissipate the heat generated by HIFU treatment, reducing its ability to induce effective thermal ablation[29].

As a result, the tumor may not be heated sufficiently to destroy the targeted tissue, leading to suboptimal treatment outcomes. These obstacles, including acoustic attenuation, respiratory motion, and heat dissipation, must be carefully addressed for HIFU to become a more reliable and effective clinical treatment for liver tumors [30].

9.2 Innovations in HIFU Systems

To address these challenges, several innovations have been introduced to enhance the effectiveness of HIFU in liver tumor treatment. One of the key advancements is adaptive focusing techniques, which involve real-time adjustments to the ultrasound beam. These adjustments help compensate for respiratory motion, ensuring better targeting accuracy by continuously aligning the ultrasound energy with the tumor as the liver shifts during breathing. Another significant innovation is the integration of advanced imaging technologies, such as MRI and ultrasound-guided HIFU systems [31]. These systems provide high-resolution imaging that facilitates precise tumor localization and enables continuous monitoring throughout the treatment, improving the overall precision and safety of the procedure. Additionally, controlled cavitation techniques have been developed to optimize the mechanical effects of HIFU. By controlling the formation and collapse of bubbles in the tissue, these techniques enhance the disruption of the tumor while minimizing collateral damage to surrounding healthy tissue. Together, these innovations—adaptive focusing, advanced imaging integration, and controlled cavitation—work to overcome the challenges of acoustic attenuation, respiratory motion, and heat dissipation, improving the clinical application of HIFU for liver tumors [32,33,34]. Figure 6 shows the integration of advanced imaging technologies, such as MRI and ultrasound-guided HIFU systems.

Figure 6: Overview of advancements in HIFU technology for enhanced precision and efficacy [26].

10. Fundamental of HIFU

HIFU is a non-invasive medical technology that uses focused ultrasound waves to target and treat tissues within the body. It delivers high-frequency sound waves to a specific point, causing localized thermal effects that lead to tissue coagulation or destruction. The primary advantage of HIFU is its non-invasive nature, allowing it to treat various medical 22 conditions, such as cancer, neurological disorders, and aesthetic treatments, without the need for surgery. It reduces the risk of infection, accelerates recovery, and minimizes scarring compared to traditional surgical procedures. The technology has gained significant attention for its ability to target deep tissues with minimal damage to surrounding healthy areas. Its application is expanding, from treating solid tumors to being explored for non-invasive brain surgery and skin rejuvenation [27].

10.1 Principles of HIFU

The principle behind HIFU lies in its ability to focus high-frequency sound waves on a small, targeted area within the body. These waves are typically generated by a piezoelectric transducer, which converts electrical energy into mechanical vibrations. As the ultrasound waves travel through the body, they are focused on the desired tissue, where their energy is concentrated. The focal point of these waves is where the intensity of the ultrasound is highest, causing localized heating that leads to tissue destruction. The heat generated at the focal point can cause coagulation or necrosis of the targeted tissue, such as tumors or unwanted tissue. In some cases, mechanical effects like cavitation can occur, further contributing to tissue destruction. Real-time imaging technologies like MRI, ultrasound, or CT scans are commonly integrated into HIFU systems to guide the procedure, ensuring that the energy is accurately delivered to the target tissue [28,29].

10.2 Specifications of HIFU

The specifications of HIFU outline its precision and versatility as a non-invasive treatment. Key parameters include a frequency range of 1–10 MHz and power output of 100–1000W, enabling effective tissue ablation. The focal spot size (1–5 mm) ensures precise targeting, while spherical or parabolic transducers focus ultrasound waves efficiently. Integrated imaging systems like MRI or ultrasound provide real-time 23 guidance, and water-based cooling systems prevent overheating. Penetration depth varies with frequency, allowing deeper or more detailed treatments, making HIFU suitable for localized areas such as tumors. The specifications of a HIFU system in Table 2 generally include several parameters that define its functionality:

Table 2. Parameters of HIFU system and its functionality

Specification	Description	References
Frequency range	1 MHz to 10 MHz	[27], [30]
Power Output	100W to1000W	[31], [33]
Focal spot size	1 mm to 5 mm	[27], [30]
Transducer type	Typically, spherical or parabolic, optimized for focusing ultrasound waves to the target tissue	[27], [30]
Cooling system	Water-based or circulating coolant to prevent overheating of the transducer and surrounding tissues	[32], [33]
Imaging System Integration	Real-time imaging technologies like MRI, ultrasound, or CT scans for accurate targeting and monitoring	[31], [34]
Penetration depth	Determined by frequency; lower frequencies for deeper penetration, higher frequencies for better resolution	[30], [32]
Treatment area	Can treat a targeted area within tissues, often used for tumors or other localized tissue ablation	[27], [31]

10.3 Design of HIFU

Ultrasounds offer a significant benefit: they can penetrate a metal object, human organ, or biological tissue without needing to cut through the transmission path to the intended target. Unlike a surgeon's scalpel during medical procedures, ultrasounds do not cause any visible scars on a patient’s skin and can still treat the desired area with high precision while minimizing the chance of harming adjacent healthy tissues. Focused ultrasound is currently utilized or holds potential for treating conditions such as prostate and breast cancer, hypertension, and even glaucoma. There are various methods to focus ultrasound through different transducer designs, and COMSOL Multiphysics® software serves as an excellent tool for simulating and optimizing these designs. Creating a transducer that can efficiently generate an ultrasound field directed at a specific area can be challenging. This task is influenced by factors such as the frequency and power of the emitted signal, the attenuation and absorption characteristics of the medium through which the ultrasound travels, and, importantly, the transducer's placement and size. Figure 7 shows the schematic diagram of the ultrasound transducer.

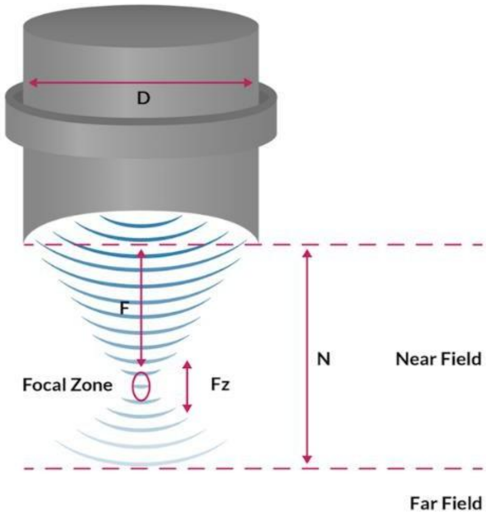

Figure 7. Schematic of the acoustic field generated by an ultrasound transducer. [34]

An ultrasound transducer used in clinical applications has several important characteristics. The near field distance (N) is a critical parameter, representing the region where sound waves constructively and destructively interfere before converging into a focused beam. It is calculated using the formula:

$$N = \frac{(D^2)f}{4c} \quad \text{(Equation 1)}$$

where D is the transducer diameter, f is the frequency of the ultrasound, and c is the speed of sound in the medium. Another key aspect is the focal distance (F), which is the distance between the transducer and the focal point, the targeted zone where imaging or therapeutic action is concentrated. Additionally, the field depth or focal zone defines the region within which the ultrasound beam remains sufficiently focused, marked by a -6 dB drop in signal amplitude from its maximum value. This zone is calculated as:

$$F_z = \frac{2F^2}{N+(\frac{F}{2})} \quad \text{(Equation 2)}$$

These parameters collectively determine the performance and effectiveness of the transducer in clinical imaging and diagnostics

11. Future Directions

While High-Intensity Focused Ultrasound (HIFU) has demonstrated promising outcomes in the non-invasive treatment of liver cancer, several areas remain open for further development and clinical refinement. Future research should focus on optimizing treatment protocols through advanced computational modeling and patient-specific customization using artificial intelligence (AI) and machine learning (ML) algorithms. Integrating HIFU with complementary therapies such as immunotherapy, targeted drug delivery, or nanoparticle-mediated ablation could enhance therapeutic outcomes and broaden its clinical applicability. Additionally, improving real-time imaging guidance—especially the fusion of MRI and ultrasound—can significantly enhance treatment accuracy and monitoring. Research into overcoming challenges such as respiratory motion, rib interference, and acoustic energy attenuation is also essential to ensure consistent and effective treatment in diverse patient populations. Large-scale clinical trials are needed to establish long-term efficacy, safety, and cost-effectiveness, ultimately paving the way for HIFU to be adopted as a standard therapeutic option for liver cancer and other solid tumors.

12. Conclusion

This study highlights the growing potential of High-Intensity Focused Ultrasound (HIFU) as a non-invasive and targeted modality for the treatment of liver cancer. By developing and analyzing a computational model, the research demonstrates that ultrasonic energy can be effectively focused on deep-seated liver tissues to induce localized thermal and mechanical effects necessary for tumor ablation. The findings confirm that with proper parameter tuning—such as frequency selection, transducer design, and acoustic energy control—HIFU can serve as a viable alternative to conventional therapies that often involve invasive procedures and systemic side effects. Although some limitations exist, particularly in treatment precision and tissue interaction complexities, ongoing technological advancements and clinical validation efforts are likely to overcome these barriers. As a result, HIFU stands poised to become a key tool in the future of liver cancer management, offering patients a safer, more precise, and recovery-friendly therapeutic solution.

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