Interaction of high intensity focused ultrasound with biological materials

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ABSTRACT

Abstract:

This work is motivated by the possible medical application of focused ultrasound in minimally invasive treatment of a variety of disorders including those associated with soft tissue or disk element disruption in the vicinity of the spine causing impingement on the spinal cord. The hypothesis is that thermal spikes induced by focused ultrasound will cause the tissues to shrink and thus restore stability to the spine and/or reverse the weakness in the structural element. A prototype setup consisting of a transducer in the shape of a spherical cap was used to conduct tests on biological materials. Our preliminary results indicate that the heating efficiency of the ultrasound energy in the focal region depends on the exciting frequency and the geometry of the focal zone depends on the material being tested. We have investigated the influence of the exciting frequency, system geometry and the specimen's material properties on the nature of low-energy focused ultrasonic wavefield using a finite element based program called Pzflex. The preliminary results of our laboratory experiments and the numerical simulations are presented in this paper. At higher excitation energies, cavitation and nonlinear effects need to be included in the simulations. These effects are under current investigation.

Keywords: focused ultrasound, HIFU, PZFlex.

1. INTRODUCTION

In the 1940's, the interaction between high intensity focused ultrasound (HIFU) and biological matters has been reported [1]. In the 1950's, William and Fry developed the first refined ultrasonic system for therapeutic applications. However, the wide spread use of therapeutic ultrasound in clinics has yet to materialize. More research still needed to be done in this area. Previous works involved using experimental methods [2] to collect the mechanical and thermal data in animal tissue, transducers design, development of theoretical methods [3,4,5] to calculate heat distribution along the axis of the model, and numerical methods such as FEM [6-9] to model therapeutic ultrasound.

To understand the effect of therapeutic ultrasound, we have to analyze the changes in tissue by the thermal and/or mechanical effects of ultrasound. Lately, the use of thermal effects in ultrasound represents the majority of the ultrasonic application. They are used for cancer therapy, birthmark removal, and surgeries in the eye and the heart.

Although more and more ultrasound is being used in clinical situations, the theory and supporting technical knowledge is still lacking. For example, in order to treat a narrow target area with minimal damage to the surrounding tissue, it is necessary to predict the path of the high-intensity ultrasound beam from the transducer to the target. It is expensive to solve this problem by experimental methods, since study using living tissue is impractical, and cost prohibitive. Tissues in the body have complex geometry and its acoustic characteristics are not currently well defined, especially for transmission of high amplitude and high frequency waves. As for theoretical solution, the PDEs could not be used to solve for the theoretical solutions for all case.

In this study, PZFlex is used to model the problem and calculate the numerical solution. PZFlex is widely used for designing transducer [6], calculating the mechanical effect of the ultrasound on tissue [7], modeling the therapeutic ultrasound [8] and calculating thermal effect of high-frequency ultrasound [9]. For this reason, PZFlex is a useful tool in understanding the engineering, biological and clinical aspects of therapeutic ultrasound.

In this paper, the mechanical effect and the thermal effect caused by high-frequency ultrasound in different material systems are calculated. The pressure distribution generated by a focused ultrasound is shown graphically. The temperature distribution in 2-D is calculated by using PZFlex. A simple uniformly loaded, focused generator with spherical geometry can not generate the highest temperature in the body contained with different biomaterials. Finally, the direction of future research is discussed.

2. PLANE WAVE TESTING

First, the mechanical effect of plane wave ultrasound passing through a thin solid cell layer between two different fluids is considered. The theoretical solution and the numerical FEM solution of the cell problem are compared to the solution generated by theoretical methods. The reflection by the second interface is extracted in a model that has three different layers of material (two fluid and one solid). In this section, the solid materials are modeled as elastic materials with no damping.

2.1 Cell Problem

The mechanical effect of the ultrasound is calculated for the symmetric (SYMM) and absorbed (ABSR) boundaries condition set by the PZFlex program. The problem of therapeutic ultrasound calculation is complex and generally the infinitely large-scale is considered while ignoring the boundaries. For FEM modeling, some displacement and stress boundary condition should be defined in ABSR boundary to simulate this kind of problems. This kind of boundary will not cause any reflection if material is homogenous. The mechanical effect created by the ultrasound is then calculated and plotted in 2-D gray equivalence graphics to show the pressure distribution. Finally, theoretical solution are compared to the of the FEM result.

(1) Problem description:

The modeling of the problem is shown in Fig1.1. From top to bottom, the total length of the propagating direction (x-direction) is 0.05 mm. The thickness of fluid layer, cell layer and water layer are 0.025 mm, 0.01 mm, and 0.015 mm respectively. The width is 0.01 mm (y-direction). The stress is loaded on the top surface of the fluid with the amplitude normalized to 1. Table1-1 gives the properties of the materials. A 2 GHz frequency ultrasound is used for the calculation.

Table1-1 Properties of materials

Material	Density	c_p	c_s
Fluid	1500	1633	0
Cell	1050	1800	80
Water	1000	1500	0

(2) Theoretical solution:

The pressures at the interface between layers are calculated by using theoretical method. We can solve for the solution by using FFT method to transform the problem from time domain to frequency domain. In the frequency domain, the displacement for the top layer is

$$w_1(\omega) = e^{-ik_1X} + R \cdot e^{ik_1X}, \qquad (1)$$

where $k_i = \dfrac{\omega}{(c_p)_i}$,

$(c_p)_i$ is the velocity of the P-wave in the i^{th} layer material,

ω is the angular frequency,

The positive direction of x-direction is shown in Fig.1.1 and the origin is located at the interface between the fluid and the cell. The displacement in the cell and water are

$$w_2(\omega) = Ae^{-ik_2X} + Be^{ik_2X}, \tag{2}$$

$$w_3(\omega) = Ce^{-ik_3(X-h)}, \tag{3}$$

where h is the thickness of the cell. A, B, R and C are constants.

Substitute the continuous conditions of stresses and displacements at the two interfaces. A system of equations (4) is obtained and the unknown coefficient C can be obtained.

$$\begin{cases} 1+R = A+B \\ -1+R = Z_{21}(-A+B) \\ Ae^{-ik_2h} + Be^{-ik_2h} = C \\ -Ae^{-ik_2h} + Be^{-ik_2h} = -Z_{32}C \end{cases}, \tag{4}$$

where

$$Z_{ij} = \frac{\rho_i (c_p)_i}{\rho_j (c_p)_j}, \tag{5}$$

Solving the system of equations, we get

$$C = \frac{-4e^{ik_2h}}{-e^{2ik_2h} - Z_{32}e^{2ik_2h} - Z_{21}e^{2ik_2h} - Z_{21}Z_{32}e^{2ik_2h} - 1 + Z_{21} + Z_{32} - Z_{32}Z_{21}}, \tag{6}$$

and,

$$\bar{\sigma}_X(\omega) = (\lambda + 2\mu)\frac{\partial w_3}{\partial X} = \rho_3 (c_p)_3^2 \frac{dw_3}{dX} = i\rho_3 (c_p)_3^2 k_3 Ce^{-ik_3(X-h)}, \tag{7}$$

On the interface between Cell and water, where $X = h$, then,

$$\bar{\sigma}_X = -i\omega\rho_3 (c_p)_3 C, \tag{8}$$

The stress near the interface ($X = 0$) between the fluid and the cell is,

$$\bar{\sigma}_0 = \rho_1 (c_p)_1^2 \frac{dw}{dX} = -i\omega\rho_1 (c_p)_1, \tag{9}$$

$$w = e^{-ik_1X}$$

Normalized $\bar{\sigma}_X$ by $\bar{\sigma}_0$, we got,

$$\bar{\sigma} = \frac{\bar{\sigma}_X}{\bar{\sigma}_0} = \frac{\rho_3 (c_p)_3}{\rho_1 (c_p)_1} C, \tag{10}$$

Now, applied the source load on the top of the fluid. The source is described as a function

$$f(t) = 19.0 \times \exp(-1.67 \times 10^9 t) - 19.0 \times \exp(-1.9 \times 10^9 t), \tag{11}$$

Transform it into frequency domain, then get

$$F(\omega) = \frac{4.87 \times 10^9}{\left(i\omega + 1.67 \times 10^9\right)\left(i\omega + 1.92 \times 10^9\right)}, \tag{12}$$

In frequency domain, the stress on the interface between cell and water under the described uniform source $f(t)$ will be

$$\bar{\sigma}_F(\omega) = \bar{\sigma}F(\omega) = \frac{\rho_3 (c_p)_3}{\rho_1 (c_p)_1} CF(\omega), \tag{13}$$

Finally, we get the numerical solution of the stress on the interface between cell and water by using $\sigma(t) = IFFT(\bar{\sigma}_F(\omega))$ as shown in Fig. 1.4.

(3) FEM results:

The 2-D pressure distribution at three given times is shown in Fig. 1.2. The result of pressure history at a single point solved using FEM is shown in Fig1.3 while the theoretical result is shown in Fig. 1.4. The same curve and behavior can be seen when compared to the results. This demonstrates that the PZFlex is a valid simulation method and can solve more complex problem that cannot be (or are not easily) solved by experimental or theoretical methods.

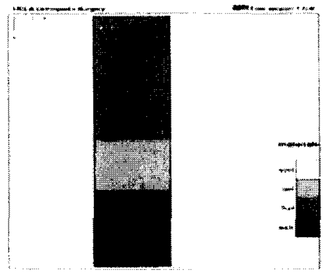


Fig1.1 Model of problem

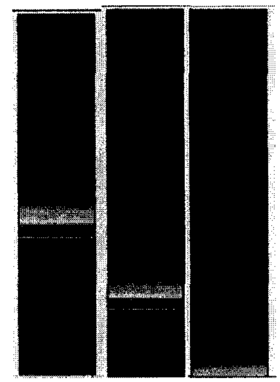
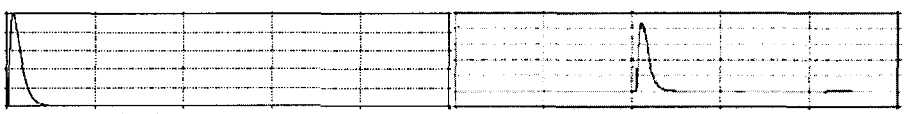


Fig1.2 Pressure distribution



(a) Source pressure (b) Pressure at a given point

Fig1.3 Pressure history calculated by PZFlex

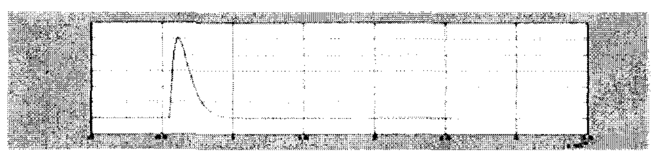


Fig1.4 Theoretical result (pressure)

2.2 Extracting the reflection signal

A new model is considered here. A high frequency pressure is loaded on the left hand side in a three layer materials system shown in Fig1.5.

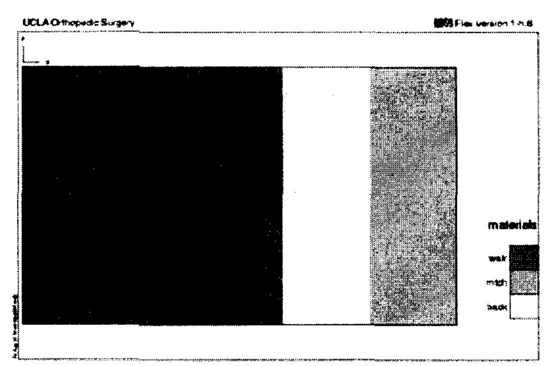


Fig1.5 Model of the problem

The ultrasound has a frequency 500 kHz and amplitude of 1. The reflection by the second interface is considered at the center point in the first layer. Using PZFlex, we can easily get the numerical solution. The properties of individual layers are listed in Table 1-2.

Table1-2 Properties of materials

Material	Density	c_p	c_s
Aluminum	2600	2800	1300
Back Material	1180	2470	1080
Water	1000	1500	0

And after numerical calculation, the pressure distribution in 2-D at two different times are shown in Fig. 1.6.

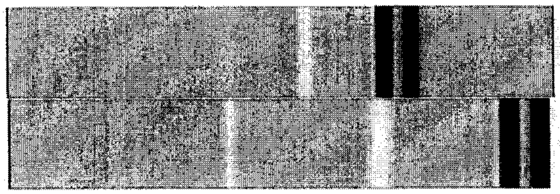


Fig 1.6 Pressure distributions (reflections by first layer and second one)

The time history of the pressure at the center point is shown in Fig1.7.

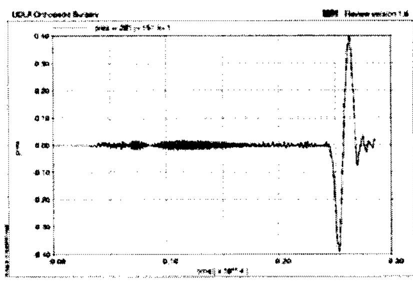


Fig 1.7 Extracted signal reflected by second layer

2. FOCUSED ULTRASOUND

In order to learn more about mechanical effect and thermal effect of the ultrasound, the simplest way is to use a focused ultrasound. From the study of optics, the focused lens can congregate a parallel beam in to a point at higher energy than an uniform beam [7], the mechanical effect of the ultrasound in a single material by a uniform load and a phase delayed load that simulates focused ultrasounds is compared by using PZFlex FEM analysis. In this section, the focused ultrasound is used and the mechanical effect is considered for three cases.

2.1 Focused wave in two layers materials

In the problem shown in Fig. 2.1, the pressure caused by a focused pressure field is calculated. The materials used are water and aluminum. The mechanical properties are listed in Table 2-1. The part above the black line is water and the rest is aluminum. The angle of lens is 60^o and the radius of the lens is 30 mm. The focal point of the lens is marked by the symbol "+" in the figure. The thickness of the water layer is 8 mm. The width and length of model is 60 mm. The frequency used is 500 kHz. The amplitude of the input pressure is normalized to one. All of the boundaries are ABSR boundaries (all the energy passes through the boundary as if this is in an infinity body).

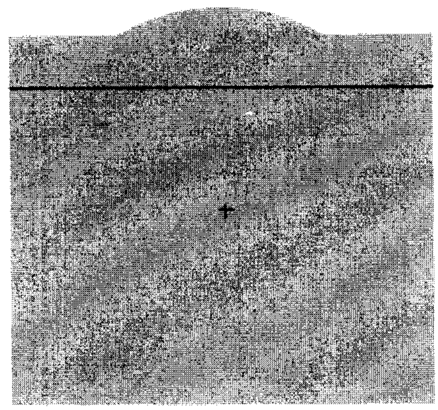
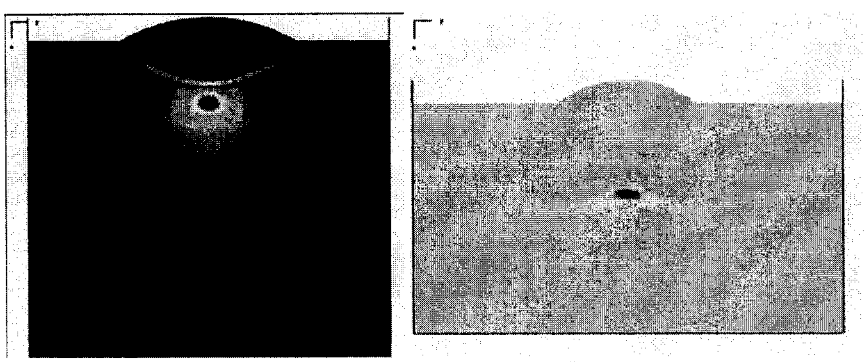


Fig 2.1 The model of problem

Table2-1 Properties of materials

Material	Density	c_p	c_s
Aluminum	2700	6400	3200
Water	1000	1500	0

After the FEM analysis, the results are shown below. The "focal points" for the two cases are shown in Fig 2.2. (a) water and aluminum and (b) water only. The input energy is the same but the pressure in the "focal point" is different for these in the two cases. Focal point pressure in water is higher than that in aluminum. From the animation created by PZFlex, the energy is reflected and refracted by the interface of water and aluminum. This problem will be analyzed further in the future. Phase delay method can be used to improve the result and to get higher pressure in the aluminum.

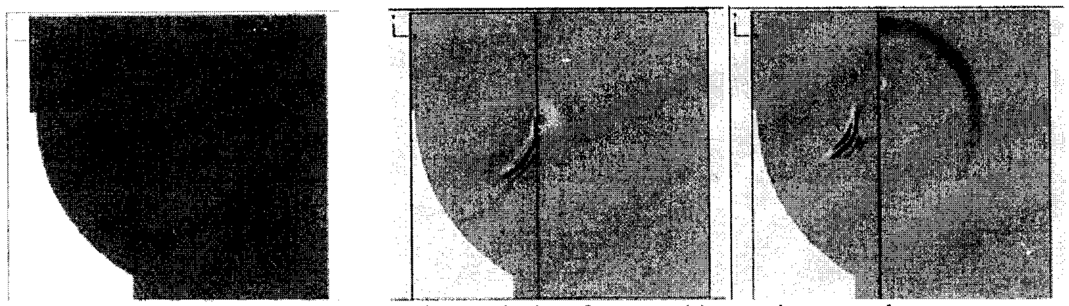


(a) In aluminium (b) In water

Fig 2.2 "focal points"

2.2 Unsymmetric geometry analysis

Consider the case where the lens is unsymmetric to the biological materials, a focused point could not be made using PZFlex FEM simulation. The model and results are shown in Fig 2.3(a), Fig 2.3(b) and (c). The materials' properties are listed in Table 2-1.



(a) Slated lens (b) Interaction on the interface (c) wave is scattered

Fig2.3 slated lens modeling

Here, the angle of the lens is 60^o. The angle between y-axis and the start edge of the lens is 30^o. High frequency pressure is uniformly loaded on the sphere surface of lens. The frequency is 500 kHz, and amplitude is normalized to one. In Fig. 2.3, the energy is divided into three parts. The first part is reflected by the interface, the second part goes along the interface and the third part is scattered.

2.3 Thin bone problem

A thin bone is placed in the water along with the focused lens. The mechanical effect of the ultrasound is calculated in the model shown in Fig. 2.4. The black arc is the lens, the middle layer is the bone, and the rest is water.

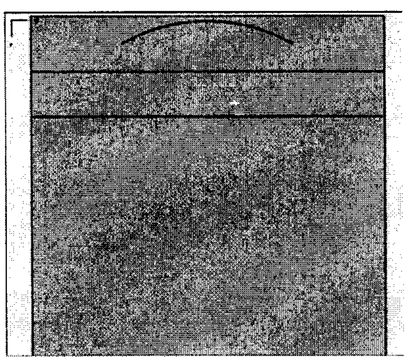


Fig 2.4 Model of problem

The angle of lens is 60^o and the radius of lens is 30 mm. The thickness of bone is 8 mm. The distance between the edges of lens to top surface of the bone is 5 mm. The input high frequency pressure has a frequency of 500 kHz and unit amplitude.

The result shows that after the ultrasound passed through the thin bone, it will be refocused. From the theory of optics, after the wave passed through the thin bone, and when the wave comes into water again, the angle direction is corrected.

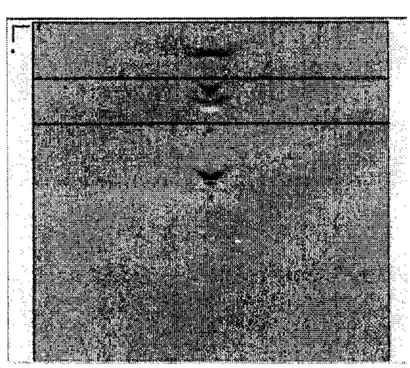


Fig 2.5 Refocused point

Now, a new problem is introduced. For clinical application, the focus point should be in the body and not in the water. If the third layer material is changed from water to another material different from water, the material of second layer, what would be the behavior of the pressure distribution in the concerned layer and how can the path of the ultrasound be corrected to get the focus point? From the thermal section, which will be discussed next, a strip area along the symmetric axis of lens is heated. This area has as high a temperature as in the BAD tissue (target area). As a result, most of the surrounding tissue is damaged. This is an important problem urgently need attention before the ultrasound can be used widely used and be effectively in the clinics. In the next section, the thermal effect is discussed.

3. THERMAL PROBLEM

Compared the mechanical effect and thermal effect by the therapeutic ultrasound, the thermal effect currently represent the majority of application for therapeutic ultrasound. In this section, a simple model is considered. A piece of biomaterial is placed in water, and the ultrasound lens is in water too. The thermal effect in biomaterial will be calculated for this simply model as well as mechanical effect. As the result of this problem, the temperature distribution in 2-D at a given time is shown graphically. The biomaterial is considered here as a viscoelastic material, and has higher damping and lower thermal parameters are used for the calculation.

3.1 Modeling and Description

As shown in Fig. 3.1, the model is plotted. Both the geometric parameters and the properties of the materials are listed in Table3-1.

Table3-1 Properties of materials

Material	Density	c_p	c_s	Q/Freq	Heat of Material	Thermal Conductivities
BIOM	3900	1881	1038	25/1MHz	4200	0.058
Water	1000	1500	0	0	4200	0.058

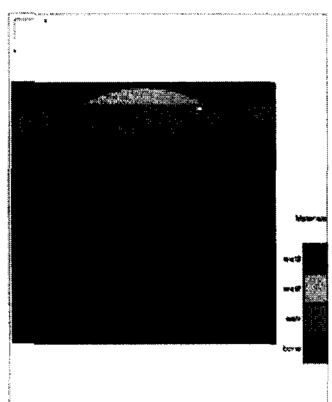
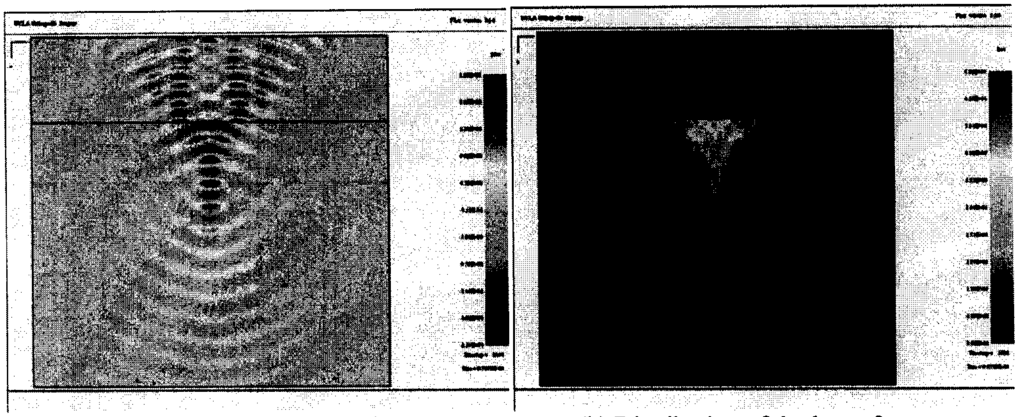


Fig 3.1 Model of thermal problem

The lens is as the same as the one in last problem; the radius of lens is 30 mm and the angle is 60°. The width and length of this model are 60 mm in x and y direction. The input ultrasound is a continuous wave with frequency of 1 MHz. High amplitude is needed; the supposed amplitude is 5 M.

3.2 Mechanical effect and Loss of energy

The results are shown in Fig. 3.2 (a) and (b). Fig. 3.2 (a) is the steady state of the mechanical effect showing the pressure distribution for the continuous ultrasound wave. Fig. 3.2 (b) is the result of the loss of energy.



(a) Steady mechanical state by continuous wave (b) Distribution of the loss of engery

Fig. 3.2 Pressure and loss

A strip area of high loss of energy is shown in Fig3.2 (b), and all of this area will be heated to high temperature.

3.3 Temperature Distribution in 2-D

The temperature, shown in Fig.3.3 has almost the same distribution as the energy loss. A strip-shaped area of tissues includes the bad tissue and lots of surrounding good tissue are damaged by high temperature.

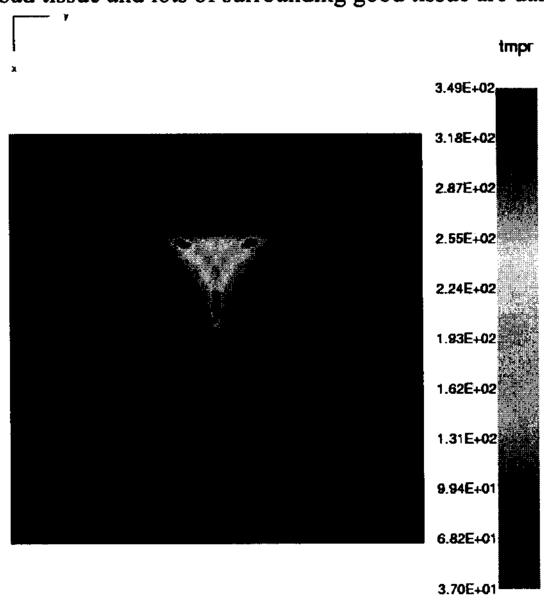


Fig 3.3 Temperature distribution in the bio-material

4. CONCLUSION AND FUTURE RESEARCH

Locating the focal point of therapeutic ultrasound in an inhomogeneous material system is an important issue that needs to be properly addressed before wider clinical application is possible. The knowledge gathered not only can reduce the amplitude of input ultrasound, but also reduce possible damage to the surrounding tissue. For the real clinic application, the material systems are complex. If the problem is not properly dealt with, the focused wave will scatter in the human body without achieving its desired effect. Lacking proper knowledge meant not being able to heat up and cause damaging to the bad tissue, or having to heating a large area for long time. The bubble caused by the application of high intensity ultrasound is another pertinent issue. The effect of these bubbles to the thermal effect and mechanical effect of the ultrasound in clinic situation is still unclear. The scattering of ultrasound by air bubbles may cause the focal point to be generated in the tissue. This is another interesting problem that will be pursued in a later time.

5. ACKNOWLEDGMENTS

The research at Jet Propulsion laboratory was conducted under a contract with NASA

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