HIGH INTENSITY FOCUSED ULTRASOUND (HIFU)

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ABSTRACT

High Intensity Focused Ultrasound (HIFU) is a medical technology that uses ultrasound waves to deliver focused energy at a specific target within the body. This non-invasive technique has gained recognition for its potential in various therapeutic applications. The principle behind HIFU involves using an ultrasound transducer to generate high-frequency sound waves. These waves are focused to a precise point, creating a concentrated area of high intensity. The energy produced can be used to achieve two main effects: thermal ablation and mechanical disruption.

In thermal ablation, the intense heat generated by the focused ultrasound causes coagulative necrosis, leading to the destruction of targeted tissue. This approach has been applied in the treatment of solid tumors, such as prostate, liver, kidney, and breast cancers. HIFU offers advantages over traditional surgical methods as it is non-invasive, avoids the need for incisions, and can be performed on an outpatient basis. It also provides real-time monitoring capabilities, allowing for precise control and adjustment of the treatment. Mechanical disruption, on the other hand, involves using high-intensity ultrasound to induce mechanical effects on tissue, rather than relying solely on thermal energy. This approach has shown promise in applications such as targeted drug delivery, where HIFU can be used to temporarily disrupt cell membranes, facilitating the delivery of therapeutic agents to specific areas.

HIFU has also demonstrated effectiveness in the treatment of various neurological conditions. In neurosurgery, it can be used to create lesions in specific brain regions, offering a non-invasive alternative to traditional surgical approaches. HIFU has been explored for the treatment of essential tremor, Parkinson's disease, and neuropathic pain, among other neurological disorders. In addition, HIFU has found applications in the field of cosmetic medicine. It can stimulate collagen production and tissue tightening, making it suitable for non-surgical facelifts, body contouring, and skin rejuvenation. HIFU treatments in this context are typically well-tolerated, with minimal discomfort and downtime. While HIFU has demonstrated significant potential, ongoing research and development efforts are focused on further refining the technology, optimizing treatment protocols, and expanding its applications. Continued advancements in imaging techniques, treatment planning software, and transducer design are expected to enhance the precision and effectiveness of HIFU procedures.

In conclusion, High Intensity Focused Ultrasound (HIFU) is a non-invasive medical technology that utilizes ultrasound waves to deliver focused energy for thermal ablation and mechanical disruption. Its applications range from the treatment of solid tumors and neurological disorders to cosmetic medicine. With ongoing research and development, HIFU holds promise as a versatile and transformative approach to various medical treatments.

Keywords: Ultrasound, Heat energy, noninvasive, medical technology

(I) INTRODUCTION

Curie brothers Pierre Curie and Jacques Curie discovered the piezoelectric effect in certain crystals in 1880 leading to the discovery of ultrasound technology. The medical ultrasound technology is continuously evolving and contributing in patient’s diagnosis and treatment. High Intensity Focused Ultrasound (HIFU) is a step forward in the field of ultrasound technology, contributing the therapeutic purpose in the radiology department.

Since decades, diagnostic ultrasound is being used but HIFU is serving the therapeutic use for tissue ablation in radiology department. HIFU uses a non-invasive thermal ablation technique. Unlike other thermal ablation techniques like radiofrequency ablation (RFA), laser, cryoablation which uses specialized needles/probes to deliver extreme temperatures to tissue cells causing necrosis. HIFU uses focused ultrasound waves to create lethal heat effect to the targeted tissue without harming surrounding tissues. HIFU can be guided through ultrasound (USg) or magnetic resonance (MRI). It is being considered as the hybrid technology in the field of radiology and is proving to be advantageous therapeutic technique.

(II) HISTORY

1942 – **First Tissue Lesion**. John G. Lynn et al. proposed the idea that ultrasound can be intensely focused to produce extreme heat and non-invasively destroy targeted disease tissue within the body.
1942 – **First Focused Ultrasound Device**. William Fry & his brother, Francis Fry with research team developed a focused ultrasound device that mechanically aligned four focused ultrasound generators to produce a pinpoint lesion without damage to the surrounding tissue.
1944 – **First Preclinical Study**.
1950 – **First Therapeutic Use**.
1955 – **Fathers of Focused Ultrasound**. Fry brothers performed partial ablation of the basal ganglia after a craniotomy.
1962 – **Focused Ultrasound and Brain**. Russell Meyers & William Fry utilized focused ultrasound to treat numerous human patients suffering from various brain pathologies, in particular Parkinson’s disease.
1964 – **First Cancer Application**. M. Oka used focused ultrasound to treat thyroid and breast cancers.

1968 – **First Brain Cancer Treatment**. Dr. Robert Heimburger (Neurosurgeon) treated brain cancer under ultrasound guidance.
1988 - 1st FDA Approval. Coleman & Lizzie developed the Sonocare CST-100 therapeutic ultrasound system to treat glaucoma. Earned FDA approval.
1990 - Focused Ultrasound for BPH. N. Sanghvi et al. developed and implemented protocol for treatment of BPH.
1991 - Focused Ultrasound for Brain Tumors.
1992 - First Combination with MRI.
1996 – First Blood Brain Barrier Application [3]

(III) PRINCIPLE

The principle is based on the physical effects of ultrasound on tissues. HIFU technology causes thermal tissue destruction with high precision and minimum damage to the surrounding tissue. The principle is similar to a childhood experiment of creating a hole in a leaf by focusing the sun rays with the help of lens over a particular point thus resulting in burning of leaf as shown in figure 1.

Figure 1: The magnifying glass converge the sunrays to a focal point on a leaf converting the energy of light waves to become hot enough to burn a leaf.

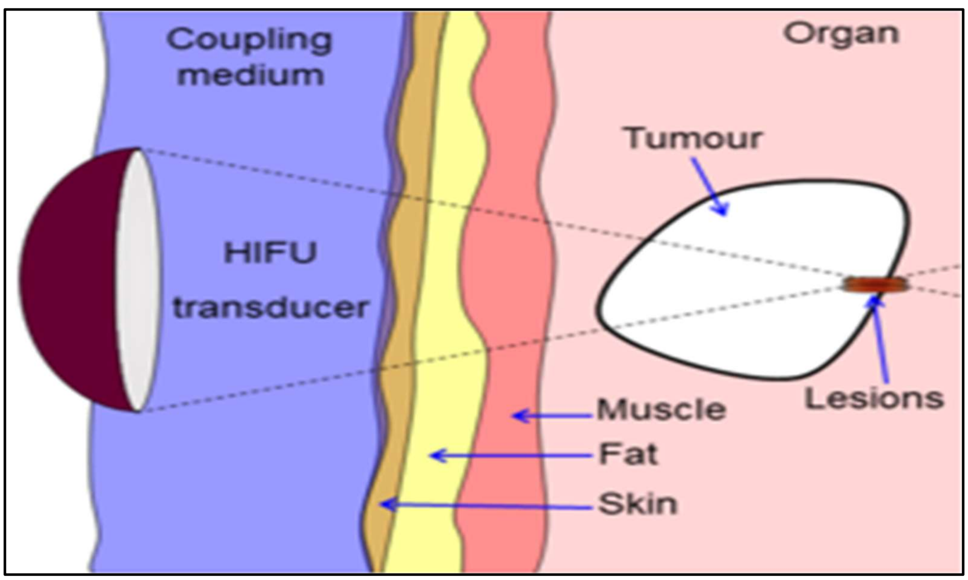

Figure 2: Illustration of HIFU principle

Therapeutic ultrasound intensity range is higher than that used in diagnostic ultrasound. Therapeutic ultrasound intensity differs depending on effect. High intensity range is used for tissue ablation.

Lower intensity range is used to induce mechanical effects on the cellular level but to create localized biological effects HIFU transducers are designed to focus or converge the beam to a point. Focusing of the ultrasound can be achieved by different methods like geometric focusing which takes advantage of spherically concave surface of HIFU transducers that helps to focus the beam at a point, another method is beam focusing which uses acoustic lens to converge the beam. Electronic focusing is also one of the focusing techniques which use phased array transducers composed of piezoelectric crystals.

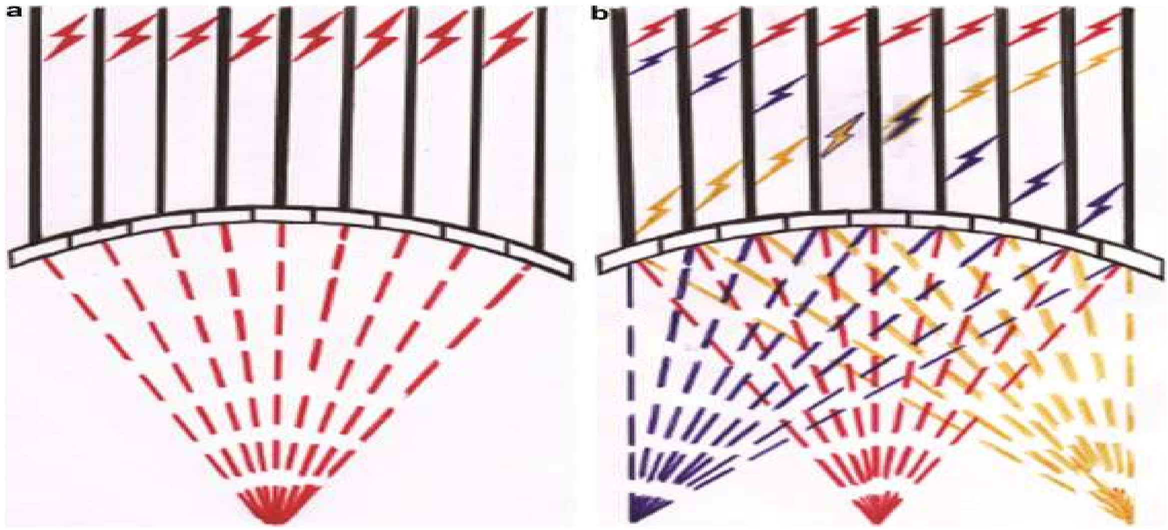

Figure 3: Electronic steering of the HIFU beam. (a) Phased array transducer is composed of multiple elements, each of which has a separate excitation signal (continuous black lines) with a specific phase. Emitted ultrasonic beams follow their corresponding phase and converge at the original geometric focus. Changing the phase of the excitation signal in (b) changes the direction of the ultrasound beams causing them to converge into a new focus [1]

(IV) PROCEDURE

When ultrasound energy interacts with tissue it either gets absorbed, reflected or deflected. The emission of wave energy is based on transducer vibration, which alternates the acoustical pressure of the coupling medium resulting in tissue movement (dilatation and contraction). Due to the fluctuations in pressure, the absorbed energy at the focal point is converted into heat. The rapid increase in tissue temperature upto 60° C or higher, resulting in tissue necrosis or coagulation leaving behind an elementary lesion.

The creation of lesion involves two main effects: thermal effect which is directly related to the tissue temperature and the other is cavitation effect i.e., presence of air bubbles in front of the transducer focus. Under high acoustic intensities, microscopic gas bubbles are formed and interact with ultrasound energy, referred as acoustic cavitation. Two types of acoustic cavitation are present: stable and inertial. Stable cavitation occurs when bubbles oscillate and grows in size, transfers the heat to the surrounding fluid resulting in mild temperature rise. Above certain pressure threshold, bubbles collapse vigorously causing damage to the nearby tissue; this phenomenon is referred as inertial cavitation[1]

Effective HIFU treatment procedure includes different stages. The diagnosis of tumor is done with the help of diagnostic ultrasound or MRI. Then the tumor visibility is ascertained with the help of diagnostic ultrasound which helps to establish a desired acoustic window for treatment delivery. The target volume is identified and localized. Another important stage is to determine the correct ultrasound exposure to ablate the tissue. In case of ultrasound imaging guidance, combination of focal peak intensity and exposure time is used which results in hyper echoic region at the target whereas in case of MR imaging guidance, this combination is varied until required temperature is attained, using MR thermometry. The acoustic energy may be delivered in different ways depending on the target volume. Smaller target volume can be ablated with single exposure keeping the transducer stationary for about 2-10s. For larger volumes, the transducer may be moved in discrete steps and fired at each position to achieve desired tissue killing. Also, transducer can be moved in predetermined trajectories to attain desired cell killing.

The final component of HIFU procedure is post- treatment assessment of tissue ablation. Contrast enhanced MR and ultrasound imaging allows visualization of vasculature. Successful HIFU ablation results in occlusion of blood vessels reducing the uptake of contrast post treatment.[5]

(V) IMAGING GUIDANCE OF HIFU

Magnetic resonance (MR) imaging and ultrasound are currently used for target tissue identification, HIFU beam localization and treatment monitoring. Each of the two has its advantages and limitations as guidance for HIFU therapy.

MRI allows precise spatial assessment of the target tissue and surrounding structures. Due to tissue cavitation, echogenic cloud is formed that limits evaluation of deeper tissues when ultrasound imaging is used. But this doesn’t happen with MR imaging. MR imaging is the only technique that provides quantitative temperature measurements using MR thermometry.

MR guided focused ultrasound surgery (MRgFUS) is limited for the treatments of tumors in moving body organs, like liver tumors, due to sensitivity to motion artifacts from respiratory movements. Ultrasound guided focused ultrasound surgery (USgFUS) lacks clinical thermometry.[1]

(VI) CLINICAL APPLICATIONS OF HIFU

(A) Non- FDA Approved Applications

- Ablation of Hepatic Tumors.

- Ablation of Breast Tumors.

(B) **FDA Approved Applications**

- Ablation of Uterine Leiomyomas.
- Ablation of Bone Metastasis.
- Ablation of Prostate Cancer.
- Neurological Applications.

(VII) ADVANTAGES OF HIFU

- The non-ionizing nature of HIFU eliminates radiation risks.
- No dose limitation allows repeated therapy.
- Low risk of injury to non-target healthy tissue as it allows precise treatment. [4]
- HIFU ablation has less heat sink effect because the heating process relies less on thermal conduction.

(VIII) LIMITATIONS OF HIFU

Organ movement during HIFU procedures can lead to incomplete target ablation or collateral damage. Ultrasound reflection by bone or gas containing tissue may cause incomplete target ablation. Poor acoustic coupling at the skin transducer interface may result in skin burns.

(IX) COMPARISON WITH OTHER TISSUE ABLATION DEVICES

HIFU	RFA
Heat generated by focusing low energy ultrasound beam.	Resistive heating by alternating radiofrequency alternating current.
Ability to focus the treatment area.	Heat given to healthy tissues too.
Good depth of penetration.	Unable to penetrate to deep tissues.
No direct contact required.	Direct contact required.
Precise and fractional heating.	Bulk heating.
Single treatment.	Several sessions.

(X) SUMMARY

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). 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. [123]

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