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Original Article

A Simulation Study on the Investigation of Thermal Effects Associated with Acoustic Radiation Force Shear Wave Interference Patterns Generation in the Liver Tissue

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A B S T R A C T

Purpose: The mechanical map of liver tissue like stiffness is as important as its anatomical image for clinical purposes like staging the liver fibrosis. Acoustic radiation force-based shear waves interference patterns elastography is an interesting independent imaging rate technique which can generate shear waves in the liver tissue in any desired depth by means of the high intensity focused, long duration push beams. Because of wave attenuation and absorption process the sound wave energy is dissipated in the tissue and due to energy conservation law is turned into heat thus like any other ultrasound imaging modality, shear waves interference patterns elastography carries the risk of tissue heating and thermal ablation specially at the focal spot. Therefore, particular attention must be paid to the thermal safety assessment to shear waves interference patterns elastography. The aim of the present simulation study is the thermal safety evaluation in the liver tissue.

Materials and Methods: The liver tissue has been simulated in the presence of its adjacent tissues like skin, muscle, ribs and intercostal muscles in 3 dimensions during shear waves interference patterns elastography. With 4 seconds exposure time and 2 MPa focal pressure.

Results: Temperature at the focal point increases from normal body temperature (37˚C) to 47˚C.

Conclusion: Thermal effects appraisal, indicates that the general tissue heating stays within the safe region.

Keywords:

Thermal Effect;

Elastography;

Liver Tissue;

Acoustic Radiation Force;

Shear Wave.

1. Introduction

Chronic liver disease like fibrosis is an essential worldwide problem. Liver tissue has the smooth surface and soft structure. Some diseases like different types of hepatitis cause liver inflammation. In response to the inflammation, the liver tissue tries to regenerate itself and the dead cells have been replaced with collagen and the tissue becomes stiffer which is called liver fibrosis. Liver fibrosis results in cirrhosis, liver defect and finally liver cancer[1].

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Elastography is a noninvasive method for assessing the liver stiffness which is proportional to the different degrees of liver fibrosis so that the liver with upper degrees of fibrosis is much stiffer than normal liver[2].

In shear wave elasticity imaging, a push signal is deeply generated by acoustic radiation force. Thecreated disturbance by the Acoustic Radiation Force (ARF) travels transversely through the tissue as a shear wave. The speed of shear wave is proportional to the underlying tissue stiffness.

Shear wave interference patterns elastography, which does not need ultrafast imaging for monitoring the shear wave movement, is an elastography technique that uses ARF as a minimally invasive excitation for liver deformation.

Nowadays, in addition to ultrasonic imaging [3], therapy [4], surgery [5, 6] and drug delivery [7], ultrasound waves can be used for shear wave generation in soft tissues [8] like liver.

While an acoustic wave propagates through a lossy medium like a soft tissue, arising from absorption and reflection of acoustic waves, ultrasonic energy turns into thermal energy. This thermal energy results in tissue heating. Therefore, a temperature distribution due to the clinical usage of ARF as the source of excitation is crucial. Generated heat and temperature rise must be in a safe region.

Wu *et al.* (1990) and Lin *et al*. (2000) computed the temperature increasing due to using a High Intensity Focused Ultrasound transducer (HIFU). Although they have considered the perfusion, their model had two layers: soft tissue and bone [9, 10].

Palmeri *et al.* (2004) investigated the temperature rise in the tissue and its relation with elasticity value under the different acoustic radiation force impulse excitation beams and focal point configurations [11].

Sheu *et al.* (2011) predicted the temperature of tumor in the liver during high intensity focused ultrasound thermal ablation, but they only considered the liver tissue without its adjacent tissues [12].

Hosseinzadeh *et al.* (2011) published a paper in which the effect of different parameters on the heated necrosis element in a cubic was investigated [13].

Tabatu *et al.* (2012) have investigated the temperature rise resulted from ARF push wave sequence at the bone-soft tissue interface. They have concerned about the time interval of excitation train from avoiding bone heating due to higher absorption [14].

Liu *et al.* (2014) have analyzed the effect of inter frame off duration in the generated heat to be in the safe region. They have discussed that the short cooling time between acoustic radiation force impulse may be dangerous at the bone tissue [15].

Nitta *et al.* (2014) have evaluated the temperature rise into a layer with and without bone in the finite element model due to using acoustic radiation force impulse imaging [16].

Hudson *et al.* (2015) developed a simulator for predicting the temperature elevation but their simulation and experiments were in and around the bone during HIFU therapy [17].

Treeby *et al.* (2015) have investigated the effect of changing the incidence angles and different degrees of bone complexity for bone sonication in 2 dimensional space in two layers consisting of bone and elastic or fluid medium in a simulation study [18].

This simulation study demonstrates the combination of acoustic and thermal simulations in K-WAVE MATLAB toolbox [19] to calculate the temperature map in the liver tissue for one of two excitation sources. Because the two sources of excitation are far enough apart from each other, we consider the thermal effects of one source.

Since it is impossible for the user to know the temperature elevation in the tissue, a simulation study has been conducted on the generated heat and safety issues using acoustic radiation force for shear waves interference patterns generation.

As acoustic waves generated from a focused transducer travel through different tissues to reach the targeted one for its deformation, the acoustic energy has been turned into heat energy due to the absorption phenomenon. Safe conditions for the liver and its surrounding tissues in the excitation duration in the case of thermal effects must be guaranteed.

In this manuscript, the liver tissue with its neighboring tissues such as skin, muscle, ribs and intercostal muscles have been simulated in 3 dimensions. The thermal effects due to using acoustic radiation force for shear wave interference patterns in the liver tissue has been investigated.

Obtained results in comparison to related references have shown that shear wave interference patterns elastography is safe for liver tissue. We continue with discussion and future works.

2. Materials and Methods

Shear wave interference patterns elastography consists of two push transducers which are responsible for liver excitation and a conventional imaging probe in order to record shear wave movement. Imaging probe is placed between excitation focused transducers.

We are going to model heat diffusion in liver due to shear wave generation using ARF. This process consists of two steps: modeling the push transducer, liver with its adjacent tissues, acquiring ultrasound beam, pressure distribution which reaches the liver through different neighboring tissues, consequently using obtained pressure field to compute thermal model and finally temperature map distribution all over the liver tissue.

Firstly an acoustic simulation has been performed to compute the volume rate of heat deposition due to the generated acoustic pressure by push transducer which here is a focused ultrasound transducer.

The volume rate of heat deposition is then used as an input to a thermal simulation to calculate the temperature map distribution.

2.1. Acoustic Simulation

Because of asymmetric in the structure of the tissue we must do our simulation in 3 dimensions.

The total volume of the simulated model is a solid cubic phantom with 10 cm length in every direction.

The first and second layers are considered as skin (fat) and muscle, so that the layer which is in contact with the transducer is skin. The third layer is the ribs in which the space between them has been filled by muscle. The width of every rib and the space between two neighboring ribs are equal to 0.5 and 1.5 cm respectively. The thickness of every layer is equal to 0.5 cm. The remaining volume is occupied by the liver.

Hence forth, z implies the main propagation axis, representing from the transducer to the focal point, x is the lateral direction and is the interconnected axis between two push transducers, and y is the elevation direction perpendicular to x.

In concave ultrasound transducers, ultrasonic energy is concentrated at the focal point which is in the form of an ellipsoid with the larger diameter in the z direction.

Here the acoustic source is defined to be a focused transducer driven by continuous amplitude-modulated sinusoid wave.

HIFU's parameters which have been used in the simulation are given in Table 1.

Table1. Spherical cap focused transducer specifications

Parameter	Value	unit
HIFU Aperture Diameter	80	mm
Radius of Curvature	50	mm
Excitation Frequency	1	MHz
Modulation Frequency	100	Hz
Surface Acoustic Pressure	0.5	MPa

The definition of the HIFU diameter and radius of curvature has been depicted in Figure 1.

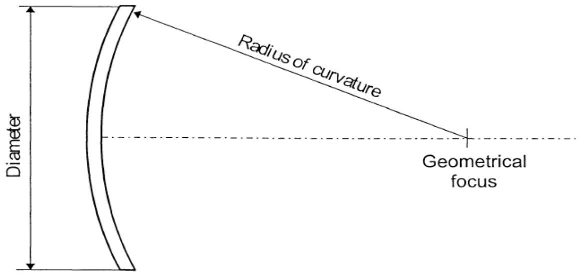

Figure 1. Schematic figure of a spherically curved transducer

A 3- dimensional picture of simulated HIFU in K-WAVE has been shown in Figure 2.

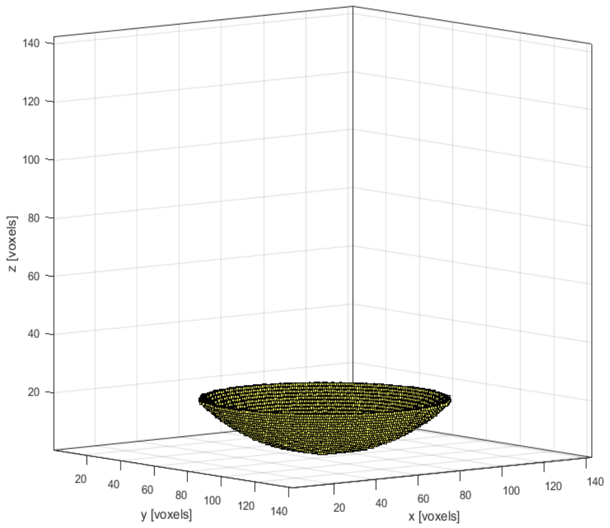

Figure 2. Focused transducer

In the shear wave interference patterns elastography we need the displacement in the range of several micrometers for elasticity estimation.

The minimum value of focal pressure for displacing the liver tissue in the range of the micrometer is equal to 2 MPa.

Because of asymmetric in the structure of tissues, we must do our simulation in 3 dimensions.

As ultrasound waves pass through different biological tissues, their intensity is exponentially attenuated. Attenuation coefficient in accordance with power-law frequency is in the form of:

$$\alpha\,(f)=\alpha_0 f^{\beta}$$

Where α_0 is absorption coefficient (at reference frequency of 1 MHz), and f and β are frequency and material specific parameters typically in the range $1\leq\beta\leq2$, respectively. In this consensus β for the liver is equal to 1.1 [20].

The acoustic properties of different applied tissues have been listed in Table 2.

Table 2. Tissues acoustic parameters have been used in simulation [3, 21]

Tissue	Compressional Wave Speed ($\frac{m}{\text{sec}}$)	Absorption Coefficient ($\frac{dB}{cm.MHz}$)	Density ($\frac{Kg}{m^3}$)
Liver	1590	0.45	1060
Rib	4080	3.54	1900
Fat	950	0.6	1450
Muscle	1590	0.75	1065

We have put a HIFU with 5 cm radius of curvature, 8 cm face diameter and 2 cm height in the center and above of the model.

In the finite difference problems the Courant-Friedrichs-Lewy (CFL) condition is used for getting a stable solution. The CFL condition is expressed as:

$$\text{CFL}=\frac{C_{max}*\Delta t}{\Delta x}<1$$

Where C_{max} is the maximum speed available in the model, Δt and Δx are the temporal and spatial steps [22].

In our simulation the maximum speed is about 4080 $\frac{m}{sec}$, the temporal and spatial steps is equal to 50 ns and 0.7mm. Based on mentioned equation CFL number is equal to 0.3, therefore our obtained answer is stable.

After the acoustic simulation was completed, we ran the simulated model and obtained the Root Mean Square (RMS) pressure in the x-z plane.

2.2. Thermal Simulation

Heat deposition per unit volume arises from acoustic pressure which has been generated by self-focusing ultrasound transducer, acting as an input in the thermal simulation.

The dimensions of the excitation transducer, ultrasonic exposure time, attenuation and specific heat coefficient of tissue affect the tissue thermal distribution.

The relation between temporal averaged acoustic intensity and Root Mean Square (RMS) acoustic pressure due to exciting a HIFU with amplitude modulated signal as input driving is given as below:

$$i=\frac{P_{rms}^2}{4\rho c_l}$$

Where $i(\frac{W}{m^2})$, $P_{rms}(pa)$, $\rho(\frac{Kg}{m^3})$, $c_l(\frac{m}{sec})$ are the averaged acoustic intensity, RMS pressure, mass density and longitudinal wave speed in the intended tissue (here liver).

The volume rate of heat deposition can be approximated using the plane wave relationship [23]:

$$Q=2\alpha i$$

Where $\alpha(\frac{Np}{m.MHz})$ is the attenuation coefficient of the liver tissue and $Q(\frac{W}{m^3})$ is the volumetric heat rate.

Because of its simplicity and considering the perfusion of tissue, the temperature elevation map which has been generated by self-focusing HIFU transducer in liver with adjacent tissues is solved through pennes bioheat transfer equation [24].

In Table 3, thermal properties of the liver tissue have been given.

Table 3. Liver tissue properties related to the diffusion

Parameter	Value	Unit
Density	1060	$\frac{Kg}{m^3}$
Thermal Conductivity	0.52	$\frac{w}{m.^\circ k}$
Specific Heat	3540	$\frac{j}{Kg.^\circ k}$

In this manuscript the perfusion is considered homogeneous in the liver tissue. The blood perfusion can act as a heat sink in the liver tissue.

The initial temperature of the tissue and blood before irradiation is considered as the normal body temperature equal to 37 degrees Celsius.

Thermal properties of blood with their values have been represented in Table 4.

Table 4. Blood properties related to the perfusion

Parameter	Value	Unit
Density	1050	$\frac{Kg}{m^3}$
Specific Heat	3617	$\frac{j}{Kg.^\circ k}$
Perfusion Rate	0.01	$\frac{1}{sec}$
Blood Ambient Temperature	37	°C

3. Results

Time domain simulation of heat diffusion in our heterogeneous medium has been calculated.

Resultant RMS acoustic pressure in the x-z plane has been demonstrated in Figure 3.

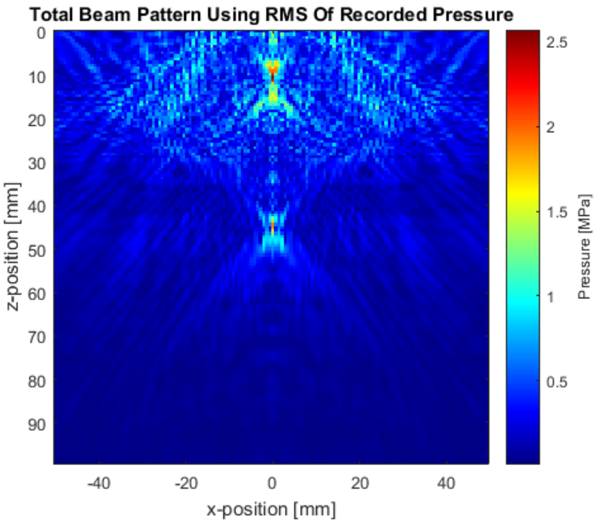

Figure 3. RMS acoustic pressure in the x-z plane in different layers from fat to liver tissue

The simulation results are presented in Figure 4.

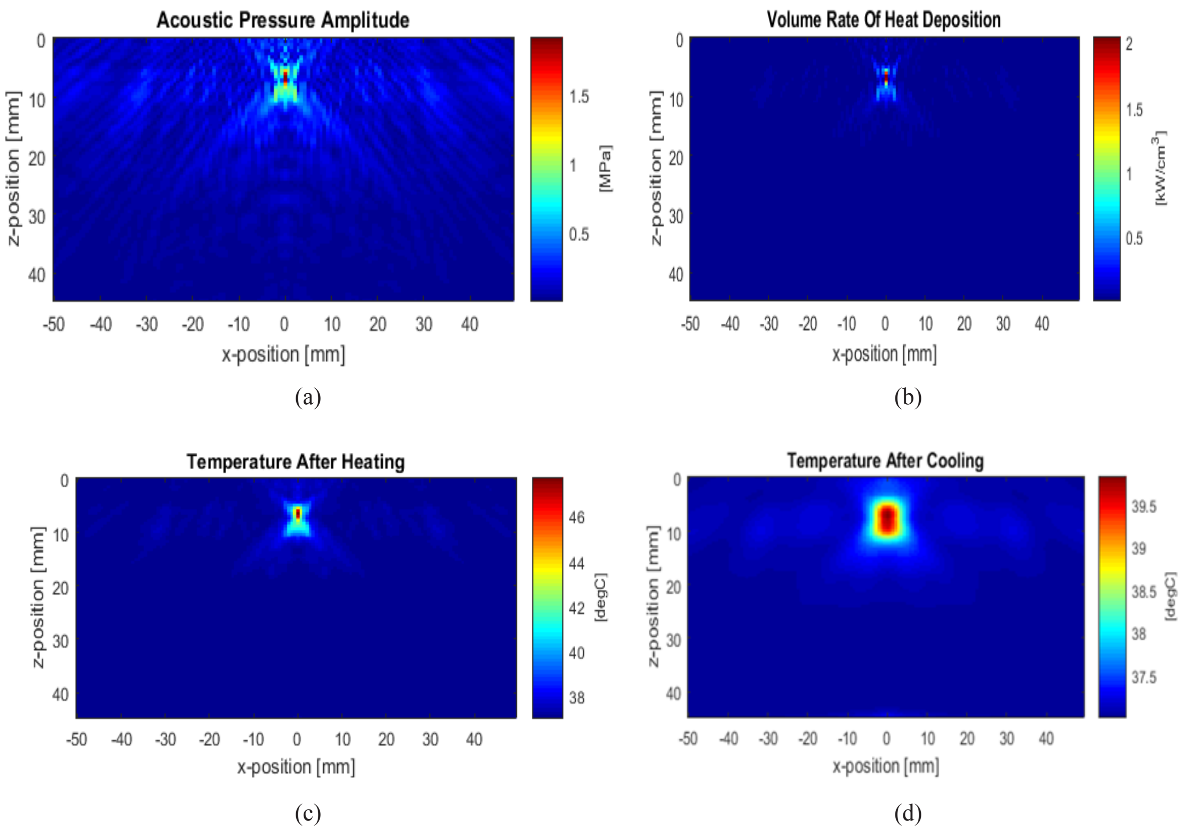

Figure 4. (a) RMS acoustic pressure. (b) Power deposition per unit volume (c) and (d) Temperature distribution field after 4 seconds heating time and then switching the heat source for 20 seconds to allowing tissue to be cool, respectively

Figure 5 which indicates the temperature at focal point in the excitation transducers on and off time is a classic heating and cooling curve.

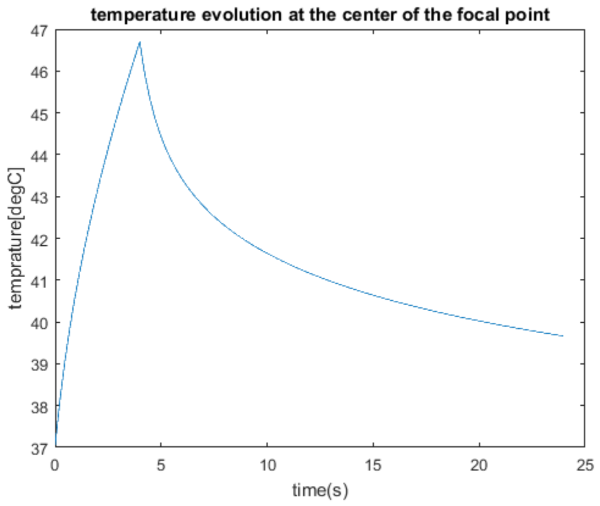

Figure 5. Temperature profile at the focal spot center in liver

4. Discussion

In the ARF-based elasticity imaging, many parameters like exposure time, acoustic intensity, attenuation coefficient of the tissue, continuous or pulsed-wave excitation are the prominent factors in the generated heat in the underlying tissues. It is clear that any increase in the radiation time or intensity rocket up the generated heat. With increasing the absorption coefficient of the tissue, more ultrasonic energy is dissipated in the tissue and is converted to the heat.

The time exposure and acoustic intensity in shear wave interference patterns elastography depends on the distance between two excitation sources and required displacement for the post processing algorithm.

Ultrasonic time exposure must be large enough so that shear waves interfere with each other.

The focal pressure should be in the range that can displace the liver tissue in the domain of many micrometers.

We have used ARF in the form of amplitude modulation or switching for shear wave creation which induces less heat compared to continuous state.

There are two sources of heating in the clinical usage of focused transducer for shear wave induction. The generated heat in the focal point and the created heat in the body surface due to impedance mismatch between the skin and the self-focusing transducer. We can decrease the generated heat in the body surface by using a lubricant gel as a matching layer.

Our post processing algorithm utilizes a Digital Image Correlation (DIC) and tracking with MATLAB which is based on axial cross correlation and is capable of detection displacements in the range of micrometer which can be achieved by the focal pressure equal to 2 MPa, so that our focal intensity is in the upper range of diagnostic ultrasound (acoustic intensity<100$\frac{W}{cm^2}$)[6, 25] .

Maximum temperature generated in the liver is equal to 47 ˚C for 4 seconds radiation, which is in the safe region based on the peak of temperature and applied time [26].

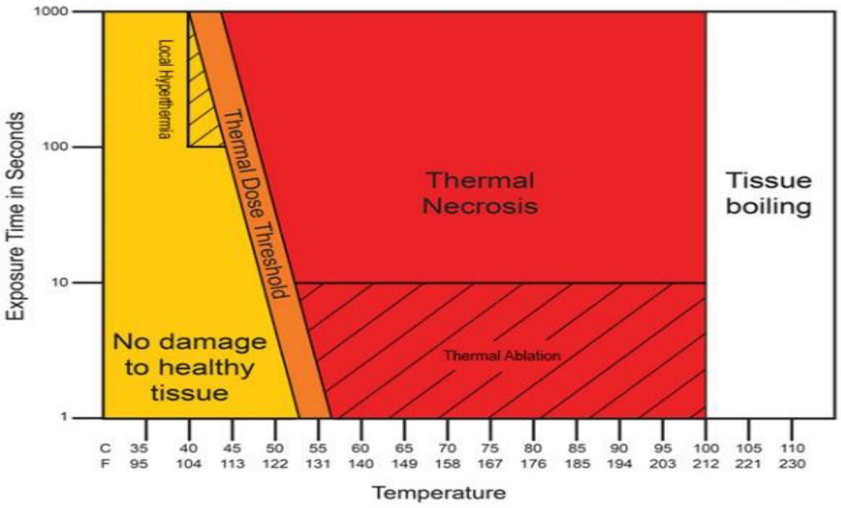

Figure 6. Illustration of the different levels of thermal dose and their biological outcomes

5. Conclusion

A common challenging problem in ARF- based elastography methods is the induced heat and temperature rise in the targeted tissue due to acoustic energy dissipation.

In our simulation study we simulated liver tissue, its adjacent tissues along with focused transducer in 3 dimensions to examine the evolution of temperature distribution in the exposure and resting time.

As results indicate we are in the safe region for the mentioned focal pressure and applied time duration. Based on the guidelines for the safe use of diagnostic ultrasound equipment which has been published by the British medical ultrasound society the maximum exposure time for being in the safe region for 10˚C temperature elevation is about 0.07 min [27].

Produced heat and temperature peak will be lower than mentioned value either by improving our image processing algorithms which are able to detect displacements less than the several micrometers or reducing the excitation time.

Future work must include modeling the different kinds of focusing push transducer and investigating the thermal effects.

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References

1- R. Bataller and D. A. Brenner, “Liver fibrosis,” *Journal of clinical investigation,* vol. 115, no. 2, p. 209, 2005.

2- R. G. Barr *et al.*, “Elastography assessment of liver fibrosis: society of radiologists in ultrasound consensus conference statement,” *Radiology,* vol. 276, no. 3, pp. 845-861, 2015.

3- T. L. Szabo, *Diagnostic ultrasound imaging: inside out.* Academic Press, 2004.

4- D. L. Miller, N. B. Smith, M. R. Bailey, G. J. Czarnota, K. Hynynen, and I. R. S. Makin, “Overview of therapeutic ultrasound applications and safety considerations,” *Journal of Ultrasound in Medicine,* vol. 31, no. 4, pp. 623-634, 2012.

5- G. Ter Haar, “Ultrasound focal beam surgery,” *Ultrasound in medicine & biology,* vol. 21, no. 9, pp. 1089-1100, 1995.

6- G. Ter Haar, “Acoustic surgery,” *Physics Today,* vol. 54, no. 12, pp. 29-34, 2001.

7- K. M. Dittmar *et al.*, “Pulsed high-intensity focused ultrasound enhances systemic administration of naked DNA in squamous cell carcinoma model: initial experience,” *Radiology,* vol. 235, no. 2, pp. 541-546, 2005.

8- K. Nightingale, S. McAleavey, and G. Trahey, “Shear-wave generation using acoustic radiation force: in vivo and ex vivo results,” *Ultrasound in medicine & biology,* vol. 29, no. 12, pp. 1715-1723, 2003.

9- J. Wu and G. Du, “Temperature elevation generated by a focused Gaussian ultrasonic beam at a tissue–bone interface,” *The Journal of the Acoustical Society of America,* vol. 87, no. 6, pp. 2748-2755, 1990.

10- W. L. Lin, C. T. Liauh, Y. Y. Chen, H. C. Liu, and M. J. Shieh, “Theoretical study of temperature elevation at muscle/bone interface during ultrasound hyperthermia,” *Medical physics,* vol. 27, no. 5, pp. 1131-1140, 2000.

11- M. L. Palmeri and K. R. Nightingale, “On the thermal effects associated with radiation force imaging of soft tissue,” *IEEE transactions on ultrasonics, ferroelectrics, and frequency control,* vol. 51, no. 5, pp. 551-565, 2004.

12- T. W. Sheu, M. A. Solovchuk, A. W. Chen, and M. Thiriet, “On an acoustics–thermal–fluid coupling model for the prediction of temperature elevation in liver tumor,” *International Journal of Heat and Mass Transfer,* vol. 54, no. 17, pp. 4117-4126, 2011.

13- M. Hosseinzadeh, M. B. Ayani, and A. E. Fakhar, “Numerical simulation of the 3 dimensional heated necrosis element under HIFU transducer,” in *Biomedical Engineering (ICBME), 2011 18th Iranian Conference of,* 2011, pp. 123-127: IEEE.

14- M. Tabaru, H. Yoshikawa, T. Azuma, R. Asami, and K. Hashiba, “Experimental study on temperature rise of acoustic radiation force elastography,” *Journal of Medical Ultrasonics,* vol. 39, no. 3, pp. 137-146, 2012.

15- Y. Liu, B. A. Herman, J. E. Soneson, and G. R. Harris, “Thermal safety simulations of transient temperature rise during acoustic radiation force-based ultrasound elastography,” *Ultrasound in Medicine and Biology,* vol. 40, no. 5, pp. 1001-1014, 2014.

16- N. Nitta, Y. Ishiguro, H. Sasanuma, N. Taniguchi, and I. Akiyama, “Experimental system for in-situ measurement of temperature rise in animal tissue under exposure to acoustic radiation force impulse,” *Journal of Medical Ultrasonics,* vol. 42, no. 1, pp. 39-46, 2015.

17- T. Hudson, T. Looi, A. Waspe, J. Drake, and S. Pichardo, “Simulating temperature distribution of high-intensity focused ultrasound during bone treatments,” *Journal of Therapeutic Ultrasound,* vol. 3, no. 133, 2015.

18- B. E. Treeby and T. Saratoon, “The contribution of shear wave absorption to ultrasound heating in bones: Coupled elastic and thermal modeling,” in *Ultrasonics Symposium (IUS), 2015 IEEE International*, 2015, pp. 1-4: IEEE.

19- B. E. Treeby, J. Jaros, A. P. Rendell, and B. Cox, “Modeling nonlinear ultrasound propagation in heterogeneous media with power law absorption using ak-space pseudospectral method,” *The Journal of the Acoustical Society of America,* vol. 131, no. 6, pp. 4324-4336, 2012.

20- H. Azhari, “Typical acoustic properties of tissues,” *Basics of Biomedical Ultrasound for Engineers,* pp. 313-314, 2010.

21- H. Azhari, “Appendix A: typical acoustic properties of tissues,” *Basics of Biomedical Ultrasound for Engineers,* pp. 313-314, 2010.

22- R. Courant, K. Friedrichs, and H. Lewy, “Über die partiellen Differenzengleichungen der mathematischen Physik,” *Mathematische annalen,* vol. 100, no. 1, pp. 32-74, 1928.

23- A. Grisey, S. Yon, V. Letort, and P. Lafitte, “Simulation of high-intensity focused ultrasound lesions in presence of boiling,” *Journal of therapeutic ultrasound,* vol. 4, no. 1, p. 11, 2016.

24- S. Ginter, "Numerical simulation of ultrasound-thermotherapy combining nonlinear wave propagation with broadband soft-tissue absorption," Ultrasonics, vol. 37, no. 10, pp. 693-696, 2000.

25- A. Shaw, "Requirement for measurement standards in high intensity focused ultrasound (HIFU) fields," *NPL Rep.,* 2006.

26- Focused ultrasound foundation. (26 january). *accelearating the development ans adoption of focused ulrtrasound*. Available: https://www.fusfoundation.org/

27- G. ter Haar, "The new British Medical Ultrasound Society Guidelines for the safe use of diagnostic ultrasound equipment," *Ultrasound,* vol. 18, no. 2, pp. 50-51, 2010.