A Review On High Intensity Focused Ultrasound (HIFU)

Shmriti[1*], Ankit Kumar[2]

[1*,2]Assistant Professor, Department of Paramedical Sciences, Subharti Medical College, Swami Vivekanand Subharti University, Meerut, India.

***Corresponding Author:** Shmriti
*Assistant Professor, Department of Paramedical Sciences, Subharti Medical College, Swami Vivekanand Subharti University, Meerut, India. Email Id: shmriti1503@gmail.com

Abstract
High Intensity Focused Ultrasound is an innovative and non- invasive therapeutic technique that uses focused ultrasound waves to thermally ablate a portion of tissue, meaning the tissue is destroyed using intense heat produced by sound waves. The intense heat causes tissue coagulation, necrosis, cavitation and heat shock in the cells. HIFU is also termed as focused ultrasound surgery (FUS). This technique aims to retain good quality life of the patient as it serves to treat neuropathic pain, uterine fibroids, prostate cancer, and tumors of bone, breast, liver, kidney, and testes. Also, research studies are being performed to temporarily open the blood brain barrier (BBB) through HIFU to allow drug absorption into blood. HIFU uses an ultrasound transducer similar to the ones used in diagnostic purpose but with high energy and an acoustic lens in order to focus sound waves to a particular point and thus raising the temperature to 70-80° Celsius. The interventional radiologist may use diagnostic Sonography with focused ultrasound (USgFUS or USgHIFU) or magnetic resonance guidance with focused ultrasound (MRgFUS). Aim is to introduce to a new innovative, non-invasive therapeutic technique in the field of radiology. The interventional radiologist can prefer USgFUS or MRgFUS. MRgFUS is being preferred the most as it monitors the degree of heating in real time. The transducer similar to the diagnostic one is used in USgFUS whereas in MRgFUS transducer is fitted in the MRI table. HIFU transducer is a cup shaped transducer fitted with an acoustic lens in order to obtain the converging beam of sound waves to focus a particular targeted tissue. The temperature is raised to 70-80° Celsius and maximum to 150°Celsius. HIFU is being considered the hybrid innovation in the radiology field which is serving as the harmless and incision less therapeutic technique in the treatment of neuropathic pain, uterine fibroids and different types of cancer. HIFU is non-invasive therapeutic technique which is replacing the surgical treatments. It has less risk, provides faster recovery time to patients by giving precise treatment using non ionizing radiation. It confirms the progress of radiology department in the field of medical science.

Keywords: HIFU, USgFUS, MRgFUS, BBB.

Introduction

HIFU is a novel, noninvasive therapy for prostate cancer and discomfort induced by disease metastasis to the bones. The ultrasonic transducer used for HIFU is similar to those used for diagnostic imaging, but it generates considerably stronger sound waves. The HIFU transducer concentrates sound waves into a tiny patch of aberrant tissue, creating enough heat to kill the cells in the same way that a magnifying glass may focus sunbeams to burn a hole in a sheet of paper. This procedure is also known as MRI-guided focused ultrasound (MRgFUS) and FUS (focused ultrasound surgery). Because of the accuracy of the approach, malignant cells may be destroyed without harming healthy tissue, and the process can be safely repeated as many times as needed. Until they reach their target, ultrasonic waves can travel through layers of tissue without causing injury.

MRI imaging is utilised to design the therapy as well as to monitor the target's temperature during the process. Patients may be under general anaesthesia (totally sleeping) or awake but sedated, depending on the ailment being treated.

History of HIFU

Wood and Loomis were the first to characterize the thermal characteristics of high-intensity US in 1927. Following that, Lynn et colleagues published in 1942 the use of a focused US generator capable of inducing targeted thermal harm to ex vivo liver specimens as well as animal brains via the intervening scalp, skull, and meninges without accidental skin injury.(2,3) The Fry brothers created a transcranial HIFU device in the 1950s that could be used after craniotomy to target deep-seated parts of the brain in primates, sparking interest in HIFU ablation to treat movement disorders such as Parkinson syndrome.(4) Several of the first studies on HIFU ablation therapy in humans were performed on the prostate and were reported in the early 1990s by Marberger and coworkers and Madersbacher et al; with subsequent advances in imaging guidance, both US and magnetic resonance imaging (MRI), allowing for treatment of a wide range of benign and malignant tumours.(5,6)

Principle of HIFU

The HIFU beam has the ability to traverse the overlying skin and tissues without causing harm and can concentrate on a specific localized area, typically limited to around 3–4 cm in diameter for treating tumors. HIFU generates a focused ultrasound beam that penetrates through the skin and surrounding tissues to induce coagulative necrosis in a targeted region, such as a tumor situated deep within the tissues. The focal point of the beam results in coagulative necrosis, creating a well-defined boundary between the ablated (dead) cells and the adjacent live cells, typically not exceeding 50 μm in width. The fundamental mechanisms responsible for tissue damage in HIFU involve coagulative thermal necrosis caused by the absorption of ultrasound energy during tissue transmission (thermal effect) and damage induced by ultrasound-induced cavitation. The heat produced by HIFU leads to a rapid temperature increase in the exposed tissue, often exceeding 60 °C, causing immediate and irreversible cell death if the exposure lasts longer than 1 second. The highly focused ultrasound beam achieves a very high intensity at the focal point, localized within a small volume of approximately 1 mm in diameter and about 10 mm in length. This focused nature minimizes the potential for damage to tissues outside the specific focal region. Additionally, the extent of thermal tissue damage is directly proportional to the duration of exposure and exponentially related to the temperature increase.10-14

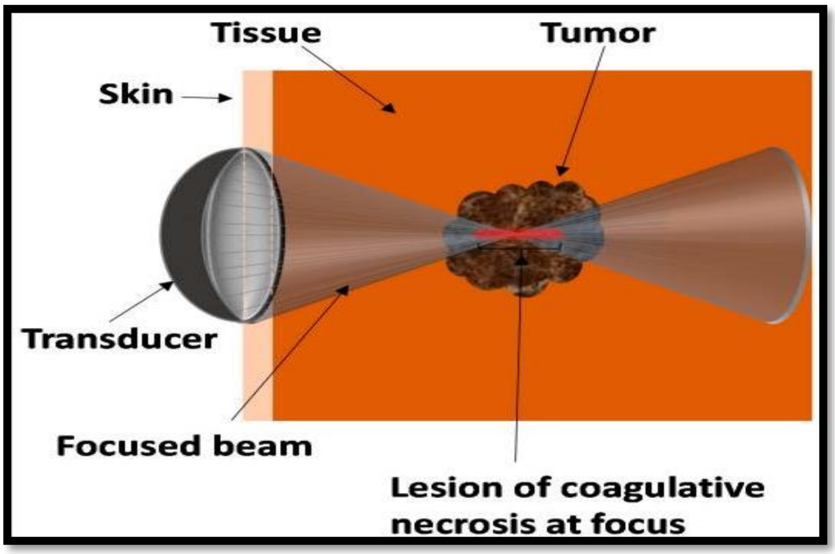

Figure 01: Principle of HIFU

Advantages of HIFU

HIFU offers several advantages over other treatments, including:

- It does not need standard surgery.
- Patients are not subjected to radiation.
- It specifically targets sick tissue while leaving healthy tissue alone.
- It has fewer adverse effects than surgery or radiation therapy.
- It's an outpatient operation with a quick recovery. Most people are able to resume their routine activities within 24 hours.

Ultrasound Thermal Ablation: Physical Properties

The physical features of high-intensity US waves allow for accurate energy deposition. Sound may carry energy in the form of waves as long as a medium is available. US is a kind of high-frequency sound (>20,000 Hz) that the human ear cannot perceive. Although radiofrequency and microwave ablation require an electrode or antenna to transmit energy to the target, HIFU can transfer energy to the target while minimising energy buildup in intervening tissues. High-intensity US is defined as US with an intensity more than 5 W/cm2, capable of causing tissue coagulation necrosis, and is most commonly used for HIFU ablation. Low-intensity US (0.125-3 W/cm2), on the other hand, causes nondestructive heating and is employed in physiotherapy. (7) When US is insonated into biological tissue, it can cause a variety of effects. Thermal ablation and acoustic cavitation are now the most therapeutically significant of these responses. HIFU thermal effects are secondary to US wave absorption. Frictional heat is produced by secondary vibrations and/or rotations of molecules to the US waves. Protein denaturation and coagulation necrosis often occur at 56°C with a one-second exposure, although temperatures over 43°C for one hour may make the tissue more sensitive to chemotherapy and radiation. (8-10)

HIFU Transducer

specific transducers constructed of piezo-active materials with unique acoustic properties suited for high-power US applications are utilised for HIFU thermoablation. In the target tissue, HIFU transducers generally produce sound intensities ranging from 100 to 10,000 W/cm2, whereas diagnostic transducers produce intensities ranging from 0.0001 to 0.1000 W/cm2. When an alternating voltage is given to piezo-active materials, they oscillate and generate US waves.(11) The most basic and least expensive transducer design is a selffocusing spherical-shaped piezo-ceramic transducer with a set aperture and focal length. More modern phased-array transducers are made up of a huge number of transducer elements, each of which may have its electrical signals modified.(12) With these more complex systems, beam steering and beam-forming capabilities are available, with the acoustic fields produced by several components converging to generate a single focus manoeuvred throughout a clinically meaningful volume, or with the ability to construct many foci concurrently. Both technologies enhance total ablation volume when compared to simpler transducer systems. Phased-array transducer designs range from 256-element phased-arrays for deep-seated tissue volume therapy to 1,000-element endorectal transducers for high-resolution prostate treatment.(13-14)

HIFU

High-Intensity Focused Ultrasound (HIFU) is a non-invasive medical procedure that utilizes ultrasound waves to target and treat specific tissues with precision. This innovative technology has gained prominence across various medical disciplines due to its ability to deliver therapeutic effects without the need for surgical incisions. Here are key aspects to consider when exploring HIFU:

1. Principle of Operation:

HIFU relies on the principle of focused ultrasound waves that generate intense heat at a specific focal point within the body. This thermal energy can be precisely directed to the target tissue, causing coagulative necrosis or cellular destruction.(15-17)

2. Clinical Application

- **Cancer Treatment:** HIFU has been employed in oncology for the treatment of localized tumors, particularly in the prostate, liver, breast, and pancreas. It offers a non-invasive alternative to traditional surgical interventions. (15-17)
- **Uterine Fibroids:** HIFU is used to treat uterine fibroids by ablating or shrinking the fibroid tissue, providing a potential non-surgical option for women seeking relief from symptoms. (15-17)
- **Neurosurgery:** In neurosurgery, HIFU has been explored for its potential in treating brain disorders and conditions, including essential tremor and certain types of brain tumors(15-17)

3. Advantages

- **Non-Invasiveness:** HIFU procedures are typically non-invasive, reducing the risks associated with traditional surgeries.
- **Precision:** The focused nature of ultrasound waves enables precise targeting of tissues, minimizing damage to surrounding healthy structures.
- **Minimal Recovery Time:** Patients often experience shorter recovery times compared to conventional surgical interventions.(17)

4. Challenges

- **Limited Depth Penetration:** The effectiveness of HIFU may be limited by the need for precise targeting, making it more suitable for superficial or easily accessible tissues.
- **Imaging and Monitoring:** Real-time imaging is crucial for monitoring the procedure, and advancements in imaging technologies are continuously improving the accuracy of HIFU treatments.(18-19)

5. Research and Development:

Ongoing research is focused on expanding the applications of HIFU, refining treatment protocols, and addressing challenges. The technology continues to evolve, with efforts to enhance its capabilities and widen its scope across different medical specialties.(20-21)

6. Regulatory Status:

HIFU devices are regulated by health authorities in various countries. Regulatory approval and guidelines may vary, and healthcare professionals must adhere to established protocols for safe and effective use.(21)

7. Future Directions:

The future of HIFU holds promising prospects as researchers and clinicians explore novel applications and refine existing protocols. Continued advancements in imaging technologies, such as real-time MRI guidance, may enhance the precision and safety of HIFU procedures. Moreover, ongoing efforts to overcome depth limitations and improve penetration into deeper tissues may expand the range of treatable conditions.(22-23)

8. Global Adoption and Accessibility:

HIFU is gaining recognition globally, and its adoption is growing in various medical centers. However, accessibility may vary, and factors such as cost, infrastructure, and regulatory approvals influence its widespread implementation. Efforts to make HIFU more accessible and cost-effective are essential for maximizing its impact on patient care.(23)

9. Combination Therapies:
Researchers are exploring the synergistic effects of combining HIFU with other treatment modalities, such as immunotherapy or chemotherapy. These combination therapies aim to enhance the overall effectiveness of cancer treatment and may offer new avenues for managing complex medical conditions. (21-22)

10. Patient Considerations:
While HIFU offers several advantages, patient selection is crucial. Factors such as tumor size, location, and individual health conditions play a role in determining the appropriateness of HIFU as a treatment option. Close collaboration between healthcare providers and patients is essential for informed decision-making. (23)

11. Ethical and Social Implications:
The introduction of advanced medical technologies like HIFU raises ethical considerations regarding informed consent, equitable access, and the potential impact on healthcare disparities. Addressing these ethical and social implications is essential to ensure responsible and equitable integration into healthcare systems. (21)

12. Training and Expertise:
The successful implementation of HIFU procedures requires specialized training for healthcare professionals. Ensuring that practitioners are well-versed in the technology, its applications, and safety measures is paramount for delivering optimal patient outcomes. (24)

Conclusion
HIFU therapy has demonstrated therapeutic achievement in the treatment of both benign and malignant tumors. Tumour control may be improved while side effects are decreased with the use of MR guidance and continuous developments in intraprocedural ablation monitoring. Furthermore, at the preliminary stage, HIFU treatment appears to be promising when combined with other therapies such as chemotherapy and radiation, and in the preclinical environment increased targeted drug/gene delivery and immune system regulation. HIFU's multimodal therapeutic capabilities offer tremendous promise in the realm of image-guided therapy, despite the fact that it is still in its early phases of development when compared to other probe-based ablative therapies.

References

1. ucsfhealth.org/treatments/high-intensity-focused-ultrasound-hifu
2. Lynn J G, Zwemer R L, Chick A J, Miller A E. A new method for the generation and use of focused ultrasound in experimental biology. J Gen Physiol. 1942;26(2):179–193
3. Wood R W, Loomis A L. The physical and biological effects of high frequency sound waves of great intensity. Philos Mag and J of Science. 1927;4(22):417–436.
4. Fry W J, Barnard J W, Fry F J, Brennan J F. Ultrasonically produced localized selective lesions in the central nervous system. Am J Phys Med. 1955;34(3):413–423.
5. Susani M, Madersbacher S, Kratzik C, Vingers L, Marberger M. Morphology of tissue destruction induced by focused ultrasound. Eur Urol. 1993;23 01:34–38.
6. Madersbacher S, Pedevilla M, Vingers L, Susani M, Marberger M. Effect of high-intensity focused ultrasound on human prostate cancer in vivo. Cancer Res. 1995;55(15):3346–3351.
7. Ter Harr G R. West Sussex: John Wiley & Sons; 2004. Therapeutic and surgical applications; pp. 407–456.
8. Kennedy J E, Ter Haar G R, Cranston D. High intensity focused ultrasound: surgery of the future? Br J Radiol. 2003;76(909):590–599.
9. Ter Haar G R. West Sussex: John Wiley & Sons; 2004. Ultrasonic biophysics; pp. 348–406.
10. Ter Haar G. Therapeutic applications of ultrasound. Prog Biophys Mol Biol. 2007;93(1–3):111–129.
11. Dubinsky TJ, Cuevas C, Dighe MK, Kolokythas O, Hwang JH. High intensity focused ultrasound: current potential and oncologic applications. AJR Am J Roentgenol 2008;190(1):191–199
12. Gavrilov LR, Hand JW. Two-dimensional phased arrays for surgery: movement of a single focus. Acoust Phys 2000; 46:390–399
13. Daum DR, Hynynen K. A 256-element ultrasonic phased array system for the treatment of large volumes of deep seated tissue. IEEE Trans Ultrason Ferroelectr Freq Control 1999;46(5): 1254–1268
14. McKenna EC. More Sites and Patients Join Clinical Trial Assessing New MR-Guided FUS System for Prostate Cancer. Focused Ultrasound Foundation; 2011
15. McDannold N, Clement GT, Black P, et al. Transcranial magnetic resonance imaging- guided focused ultrasound surgery of brain tumors: Initial findings in 3 patients. Neurosurgery. 2010;66(2):323-332.
16. Kennedy JE. High-intensity focused ultrasound in the treatment of solid tumours. Nat Rev Cancer. 2005;5(4):321-327.
17. Stewart EA, Rabinovici J, Tempany CM, et al. Clinical outcomes of focused ultrasound surgery for the treatment of uterine fibroids. Fertil Steril. 2006;85(1):22-29.
18. Tempany CM, Stewart EA, McDannold N, et al. MR Imaging–guided Focused Ultrasound Surgery of Uterine Leiomyomas: A Review of Treatment Principles and Current Outcomes. Radiology. 2007;245(1):29-39.

19. Elias WJ, Huss D, Voss T, et al. A pilot study of focused ultrasound thalamotomy for essential tremor. N Engl J Med. 2013;369(7):640-648.
20. Napoli A, Anzidei M, De Nunzio C, et al. Real-time Magnetic Resonance–guided High-intensity Focused Ultrasound Focal Therapy for Localized Prostate Cancer: Preliminary Experience. Eur Urol. 2013;63(2):395-398.
21. Kennedy JE, ter Haar GR, Cranston D. High intensity focused ultrasound: surgery of the future? Br J Radiol. 2003;76(909):590-599.
22. Wu F, Wang ZB, Chen WZ, et al. Extracorporeal focused ultrasound surgery for treatment of human solid carcinomas: early Chinese clinical experience. Ultrasound Med Biol. 2004;30(2):245-260.
23. Pfeiffer D, Berger J, Gross AJ. Precision and feasibility of transrectal high-intensity focused ultrasound (HIFU) treatment in localized prostate cancer. Eur Urol. 2005;47(1):34-41.
24. Hurwitz MD, Ghanouni P, Kanaev SV, et al. Magnetic Resonance–Guided Focused Ultrasound for Patients With Painful Bone Metastases: Phase III Trial Results. J Natl Cancer Inst. 2014;106(5):dju082.