

## Effective Therapeutic Treatment of Deep-Seated Brain Tumours with High Intensity Focused Ultrasound (HIFU) for Better U-Healthcare

VR Singh<sup>1\*</sup> and Kanika Singh<sup>2</sup>

<sup>1</sup>Professor, Chair, IEEE-IMS/EMBS Delhi, National Physical Laboratory, New Delhi, India

<sup>2</sup>Pusan National University, Busan, South Korea

\*Corresponding Author: VR Singh, Professor, Chair, IEEE-IMS/EMBS Delhi, National Physical Laboratory, New Delhi, India.

Received: May 03, 2020; Published: June 18, 2020

### Abstract

Cancer is a deadly disease and its diagnosis and treatment are required to be undertaken on priority basis, preferably at an early stage. Several conventional techniques are used presently in the hospitals but for an effective and reliable diagnosis and treatment of the disease, more efforts are required to be made on the development of new techniques, like focal ultrasound hyperthermia system, etc.

In the present research, development of a high intensity focal ultrasound (HIFU) system is presented for the treatment of deep seated brain tumour, in particular. Thermal profile under the focal beam is studied and plotted in the brain at different locations by using an array of temperature sensors. A non-contact double probe through transmission technique is also developed and used to monitor thermal profile pattern inside and outside the tumours. This thermal pattern is then correlated with the intensity of ultrasound.

Design and development of the ultrasound system are discussed here, in detail. Case studies are given about the treatment of cyst, tumour and cancerous cells, etc, particularly for the deep seated brain tumours, in an effective manner. RFID Chips and Wireless Sensor Networking (WSN) are used, along with the transducer systems, for ubiquitous health care applications in different environments. This contribution would be a new direction in the field of biomedical engineering for monitoring and control of the health condition of a patient, in a better way.

**Keywords:** Cancer; Focal Ultrasound; Tumour; Ablation; Hyperthermia; U-Healthcare

### Introduction

The presence of deep seated brain tumours is a serious problem for the patients [1,2] and It becomes difficult to remove such tumours with conventional techniques. The surgery has, however, been the only practical solution for such problems for long time, though in most of the cases, patients have not survived. In order to solve the problem, radiological and ultrasound techniques have been developed [3-5]. Focusing of ultrasound beam has given more intensity to get a focal lobe to destroy the abnormality [6-8]. A smart sensor has been explored to measure output parameters of the transducer [9]. Further, efforts have been made to get focal ultrasound of high intensity, which is found to be more useful to remove these tumours [6-8,10,11]. Although, some findings are reported on the use of high intensity focal ultrasound [3-5], yet more research is required to be pursued to make the system clinically acceptable for better results. Generally, imaging techniques are used simultaneously to detect the presence of tumours with their particular location.

Biological aspects of tumours in the brain are given to explain the types of tumours with the location inside the brain. Main emphasis is placed on the benign brain tumours, to understand the pathological aspects and the causes of brain tumours [1,2].

Thermal profile patterns [12,13] have been studied in the focal lobe and in the surrounding of the existing tumour at different locations, by using a thermos-couple temperature probe as well as by having a non-contact double probe ultrasonic through- transmission technique [14-18]. Numerical modelling [14] of thermal patterns, deep heating and hyperthermia [15-17] give good indication of clinical treatment. Basic biological tissues and tumours have been evaluated for ultrasonic, physical and chemical properties [19-26] to understand their complexity.

The ultrasonic data from the tumour under treatment has been studied to telemeter the information [27] by using WSN (Wireless Sensor Networking) and biotelemetry [34] for better U-health care [28-33].

In the present study, development of a high intensity focused ultrasound (HIFU) is described for the treatment of deep seated brain tumours. Thermal profile patterns in the tumours under focussed ultrasound have been measured and mapped by using temperature sensors. Clinical experience of the HIFU on *in vitro* tissue samples in the Laboratory and on the *in vivo* patients in the hospital has been discussed. Application of HIFU in U-health care for old age patients living in remote areas, has also been studied.

### Biological aspects and treatment techniques

#### Brain anatomy and abnormalities

Anatomy of the inside of the brain gives a clear indication of important parts of the brain [1]. Generally, the supra-tentorium contains the cerebrum, ventricles (with cerebrospinal fluid), choroid plexus, hypothalamus, pineal gland, pituitary gland, and optic nerve. The infratentorium contains the cerebellum and brain stem. The brain is the controller of every function of the body, including vision, hearing, speech, and movement. If the brain cancer grows, it damages areas that control these functions, leading to complications like headaches, seizures, vision and hearing loss, etc [1,2].

#### Brain tumour types

A brain tumour is explained [1,2] as a mass of abnormally growing cells in the brain or skull. The tumour can be benign (noncancerous) or malignant (cancerous). Generally, the brain tumours are two types, primary and secondary. Primary tumours start growing in the brain tissue, while secondary tumours spread to the brain from another area of the body. The cancer arises from the brain tissue and spreads further. All types of brain tumours, benign or malignant, are serious and are required to be treated in time. The growing tumour, generally, compresses and damages other structures in the brain. The most common types of brain tumours are metastatic brain tumours (Figure 1) that arise elsewhere in the body (such as the breast or lungs) and migrate to the brain, usually through the bloodstream. These metastatic tumours are considered cancer and are malignant. Such tumours affect the brain for about 25% patients with cancer but about 40% of people with lung cancer develop metastatic brain tumours. Presently, with innovative surgical and radiation approaches, survival rate of the patients is better now with improved quality of life [2].

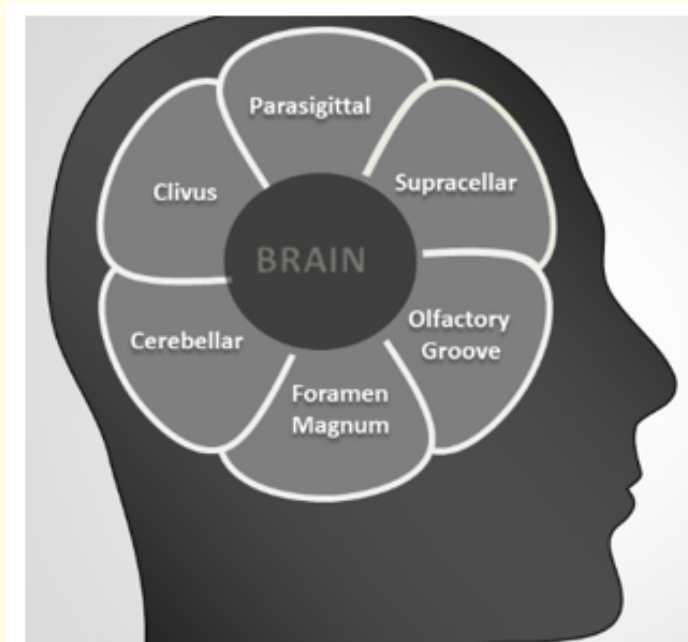


Figure 1: Abnormality locations in the brain due to cancer [1,2].

**Different types of benign brain tumours [1,2] are given as follows:**

- Chordomas are benign, slow-growing tumours that are most prevalent in people ages 50 to 60. Their most common locations are the base of the skull and the lower portion of the spine. Although these tumors are benign, they may invade the adjacent bone and put pressure on nearby neural tissue. These are rare tumors, contributing to only 0.2 percent of all primary brain tumours.
- Craniopharyngiomas are of benign nature, but are difficult tumours to get them removed as their location is near to the critical structures deep in the brain. These arise from a portion of the pituitary gland (the structure that regulates hormones in the body), as most of the patients need some hormone replacement therapy.
- Gangliocytomas, gangliomas and anaplastic gangliogliomas are rare tumours that include neoplastic nerve cells which are differentiated but occur primarily in the young adults.
- Glomus jugulare tumours are mostly benign which are located just under the skull base, at the top of the jugular vein. There are common form of glomus tumour and are only 0.6% of neoplasms of the head and neck.
- Meningiomas are also mostly benign intracranial tumours, comprising 10 to 15% of brain neoplasms, with small percentage as malignant. These tumours originate from the meninges, the membrane-like structures that surround the brain and spinal cord.
- Pineocytomas are, generally, benign lesions and arise from the pineal cells, occurring in the adults. These are also called as non-invasive, homogeneous and slow-growing.
- Pituitary adenomas are the intracranial tumours after gliomas, meningiomas and schwannomas. Mostly, these are adenomas as benign and slow-growing. These malignant pituitary tumours do not spread to other parts of the body.
- Schwannomas are common benign brain tumours in adults and these arise along nerves, comprised of cells that normally provide the “electrical insulation” for the nerve cells. Schwannomas often displace the other part the normal nerve instead of invading it.
- Acoustic neuromas are the most common schwannoma, arising from the eighth cranial nerve, or vestibular cochlear nerve, which travels from the brain to the ear. These are also benign tumours and can cause serious complications. Other locations are the spine and along the nerves going to the limbs.
- Medulloblastomas usually arise in the cerebellum, most frequently in children. They are high-grade tumours, but are usually responsive to radiation and chemotherapy.
- Oligodendrogliomas are derived from the cells that make myelin, working as the insulation for the wiring of the brain.
- Hemangioblastomas are slow-growing tumours, commonly located in the cerebellum, originating from blood vessels, which are large in size and are accompanied by a cyst, occurring in the ages of 40 to 60.
- Rhabdoid tumors are rare but are highly aggressive tumours that tend to spread throughout the central nervous system, appearing in multiple sites in the body, especially in the kidneys, in young children and adults.

**Causes of brain tumours**

Brain tumours arise when certain genes on the chromosomes of a cell are damaged and no longer function properly. These genes regulate the rate at which the cell divides and repairs genes to fix defects of other genes. Environmental factors are also responsible for

the damage, giving the environmental injury to the genes, to develop brain tumour [1,2]. Thus, tumours produce substances that block the immune system from recognizing the abnormal tumour cells and eventually overpower all internal and external deterrents to its growth. These tumours can produce substances called angiogenesis factors to promote the growth of blood vessels, to increase the supply of nutrients to the tumour, to become dependent on these new vessels.

### **Treatment techniques for brain tumour**

The brain tumours (whether primary or metastatic, benign or malignant) usually are treated with surgery, radiation, cryo-surgery, ultrasound, hyperthermia and/or chemotherapy- alone or in various combinations. Sometime, radiation and chemotherapy are used together for malignant, residual or recurrent tumour. Each technique [3-5,10-12,19,20] has its side-effects and risks to the patient.

#### **Surgery**

Surgical surgery is the conventional manual method. The neurosurgeon opens the skull through a craniotomy to access the tumour to remove it, by taking precaution so that the patient does not lose speaking and walking. Alternately, surgery is made by having stereotactic biopsy before craniotomy. A frame is attached to the patient's head and a scan is obtained. A small hole is then drilled in the skull to allow access to remove the tumour or lesion [1-3].

#### **Radiation therapy**

Radio-therapy includes RF and microwave therapy. If surgery fails, radiation therapy may be used by having high-energy X-rays to kill cancer cells and abnormal brain cells and to shrink tumours. A conformal coverage of the tumour is easily made with Standard External Beam Radiotherapy, or by using 3-dimensional conformal radiotherapy (3DCRT) including intensity-modulated radiotherapy (IMRT). Proton Beam Treatment can be used with radioactivity to locate the tumour, to give less damage to the surrounding structure. Also, Stereotactic Radiosurgery (such as Gamma Knife, Novalis and Cyberknife) technique focuses the radiation with many different beams on the target tissue, to give less damage to tissues adjacent to the tumour [1-3].

#### **Chemotherapy**

Chemotherapy refers to use of drugs to kill cancerous cells This technique is effective for specific paediatric tumours, lymphomas and some oligodendrogliomas, and gives good survival rate in case of the most malignant primary brain tumours, The chemotherapy kills the inflicting cell damage to get repaired by normal tissue than tumour tissue [1,2]. The resistance to chemotherapy involves survival of tumour tissue that does not respond to the drug, or to show inability of the drug to pass from the bloodstream into the brain. The goal of another class of drugs is not to kill the tumour cells but, rather, to block further tumour growth.

#### **Cryo-surgery**

Cryo-surgery kills the cancerous cells by freezing them. A freezing machine at low temperature is developed and used to treat abnormal swelling and cist etc [1,2,10].

#### **Laser therapy**

Laser Thermal Ablation is a newer technique that some centres are using to treat smaller tumours, particularly in areas that may be more difficult to reach using previous open surgery procedures. This involves placing a tiny catheter within the lesion, possibly completing a biopsy, then using laser to thermally ablate the lesion. This technique is only more recently used in brain tumour treatments, therefore the long term efficacy has not been established [1,2].

#### **Ultrasound cancer therapy**

Ultrasound therapy is used for the treatment of tissue abnormality, due to heat generated by ultrasonic vibrations. As reported [24,25], the treatment of deep-seated tumours, particularly of the oesophagus, has been primarily surgical, as the irradiation has not proved successful. The radiation therapy has not successfully eradicated the deep-seated neoplasms to destroy the tumour, avoiding adverse effect upon the skin and overlying tissues. Thus, clinically, as well as pathologically, deep-seated carcinomas are amenable to external radiation therapy, particularly, for curability of carcinomas located in accessible positions. Thus, two types of cancer at effective control by irradiation are cancer of the oesophagus and cancer of the lung [1-3,10,11,16-18,24,25].

#### **Hyperthermia technique**

Focal ultrasound therapy is preferred to be used for tumour therapy. Generally, local tumour hyperthermia is the elevation of tissue temperature between 42.5°C to 45°C for 30 minutes or longer [3-8,11,15-18,24,25].

The temperature elevation depends on the transducer frequency, intensity and duration of irradiation and thermal characteristics of the medium. The heat generated in a living tissue is classified into two groups hyperthermia and thermotherapy. In thermotherapy, high temperatures are employed which give rise to rapid tissue necrosis, while the hyperthermia is characterised by lower temperatures between 41 - 47°C.

A comparison of hyperthermia modalities is given in table 1, with the frequency range, effectiveness, and technical features. However, the high intensity focussed ultrasound (HIFU) is developed here for effective tumour therapy [4,24].

S.No	Parameter	Radio frequency				Microwave	Ultrasound
		0.5-1.0		10-30			
1	Frequency	0.5-1.0		10-30		>300	0.5-5
2	Technique	RF Heating	Local current field	Capacitive coupling	Inductive coupling	Radiation source direct coaxial application	Direct contact treatment through water bag
3	Focusing	-	-	-	-	Not good	Very good
4	Localization	Very good	Very Good	Poor	Good	Very Good	Excellent
5	Advantages	-	Simple, cheap, can be used with radio-active sources	Can heat large volumes	Used for superficial, but not good for deep tissue	High temperature available, capable of forming large lesions in presence of blood perfusions	Inexpensive, good depth of penetration, Fast development of high intensity focused ultrasound
6	Disadvantages	Needs expensive high power	Invasive	Damage the tissues	Non-uniform heating	Difficult to predict thermal patterns, poor penetration	Expensive equipment, small ablations

Table 1: Comparative features of hyperthermia modalities

Physical aspects

Physical principle of HIFU

HIFU produces an effect on the tumour in the tissue to create heating, cavitation and mechanical forces. The thermal and cavitation mechanisms are, however, the main factors [3-8,16,17]. In the tumour, the thermal heating is caused by absorption of ultrasonic energy by the tissue, to give a rise in temperature of the tissue, which is dependent on the intensity of the ultrasound energy and the acoustic (ultrasound) absorption coefficient of the tissue. In HIFU, the ultrasonic intensity at the beam focus is much higher than that outside of the focus. This gives the generation of tissue temperature elevation, in the focal zone of the beam causing tissue coagulation and denaturing of the tissues within seconds [11,13].

Figure 2 shows the focussing mechanism with focal lobe and its intensity patterns. The physical mechanism involves the ultrasonic energy to pass through a viscous medium such as human soft tissue and the intensity of the beam is attenuated. This attenuation depends on both the energy that is absorbed by the medium as well as the energy that is scattered from interfaces or inhomogeneities within the tissue. However, most of the attenuation is related to tissue absorption, and hence almost all of the energy from the primary ultrasound beam results in the tissue heating, which is used for therapeutic purposes [3-7,13,14].

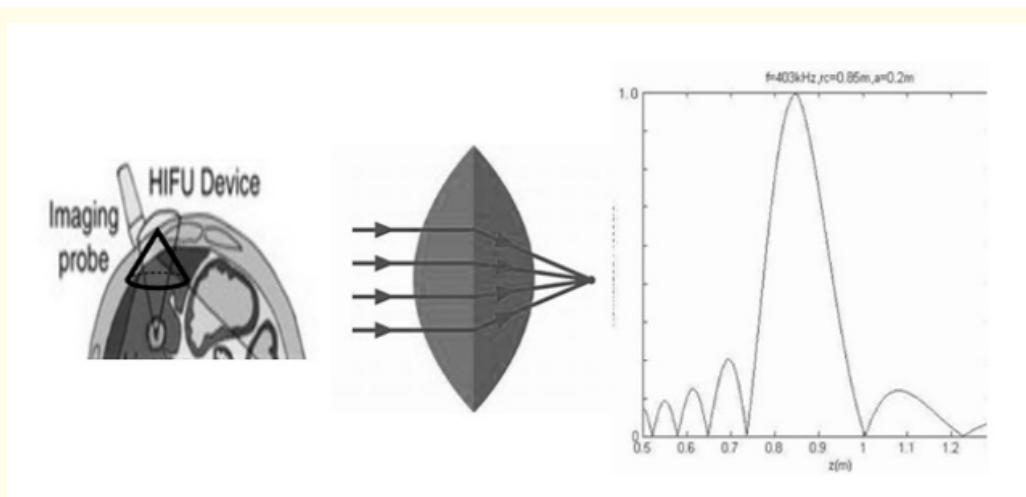


Figure 2: Focussing mechanism of focal ultrasound with intensity pattern [3-7].

### Theoretical thermal modelling of temperature profile in tumour under ultrasound

When an ultrasonic wave propagates in a soft tissue medium, it gets attenuated due to viscosity of the medium, and the absorbed ultrasonic energy is transformed into heat. The amplitude attenuation coefficient ( $\alpha$ ) depends on the type of tissue temperature and ultrasonic frequency. The thermal mathematical models are developed to understand actual exposure conditions [3-7,12-14].

A theoretical thermal model [20] has been developed in the present study by using linear bio-heat transfer equation.

The linear bio-heat transfer equation is the accepted model. The tissues are considered as a homogeneous absorptive medium, the acoustic characteristics like impedance of soft tissues is equivalent to that of water. The absorption gives relaxation to processes and therefore at every point, in a region traversed by ultrasound, heat is produced by absorption at a time averaged per unit volume. This is proportional to the square of these local pressure amplitudes. The pressure amplitude distribution in the near field of focussed transducer is highly non uniform, and thus the distribution of heat source function is non uniform.

Thus, the temperature elevation generated by absorption of ultrasound is found [14] from the linear bio heat transfer equation:

$$C_v = k \nabla^2 T - C_v \delta T / \tau + q_v \quad (1)$$

where  $\delta T$  is the temperature rise above the ambient level,  $\dot{T}$  is rate of temperature rise,  $K$  the thermal conductivity coefficient and  $C_v$  the heat capacity per unit volume for the medium,  $q_v$  the heat source function, which is defined as the rate of heat production per unit volume and  $\tau$  the time constant for perfusion as:

$$\tau = C_v L^2 / K \quad (2)$$

where  $L$  is the perfusion length.

The intensity is equal to  $\frac{1}{2} P_0^2 / \rho_0 c$  where  $p_0$  is the pressure amplitude. When the linear acoustic wave propagates, the attenuation is due to absorption arising from volume relaxation. The heat source function  $q_v$  is equal to  $2\alpha I$ . The heat state temperature elevation  $\delta T$  at any point in the system can be found by solving this differential equation, by using certain approximations.

For a tissue sample homogeneous in nature, having with spherical medium of diameter  $d_s$  and thermal conductivity  $K$ , the temperature elevation  $\delta T$  at the centre of the sample is given by:

$$\delta T = 8\alpha I(z) t / \rho c_m \int_0^u \text{erfc} u \, du \quad (3)$$

where  $\alpha$  is the absorption coefficient in  $N_p/cm$ .  $c_m$  is the specific heat per unit mass,  $\rho$  the density,  $I(z)$  the intensity in  $Watts/cm^2$  and  $\text{erfc}$  is the complementary error function.  $A = d_s / (4kt)^{1/2}$  and thermal diffusivity  $k = K / \rho c_m$ . By considering the complementary error function in Equation 3, as 2, 1, 0,  $u$  has values from  $-\infty, 0, \infty$  respectively. When time  $t$  is small, Equation 3, becomes:

$$\delta T_1 = 2\alpha I(z) t / \rho c_m \quad (4)$$

According to equation 4 in initial phase, where the time  $t$  is too short for appreciable heat conduction to occur, the temperature elevation  $\delta T$  is linearly proportional to time  $t$ . After a long time equation 4, simplifies to

$$\delta T_{III} = I(z) \alpha d_s^2 / 4K \quad (5)$$

The temperature elevation is independent of time during the last phase.

### Material and Methods

The materials used in the present work and the techniques applied are as follows.

## Design and development

### Design of focal ultrasound therapy system

The main features of the focal ultrasound system are as follows:

- The system is non-invasive
- It can penetrate effectively to mid-body plane at frequency with tissue wavelength of a few mm.
- The transducer can be focused within the tumor or treatment volume.
- This system is the best for local treatment of deep seated tumors with hyperthermia.
- This technique is good for deep, good large and/or highly vascular tumors.
- This can control easily coagulation of graded volumes (cytoreduction) with focused ultrasound.

Local hyperthermia planning is made by adopting the similar controls as in X-Ray machine. Geometrical treatment planning is made by following thermal treatment plan, transducer probe insertion at treatment volume location, treatment execution by exciting the transducer from RF generator and measurement of temperature by using thermocouples, inserted in the skull [3-8,16-18].

### Design of high intensity focussed ultrasound system (HIFU) system

High intensity focused ultrasound or HIFU is a treatment technique [3-7,11,16-18]. The machine gives off high frequency sound waves, which deliver a strong beam to a specific part of a cancer or tumour. Some cells die when this high intensity ultrasound beam is focused directly onto them. The main advantage of this technique is that it only uses sound waves to kill the cancer cells, it has no side effects. In general, high intensity focused ultrasound can easily be used for the treatment of cancer problems related to prostate, kidney, pancreatic, liver or bladder and brain abnormality.

Generally, PZT-4 (lead-zirconium-titanate) material has been used to develop this ultrasonic transducer having frequency of 1 MHz, in the present case (Figure 3). Acoustic lens [15] is shown at the front of transducer dis element having a rubber balloon filled with saline solution for better impedance matching with the skull or the tissue [6-8]. Figure 3 gives the hardware components of the measurement set up of HIFU system including RF excitation generator, RF amplifies, temperature probe and transducer with focal lens assembly [3-8,16-18], for tumour destruction [24,25].

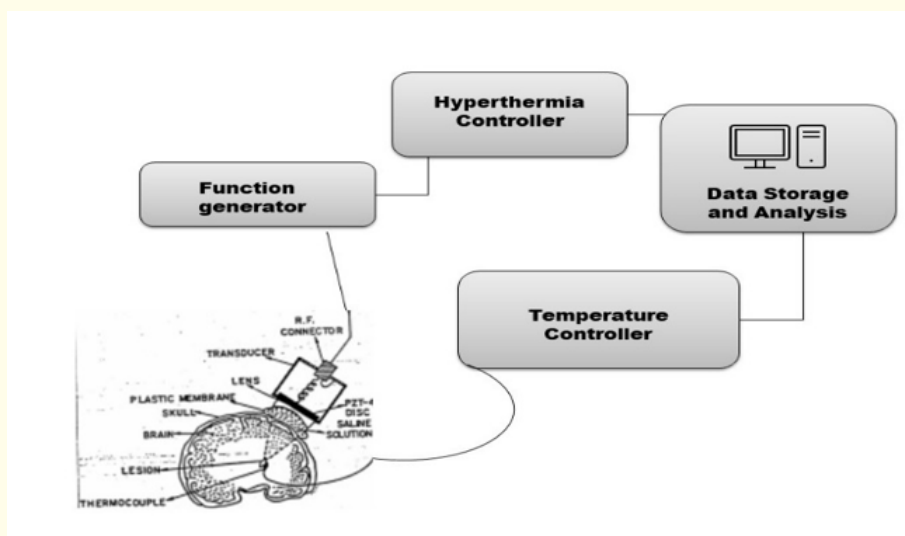
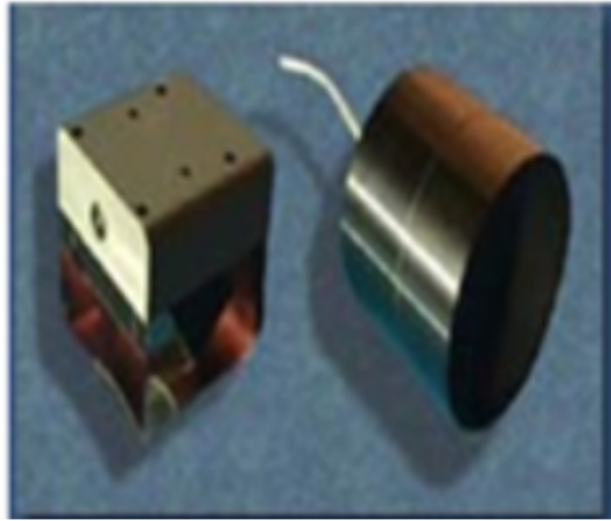


Figure 3: HIFU measurement set up for tumour treatment [6-8].



### Design and fabrication of piezo-composite based ultrasonic transducer

Further, a new composite material has been developed to fabricate a high power therapeutic transducer to give ultrasonic power up to 100 Watt, by having integral focusing lens. This ultrasound hyperthermia transducer has piezo-composite disc, membrane couplant and thermos-couple probe for thermal profile monitoring [7-9]. Figure 4 shows the photograph of piezo-composite based high power transducer.



*Figure 4: Piezo-composite based high power therapeutic transducer [6-8].*

## Results and Discussion

### Effective ultrasonic intensity of HIUF and transducer performance optimisation

The intensity pattern of the HIFU transducer is described in section physical principle of HIFU above. Several mechanical and cavitation factors are responsible for treatment of the tumour with ultrasound. The thermal elevation and intensity in the tumour under focal ultrasound are important parameters. The treatment with other modalities says chemotherapy becomes faster [3-8].

Thus, the local heating by focused ultrasound is found to be useful in curing of the tumours.as the complex tumour. The therapy depends on the thermal dose or several complex reactions like denaturation of proteins, deactivation of enzymes, low pH and inadequate microcirculation.

### Penetration depth and focal lobe area

Focal lobe is the area/volume of focussing at the tumour portion to be destroyed/treated, part by part, in different sittings of the patient at different intervals. Point focussing does not work effectively, for focal ultrasound. Dosage rate is set for a particular time duration, so that there is no itching, pain or discomfort to the patient. Optimum safety limits have been obtained by making different measurements under different conditions [3-7].



**Location detection and dosage rate**

The exact location of a tumour deep seated in the brain has been found by using conventional diagnostic imaging techniques like MRI (Magnetic Radiological Imaging) and ultrasound, etc. Dosage rate has been calculated by using the theory given in section physical principle of HIFU above.

**Frequency optimisation**

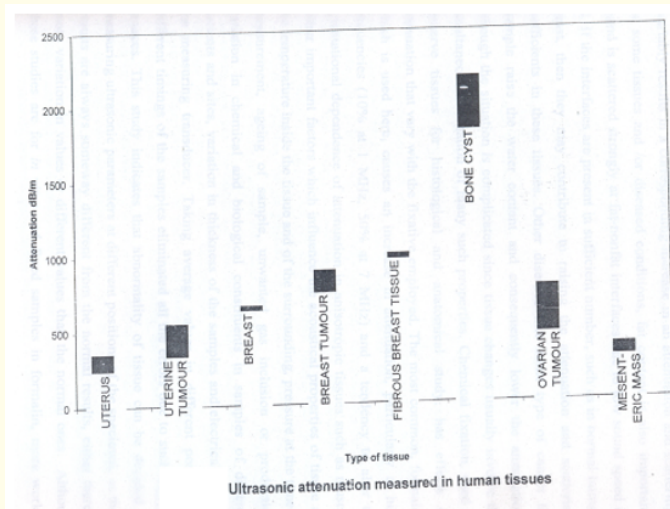
The optimum frequency of the HIFU transducer has been measured as 1.0 MHz in the present HIFU design, to accommodate the tumour volume under treatment. In some cases, the frequency could vary from 0.80 MHz to 1.20 MHz. A particular point is selected to get maximum intensity for more effective treatment [6-7].

**Ultrasonic parameters of tumour**

Ultrasonic propagation study has been carried out by using a double-probe-through- transmission technique. Table 2 gives the average ultrasonic values of acoustic velocity and attenuation at 3 MHz in different types of *in vitro* tumours, like giant cell, lymphoma, chonbro sarcoma and osteogenic sarcoma [19,21-25]. The comparison of results has been obtained based on such measurements (Figure 5), for various soft and hard human biological tissues, showing that harder is the tissue, higher is the velocity and vice-versa. The study helps in understanding the biochemical, biological and pathological characteristics of the tissues.

Tumor Type	Average	Attenuation
Giant Cell	2106 ± 1.49%	26.06
lymphoma	2304 ± 1.04	29.00
Chonbro sarcoma	2677 ± 0.44	74.40
Osteogenic Sarcoma	3586 ± 0.74	73.08

**Table 2:** Ultrasonic measurement values in tumours at 3 MHz [19,21-26].



**Figure 5:** Ultrasonic attenuation in human tissues [21-26].

### Thermal profile mapping

The thermal profile under the focal beam has been studied and plotted at different locations of the brain by using temperature sensors. In this case, thermocouples. A non-contact double probe through transmission technique has also been developed and used to monitor thermal profile inside and outside the tumours. The thermal pattern is correlated with the intensity of ultrasound [6-8,12,16-18]. Figure 6 shows the photograph of measurement set up for thermal profile evaluation of for *in vitro* tumour under focussed ultrasound with temperature sensors at different locations. The *in vitro* tumour samples were collected from local hospitals like AIIMS (All India Institute of Medical Sciences) and Safdarjung Hospital in New Delhi, India.

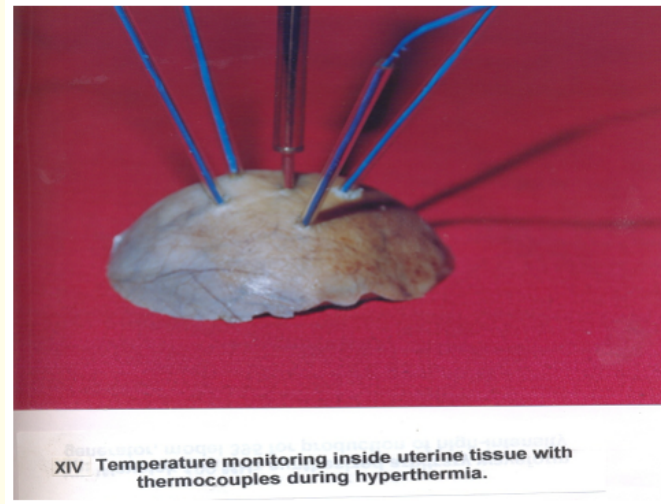


Figure 6: Thermal profile study in the tumour, *in vitro*, by using thermocouple sensors for HIFU system.

### Thermal modelling

A number of simulations have been performed [12-14] at different intensities ranging from 1 W/cm<sup>2</sup> to 12 W/cm<sup>2</sup> at 1 MHz frequency. Figure 7 depicts the increase in tissues temperature with time at different intensities. Initially, the tissue temperature increases rapidly, and then slowly with the increased time. The temperature elevation becomes independent of exposure time and depends upon ultrasonic intensity. At the end of 400 seconds of exposure, an elevation of 0.12°C has been achieved at 1 W/cm<sup>2</sup> whereas at 12 W/cm<sup>2</sup> an elevation of 2.46°C has been achieved. Tumour cells are more sensitive to heat in the temperature range 42 - 44°C than the normal tissues. The temperature range used here is between 41-47°C called Hyperthermia.

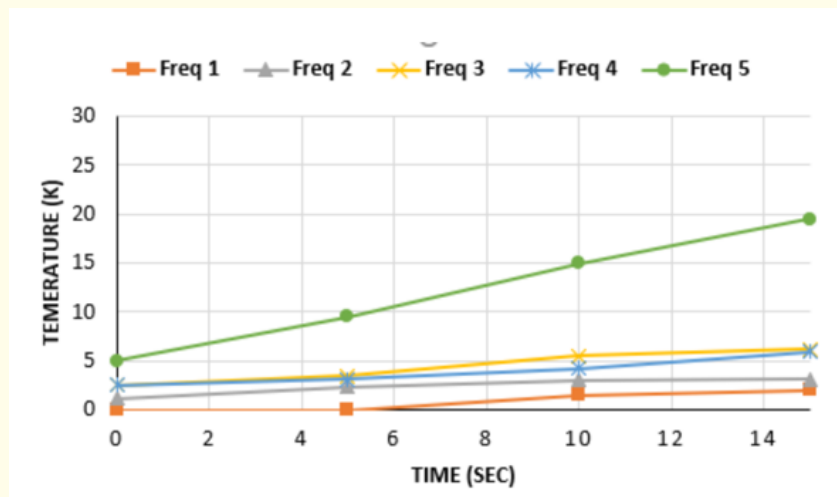


Figure 7: Tumour ablation with HIFU for particular dosage duration [6-8,12,13,16-18].

The tissue is considered as a homogenous absorptive medium. The assumed acoustic parameters [14] of the tissue are approximately equal to water, as given below (Table 3).

Parameter	Value
Density of tissue ( $\rho$ )	1032 Kg/m <sup>3</sup>
Time (t)	Variable s
Temperature (T)	Calculated in °C and K
Specific heat of blood ( $c_b$ )	3370 J/Kg°C
Specific heat of tissues ( $c_m$ )	3370 J/Kg°C
Thermal conductivity of (K) tissue	0.5 W/m°C
Absorption coefficient ( $\alpha$ )	03-.09 N <sub>p</sub> /c

**Table 3:** Tissue parameters in thermal modelling.

The ultrasonic exposure to the tissues depends upon the transducer geometry, frequency of the wave, velocity of ultrasonic beam, attenuation in intervening tissues, acoustic reflection and refraction. In the exposed tissue areas, energy is partly absorbed and converted into heat. Temperature elevation depends on the heat conduction, cooling effect due to blood flowing out of the exposed tissue volume into surrounding regions, and additional conduction and perfusion occurring in the unexposed regions conveying heat to distant parts leading to steady state, as thermal losses out of the body balance the effect of absorbed energy.

It has been observed clinically that the thermal dose kills the cells at the peak temperature, resulting into cell death. The treatment time may span from few minutes to few hours. The increase in tissue temperature with increase in acoustic intensity has also studied. Thus, the present simulation model for temperature elevation using focused ultrasound is useful for tumour ablation [12,13].

The magnitude of temperature elevation depends on the acoustic frequency, intensity, duration of irradiation, and the thermal characteristics of the tissue medium. This system can be designed by simulating the various parameters with the aim to focus all the acoustic energy into a small target area, for an effective treatment.

**Clinical effectiveness**

The ultrasound induced temperature elevation and cavitation effects are responsible for thermal modelling [12-14] of ultrasonically induced hyperthermia developed for a focused ultrasonic system to monitor temperature rise in the particular area and volume of the target tissue deep inside the living body [10,11,16-18,21-25]. The induced hyperthermia depends on the type of biological tissue, acoustic intensity and exposure duration. Treatment time is also important.

**Application in U-health care**

HIFU system can easily be used for ubiquitous health care application, to monitor and control the condition of say, old age patients, living in remote isolated areas. WSN (Wireless Sensor Networking) is used, as shown in figure 8 and 9, for monitoring the health condition of the patient. Electrical output signal of the HIFU system has been transmitted to the main city hospital from the patient to enable the doctor to study the diagnostic results and send back the advice for initial treatment at site. WSN based and cloud-based HIFU systems have been developed, which become very useful systems for U-health care [27-33] very effectively.

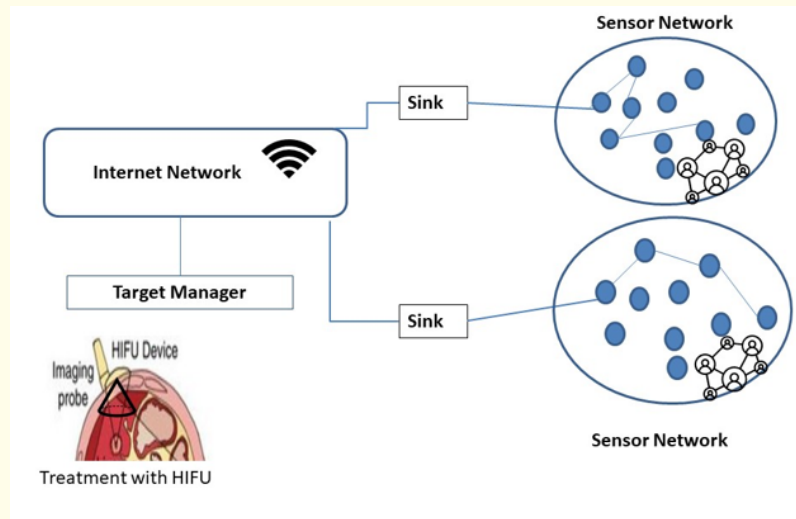


Figure 8: WSN in HIFU system [27].

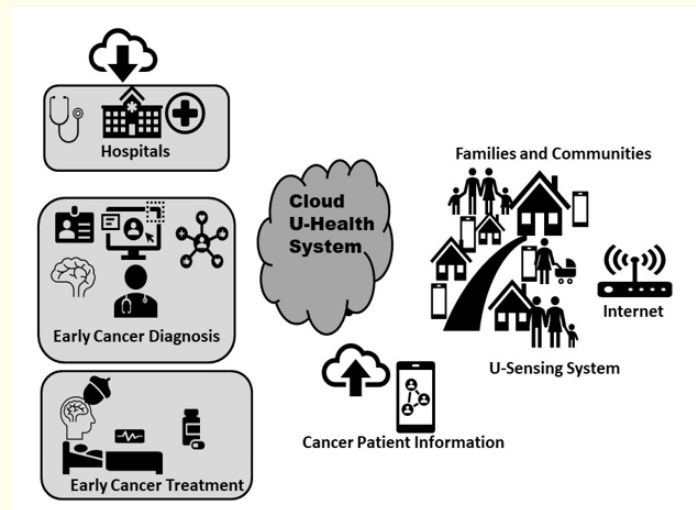


Figure 9: Cloud based sensing for HIFU system.

The use of biotelemetry is also a good solution for remote health care [34]. The development of biotelemetry has been made for improving healthcare, particularly for the rural and remote population. However, the biotelemetry system, when implemented with U-sensor technology has been found to give better health care in an effective manner.

## Conclusion

Development of methodology for a high-intensity-focal-ultrasound (HIFU) system has been described for effective therapeutic treatment of deep-seated brain tumours. Biological aspects and physical propagation of ultrasound in the tissues have been discussed in

brief. Thermal profile measurements have been made under focal ultrasound beam which become an index of dosage level for a particular treatment. A comparison of different therapeutic techniques with ultrasound have been presented. Practical application of HIFU system for U-health care, by using WSN (Wireless Sensor Networking), and cloud based approach have been studied and discussed.

### Bibliography

1. Bignold Leon. "Principles of Tumors". Elsevier Publisher (2015)
2. Pardee B Stein GaryS. "The Biology and Treatment of Cancer". Wiley Inc (2008)
3. Fry FJ. "Precision high intensity focusing ultrasonic machines for surgery". *American Journal of Physical Medicine* 37.3 (1958): 152-156.
4. Lele PP. "Production of deep focal lesions by focused ultrasound--current status". *Ultrasonics* 5 (1967): 105-112.
5. Ernst Martin and Beat Werner. "Focused ultrasound surgery of the brain". *Current Radiology Reports* 1 (2013): 126-135.
6. Singh VR. "Ultrasound hyperthermia control system for deep-seated tumours: *Ex vivo* study of excised tumours, modeling of thermal profile and future nanoengineering aspects". *IRBM (Innovation and Research in BioMedical Engineering)* 29.5 (2008): 326-336.
7. Singh VR. "Computer controlled ultrasonic hyperthermia system". *Journal of Scientific and Industrial Research* 58 (1999): 112-117.
8. Singh VR., *et al.* "Transient cavitation and associated mechanisms of stone disintegration". *ITBM (Innovation and Technology in Biology and Medicine)* 21.1 (2000): 14-22.
9. Singh VR. "Smart sensors: physics, technology and applications". *Indian Journal of Pure and Applied Physics* 43.1 (1995): 7-16.
10. Hsiao YH., *et al.* "Clinical application of high-intensity focused ultrasound in cancer therapy". *Journal of Cancer* 7.3 (2016): 225-231.
11. Shehata IAE., *et al.* "High intensity focused ultrasound: The fundamentals, clinical applications and research trends". *Diagnostic and Interventional Imaging* 99.6 (2018): 349-359.
12. Nyborg WL and Steele RB. "Temperature elevation in a beam of ultrasound". *Ultrasound in Medicine and Biology* 9.6 (1983): 611-620.
13. Wu J and G Du. "Temperature elevation generated by a focussed Gaussian beam of ultrasound". *Ultrasound in Medicine and Biology* 16.5 (1990): 489-498.
14. 'O' Brien KT and Mekkaoci AM. "Numerical simulation of the thermal fields occurring in the treatment of malignant tumours by local hyperthermia". *Journal of Biomechanical Engineering* 115.3 (1993): 247-253.
15. Singh VR and Malik R. "Development of acoustic lens for biomedical applications". *Biomedical Engineering: Applications, Basis and Communications* 7 (1995): 598-602.
16. Diederich CJ and Stauffer PR. "An assessment of the deep heating capabilities of a rotating multi transducer ultrasound hyperthermia system". *IEEE Ultrasonic Symposium* 2 (1992): 1255-1259.
17. Gerweck LE. "Hyperthermia in cancer therapy: The biological basis and unresolved questions". *Cancer Research* 45.8 (1985): 3408-3414.
18. Hill CR and Tenhaar GR. "High intensity focused ultrasound - potential for cancer treatment". *The British Journal of Radiology* 68.816 (1995): 1296-1303.
19. Duck FA. "Physical properties of tissues". Academic Press limited London, England (1990).

20. Sassaroli E., *et al.* "Modelling focused ultrasound exposure for the optimal control of thermal dose distribution". *The Scientific World Journal* (2012): 252741.
21. Scott SJ, *et al.* "Interstitial ultrasound ablation of vertebral and paraspinal tumours: Parametric and patient-specific simulations". *International Journal of Hyperthermia* 30.4 (2014): 228-244.
22. Malik R and Singh VR. "Tumour therapy modelling under focussed ultrasound". Proceeding International Conference on Instrumentation, Bangalore, India. Proceedings of ICI-1996. Special issue of the Journal of Instrument Society of India (1996).
23. Bhatia KG and Singh VR. "Ultrasonic propagation in breast tissue with ductal carcinoma". *Indian Journal of Pure and Applied Physics* 40.7 (2003): 515-519.
24. Gerweck LE. "Hyperthermia in cancer therapy: The biological basis and unresolved questions". *Cancer Research* 45.8 (1985): 3408-3414.
25. Roemer RB. "Engineering aspects of hyperthermia therapy". *Annual Review of Biomedical Engineering* 1 (1999): 347-376.
26. Bhatia KG and Singh VR. "Ultrasonic characteristics of leiomyoma, *in vitro*". *Ultrasound in Medicine and Biology* 27.7 (2001): 983-987.
27. Singh VR and Singh Kanika. "Wireless sensor networks for biomedical applications in cancer hyperthermia". Proceeding IEEE International Conference on Engineering in Medicine and Biology (EMBC 2008), Vancouver, Canada (2008): 5160-5163.
28. Singh VR. "Advanced diagnostic imaging sensors and therapeutic treatment devices for U-health care". Proceedings National Conference on Medical Instrumentation, Biomaterials and Signal Processing (NCMBS-20), Department of Biomedical Engineering, Deenbandhu Chhotu Ram University of Sci and Tech., Murthal, Sonapat, Haryana, India (2020).
29. Singh VR. "Advanced ultrasonic and acoustic sensors and instrumentation systems for U-health care applications". Proceeding Annual Physics Symposium (APS-2020) - International Year of Sound (IYS 2020) Celebration, Department of Physics and Centre for Research, St Teresa's College (Mahatma Gandhi University), Ernakulam, Kerala, India (2020).
30. Singh VR. "Nano-cancer technology: New diagnostic and therapeutic devices". Proceeding ICIP, University of Dhaka, Bangladesh (2017).
31. Singh VR. "Advanced nano-sensors, bio-devices and bio-medical systems for U-health care". Proceeding 4<sup>th</sup> IEEE Middle East Conference on Biomedical Engineering (MECBME 2018), Tunis, Tunisia (2018).
32. Singh VR. "Advanced nano-diagnostic imaging sensors and therapeutic devices for U-health care". Proc IEEE UBISym Symposium on Healthcare Engineering, Universidade da Beira Interior (UBI), IEEE-SB, Covilha, Portugal (2018).
33. Singh VR. "Advanced nano-ultrasonic diagnostic sensors and therapeutic devices for health care applications". Proceeding 3<sup>rd</sup> IEEE South African Biomedical Engineering Conference (SABEC 2018), Spier Wine Estate, University of Stellenbosch, Stellenbosch, South Africa (2018).
34. Singh Kanika. "Biotelemetry: could technological developments assist healthcare in rural India". *Rural and Remote Health* 5.2 (2005): 230-234.

**Volume 3 Issue 7 July 2020**

**© All rights reserved by VR Singh and Kanika Singh.**