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Acoustic and Thermal Analysis in Blood Vessel into Muscle for Pressure Study Related to Cavitation

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***Abstract* – The acoustic cavitation during the application of ultrasound has been witnessed with their effect in different media. For clinical applications, it has been showed as an undesired effect. The use of Finite Element Method has been related to computational solutions for solving problems of real life for clinical problems or therapeutic uses. This paper presents a simulation made with the Finite Element Method for the acoustic and thermal analysis in muscle and a blood vessel with a transducer of 20 mm of radius, for the comparison of behavior between both tissues and their possible relation with the acoustic cavitation phenomenon. The result obtained shows the map acoustic pressure distribution with a higher pressure in the blood vessel than the muscular tissue, and a temperature increase lower than 7 °C from the initial temperature (37.5 °C) in the blood vessel. This work was made as an approximation of our main goal of study of acoustic cavitation.**

Keywords – Acoustic pressure, Finite Element Method, Focused Ultrasound, Thermal distribution.

I. Introduction

Ultrasound has been proved as an effective tool in the application of therapeutic application [1][2]. The use of ultrasound in a focused way have been allowed to produce a considerable damage only in a specific area [3]. One of the applications in the las years has been the opening of the blood-Brain Barrier (BBB) in a reversible way with low produced in surrounding tissue [4]–[7]. During the application of ultrasound has been presented the phenomenon of acoustic cavitation [8]. This phenomenon has been undesired for some investigation groups due to the uncontrolled damage generate in tissue [9]. Other groups have been tried to be controlled for the understanding and the improvement in the use of the ultrasound techniques [10][11].

The use of computational systems for the simulations of tissue during ultrasound applications has been done in past years [12]. Using the Finite Element Method for solving mathematical problems in real life problems aboard different topics such as the use of transducer that positioned a focus in a specific area [13], to approach an estimation of tissue damaged in tissue. This damage generated is accompanied to temperature increases studies due to the acoustic power generated by the transducers [14]. Although these computational tools have been helping for the solution of different phenomena, the acoustic cavitation effect has been very difficult to simulate [15]; some studies are focused in the behavior of a bubble [16], or approximations of what the phenomenon could be approached to the reality [17]. These types of simulations are often pending to the experimentation for the validation of simulated results obtained, that is the reason for called an approximation [18].

In this paper is presented a computerized simulation of a focused transducer that generates a focus in a simulated muscle tissue with a blood vessel in it. The transducer is able to generate the focus in the vessel and the muscle with the purpose to determine the acoustic pressure generated in both tissues. Also, is presented the thermal distribution generated from the acoustic pressure generated by the transducer. This study will support the main study of acoustic cavitation that is developed by our investigation group.

II. Methods

A. Theoretical basis

To understand the propagation of the ultrasound and the thermal effect in tissue, the solutions were solved by the differential equations of acoustic propagation and heat propagation. The acoustic power of the FUS transducer can be related to his radiation forced proportioned by [19]:

$$P = \frac{2c_0 f}{1 + cos\theta} \tag{1}$$

where c_0 is the speed of sound, f is the work frequency of the transducer. The value θ is given by $\theta = {}^{d}/_{D}$, where d is the aperture radius, and D is the focal length. The ultrasonic propagation can be explained by the acoustic wave equation, that is related to its normal acceleration given by [20]:

$$a_0 = \frac{\omega}{\rho c} p e^{j(\omega t + \pi/2)} \tag{2}$$

where a_0 is the normal acceleration, ρ is the density of the material, c is the speed of sound, and p is the pressure of the radiator. The heat propagation studied can be explained with the Pennes bioheat thermal equation given by:

$$\rho C_p \frac{\delta T}{dt} + \nabla \cdot (-k \nabla T) = Q \tag{3}$$

where ρ is the density of the medium, C_p is the heat capacity at constant pressure, k is the thermal conductivity, T is the initial temperature, and Q is the external heat source. The external heat source can be determined from the pressure generated by:

$$Q = \frac{\alpha p^2}{\rho c} \tag{4}$$

where ρ is the acoustic absorption coefficient.

B. Finite element analysis

For solving the main differential equations presented, the simulation was made with the Finite Element Method (FEM) using COMSOL Multiphysics (COMSOL Inc., Sweden) on a workstation with 32-GB RAM and 3.20-GHz 4-core processor.

For the FEM solution, it was implemented a 2D geometry that consists of a concave transducer of 20 mm of radius, immersed in a tank filled with water that works as a transmission medium. This water tank, which contains the tissue sample, was made with similar properties to the laboratory, to avoid acoustic rebounds between the transducer and the medium. Inside the tank, it is placed a smooth muscle phantom of 12 mm per side, which contains a blood vessel. This vessel has a diameter of 3 mm [21] and the same size in length as the phantom (see Fig. 1). The transducer was made with similar parameters of dimensions of a real transducer that has been studied in the past [22]. Also, the geometry proposed will help for the studies of acoustic pressure and soft tissue heating that will be explained later.

In the Fig. 1, it is also showed every domain of the simulation. Domain 1 represents the medium in which the tissue is submerged, in this case is water; the domain 2 is the muscle, and domain 3 is the blood vessel; the curve boundary represented with the red color is the radiator boundary of the transducer. The boundaries marked with blue were set to match the acoustic impedance of water to reduce reflections produced by the transducer boundary. For thermal purposes, those same boundaries were set to an initial condition temperature of 37.5 °C.

The simulation was carried out in two parts. The first part consists in a frequency analysis to study the acoustic emission of the transducer and analyze the acoustic pressure behavior generated. The main interest of this was observe the focus and the acoustic pressure produced in the muscle and the blood vessel. In the specific case of the model, the blood vessel contains blood in a stationary moment. Other components of erythrocytes do not affect the simulation as it were taken with the same properties and are not included in the model. The study in this first step was made in a bandwidth of frequencies starting in 100 kHz and finishing at 3 MHz, with steps of 100 kHz. The focus generated from the best-case should has the size to cover part of both tissues but narrow enough to escape to undesired areas of the simulation.

The second part consists in the thermal distribution generated by the acoustic pressure produced at the beast-case of work frequency by the transducer. Since there is not a maximum temperature estimated, it is expected that the reached temperature does not create considerable damage in both, muscular tissue, and blood vessel. The study was made as a time dependent analysis during 60 seconds with steps of 0.5 seconds. The results obtained from acoustic pressure and tissue heating could be a studied as a first approximation with the acoustic cavitation effect studied by our investigation group.

The mesh applied in the model was established according to the wavelength (λ) of the materials of the model. The wavelength obtained was divided by 7 as a minimum and 5 as a max value, which has proved to be a good mesh for acoustical problems [23]; convergence was verified with smaller meshes having an error of 0.01% between the chosen one and a mesh of 12 elements per wavelength. For the materials added to the geometry, table 1 shows the properties applied at every domain for both acoustic and heating studies.

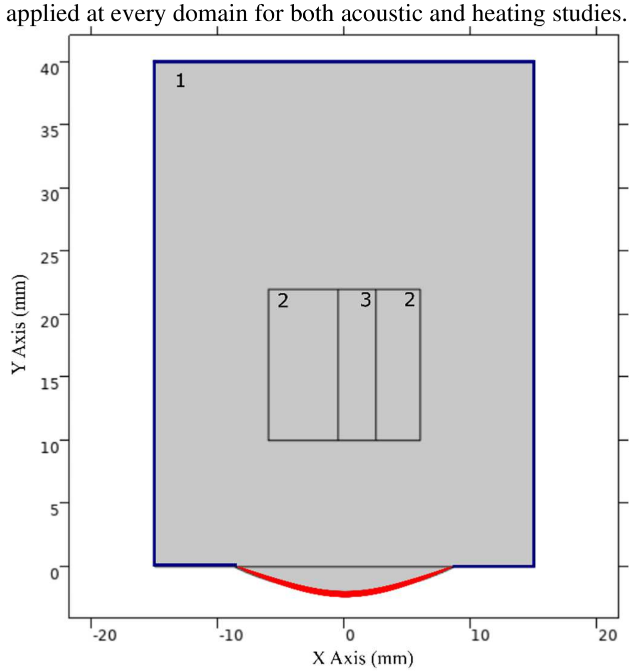

Fig. 1 – Geometry of the simulation. Every domain represents a different material of element of the model: 1 is the transmission medium, 2 represents the muscle tissue, and 3 is the blood vessel. The blue boundaries are the water tank, and the red boundary represents the face of the transducer.

TABLE 1.- Acoustic and thermal properties of simulated tissue [24][25]

Domain	Speed of sound (m/s)	Attenuation (Np/m)	Heat capacity (J/(kg·K))	Thermal conductivity (W/(m·K))	Density (kg/m^3)
Water	1500.00	0	4178.00	0.60	997.00
Muscle	1575.00	7.11	3241.00	0.49	1090.00
Blood	1578.20	7.02	3212.00	0.46	1055.00

III. Results and Discussion

The results obtained from de model explained before present the acoustic pressure generated in two different media by a concave transducer and the thermal distribution with the temperature increases reached in the sample of tissue designed.

In fig. 2 it is showed the acoustic pressure generated by the transducer in the medium and the phantom with the blood vessel in it at a frequency of 2 MHz. The transducer was positioned in a way that the focus aboard enough area of both tissues. However, due to the characteristic in the acoustic properties of the materials, the focus was "stronger" in the blood vessel. Still counting with this displacement, the acoustic pressure still aboard part of the muscular tissue what would allow us to compare the pressure in both tissues.

For the case of the muscular tissue was 1.4 kPa, and in the blood vessel was of 1.8 kPa. The acoustic pressure generated in any medium will produce the acoustic cavitation effect. Although it is difficult to simulate the cavitation effect, we could assume that the higher acoustic pressure generated could produce a major effect for the phenomenon, for our results the higher acoustic produced was in the blood vessel. If we took this to an experimental work, the easiest detection on the phenomenon would be in this area, using specific equipment.

For the main goal of our investigation group, which is the study of the acoustic cavitation during the opening of the blood-brain barrier, this could be presented as an approximation for the behavior of the phenomenon in blood vessels. Also, if we improve the properties or other elements in the components of the model the result could be different due to other media included in the composition of a real organ or tissue, the presence of erythrocytes or the flow of blood in the vessel. The presence of the wall also was omitted due to the high pressure generated would break it due to their physical characteristics. Even mentioned that, and as it was mentioned before, simulate the phenomenon has been very difficult, so it can be concluded that the obtaining of different values of acoustic pressure it can be inferred that at higher acoustic pressure, it would be higher the presence of the phenomenon.

In the study of the second step, the thermal distribution is showed in Fig. 3. The heating of the tissue was performed according with the acoustic pressure generated in the first step, explained before. The initial temperature of the tissue was 37.5 °C, and the maximum increase obtained was less than 7 °C during the time of application, mostly in the blood vessel than the muscle due to the location of the focus generated. These results showed us that the damage produce in both tissues could be considered reversible due to do not reach a higher temperature of 45 °C.

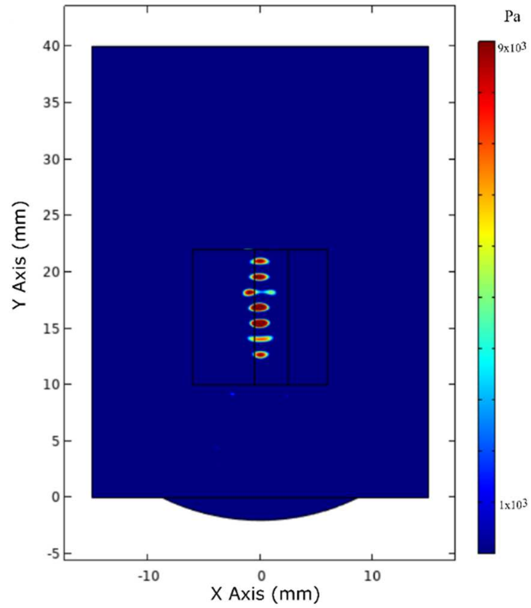

Fig. 2 – Acoustic pressure generated by the transducer at a frequency of 2 MHz.

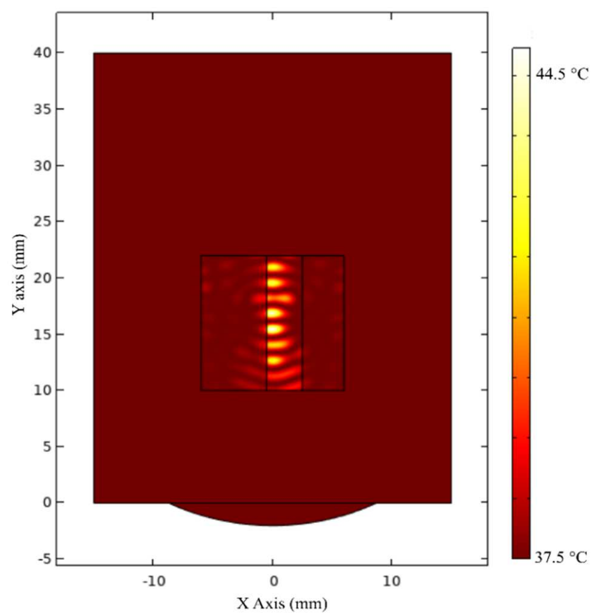

Fig. 3 – Heating pattern obtained from the acoustic pressure generated before.

If we compare the results simulated obtained with application in experimental application [26][27],the temperature increase does not perform irreversible damage. For our purposes, temperature increases showed in the simulation, although could have an impact in the phenomenon, could not be the most important factor to consider due to the nature in which the cavitation acoustic presents. Even so, the result obtained (about heating pattern) shows a temperature increase interesting with the low damaged produced. In the same way, the results obtained, being an approximation with the acoustic cavitation effect, is not validated yet in a complete form. The road to validation would include the use of experimental equipment with the specifications that were described previously in past sections.

IV. Conclusions

The objective of this paper was to present a computational model of a focused concave transducer able to generate a focus in a specific area. This area abord in the simulated tissue sample a portion of smooth muscle and other of the vessel. The results and discussion section mentioned the graphs and data obtained from the transducer simulation able to generate a focus able enough to cover both parts of the sample modeled tissue. The acoustic pressure generated of the focus in the muscle was lower (1.4 kPa) than the produced in the blood vessel (1.8 kPa). Previous results [28], it has been obtained a stable percentage value of probability for acoustic cavitation been determined. Comparing with the results obtained in pressure emitted could be difficult due to the differences of transducers employed in both cases.

With the acoustic map produced, it was determined a maximum temperature increase of 7 °C from the initial temperature (37.5 °C) at the vessel and a maximum increase of 4°C in the muscle, due to the localization of the focus. As an approximation, the results could be considered favorable, pending of experimental validation. These acoustic pressure and heating distribution generated in the tissue could work as a tool for the understanding part of the total reach from the acoustic cavitation phenomenon, which is the main objective of investigation by our investigation group. For experimental application in the future, it will start with the instrumental application for the validation of results, that is beyond this paper.

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References

[1] O. Al-Bataineh, J. Jenne, and P. Huber, "Clinical and future applications of high intensity focused ultrasound in cancer," *Cancer Treat. Rev.*, vol. 38, no. 5, pp. 346–353, 2012, doi: 10.1016/j.ctrv.2011.08.004.

[2] M. J. K. Blomley, J. C. Cooke, E. C. Unger, M. J. Monaghan, and D. O. Cosgrove, "Science, medicine, and the future: Microbubble contrast agents: a new era in ultrasound," *Bmj*, vol. 322, no. 7296, pp. 1222–1225, 2001, doi: 10.1136/bmj.322.7296.1222.

[3] V. Y. T. Cheung, "High-intensity focused ultrasound therapy," *Best Pract. Res. Clin. Obstet. Gynaecol.*, vol. 46, pp. 74–83, 2018, doi: 10.1016/j.bpobgyn.2017.09.002.

[4] J. J. Choi, K. Selert, Z. Gao, G. Samiotaki, B. Baseri, and E. E. Konofagou, "Noninvasive and localized blood-brain barrier disruption using focused ultrasound can be achieved at short pulse lengths and low pulse repetition frequencies," *J. Cereb. Blood Flow Metab.*, vol. 31, no. 2, pp. 725–737, 2011, doi: 10.1038/jcbfm.2010.155.

[5] K. F. Timbie, B. P. Mead, and R. J. Price, "Drug and gene delivery across the blood-brain barrier with focused ultrasound," *J. Control. Release*, vol. 219, pp. 61–75, 2015, doi: 10.1016/j.jconrel.2015.08.059.

[6] N. McDannold, N. Vykhodtseva, and K. Hynynen, "Effects of Acoustic Parameters and Ultrasound Contrast Agent Dose on Focused-Ultrasound Induced Blood-Brain Barrier Disruption," *Ultrasound Med. Biol.*, vol. 34, no. 6, pp. 930–937, 2008, doi: 10.1016/j.ultrasmedbio.2007.11.009.

[7] G. Samiotaki, F. Vlachos, Y. S. Tung, and E. E. Konofagou, "Permeability and reversibility timeline study of the focused-ultrasound induced blood-brain barrier opening at distinct pressures and microbubble sizes in vivo," in *IEEE International Ultrasonics Symposium, IUS*, 2011, pp. 1494–1497, doi: 10.1109/ULTSYM.2011.0370.

[8] Y. Shin and U. Shin-Ichiro, "Cavitation detection with subharmonic emissions by low intensity sustaining ultrasound," *Proc. - IEEE Ultrason. Symp.*, pp. 772–775, 2008, doi: 10.1109/ULTSYM.2008.0185.

[9] Y. Qiao, H. Yin, Z. Li, and M. Wan, "Cavitation distribution within large phantom vessel and mechanical damage formed on surrounding vessel wall," *Ultrason. Sonochem.*, vol. 20, no. 6, pp. 1376–1383, 2013, doi: 10.1016/j.ultsonch.2013.03.007.

[10] H. Chen, T. Khokhlova, Y. Wang, and W. Kreider, "Passive Cavitation Detection During Pulsed Hifu Exposures of Ex Vivo Tissues and in Vivo Mouse," vol. 40, no. 7, pp. 1523–1534, 2015, doi: 10.1016/j.ultrasmedbio.2014.01.007.PASSIVE.

[11] B. Hu *et al.*, "Stable cavitation using acoustic phase-change dodecafluoropentane nanoparticles for coronary micro-circulation thrombolysis," *Int. J. Cardiol.*, vol. 272, pp. 1–6, 2018, doi: 10.1016/j.ijcard.2018.06.027.

[12] S. Grudzenski *et al.*, "Simulation, Implementation and Measurement of Defined Sound Fields for Blood–Brain Barrier Opening in Rats," *Ultrasound Med. Biol.*, vol. 48, no. 3, pp. 422–436, 2022, doi: 10.1016/j.ultrasmedbio.2021.10.003.

[13] D. A. Hernández, M. I. Gutiérrez, A. Vera, and L. Leija, "Simulation and in vivo Validation of Craniotomies in Rats for the Disruption of the Blood Brain Barrier with Focused Ultrasound for Drug Delivery," *14th Int. Conf. Electr. Eng. Comput. Sci. Autom. Control. CCE 2017*, pp. 2–6, 2017.

[14] T. Wessapan and P. Rattanadecho, "Acoustic streaming effect on flow and heat transfer in porous tissue during exposure to focused ultrasound," *Case Stud. Therm. Eng.*, vol. 21, no. April, p. 100670, 2020, doi: 10.1016/j.csite.2020.100670.

[15] H. Chen, W. Kreider, A. A. Brayman, M. R. Bailey, and T. J. Matula, "Blood vessel deformations on microsecond time scales by ultrasonic cavitation," *Phys. Rev. Lett.*, vol. 106, no. 3, pp. 1–4, 2011, doi: 10.1103/PhysRevLett.106.034301.

[16] A. L. K. Karen E. Morgan, John S. Allen, Paul A. Dayton, James E. Chomas and and K. W. Ferrara, "Experimental and Theoretical Evaluation of Microbubble Behavior: Effect of Transmitted Phase and Bubble Size," vol. 1, no. 3, pp. 1–16, 2010, doi: 10.1109/58.883539.

[17] J. J. Choi, M. Pernot, T. R. Brown, S. A. Small, and E. E. Konofagou, "Spatio-temporal analysis of molecular delivery through the blood-brain barrier using focused ultrasound," *Phys. Med. Biol.*, vol. 52, no. 18, pp. 5509–5530, 2007, doi: 10.1088/0031-9155/52/18/004.

[18] D. Andrews, "Modelling of Ultrasonic Transducers and Ultrasonic Wave Propagation for Commercial Applications using Finite Elements with Experimental Visualization of Waves for Validation," *Cambridge Ultrason. Ltd*, pp. 228–239, 2012, doi: 10.4324/9780203126790.

[19] Y. Zhou, "Acoustic power measurement of high-intensity focused ultrasound transducer using a pressure sensor," *Med. Eng. Phys.*, vol. 37, no. 3, pp. 335–340, 2015, doi: 10.1016/j.medengphy.2015.01.014.

[20] M. I. Gutierrez, S. A. Lopez-Haro, A. Vera, and L. Leija, "Experimental Verification of Modeled Thermal Distribution Produced by a Piston Source in Physiotherapy Ultrasound," *Biomed Res. Int.*, vol. 2016, pp. 1–16, 2016, doi: 10.1155/2016/5484735.

[21] V. P. Crabtree and P. R. Smith, "Dimensional analysis of blood vessels in the pressure myograph," *Opt. Biopsies Microsc. Tech. III*, vol. 3568, no. January 1999, pp. 46–52, 1999, doi: 10.1117/12.336816.

[22] D. Hernández, "Propuesta de un protocolo experimental basado en craneotomías para la apertura temporal de la barrera hematoencefálica por acción del ultrasonido focalizado para permitir el paso de químicos macromoleculares al cerebro de

roedor." Ciudad de México, p. 113, 2017.

[23] S. Marburg, *Computational Acoustics of Noise Propagation in Fluids - Finite and Boundary Element Methods*. 2008.

[24] K. Giering;, O. Minet;, I. Lamprecht;, and G. Muller, "Review of thermal properties of biological tissues," *SPIE Opt. Eng. Press*, vol. 044, no. August 2018, pp. 45–65, 1995, doi: 10.1007/978-3-319-95432-5_4.

[25] A. Feldmann, P. Wili, G. Maquer, and P. Zysset, "The thermal conductivity of cortical and cancellous bone," *Eur. Cells Mater.*, vol. 35, no. 2000, pp. 25–33, 2018, doi: 10.22203/eCM.v035a03.

[26] S. Xu *et al.*, "Correlation Between Brain Tissue Damage and Inertial Cavitation Dose Quantified Using Passive Cavitation Imaging," *Ultrasound Med. Biol.*, vol. 45, no. 10, pp. 2758–2766, 2019, doi: 10.1016/j.ultrasmedbio.2019.07.004.

[27] A. D. Maxwell, C. A. Cain, T. L. Hall, J. B. Fowlkes, and Z. Xu, "Probability of Cavitation for Single Ultrasound Pulses Applied to Tissues and Tissue-Mimicking Materials," *Ultrasound Med. Biol.*, vol. 39, no. 3, pp. 449–465, 2013, doi: 10.1016/j.ultrasmedbio.2012.09.004.

[28] J. A. Rodriguez Ramirez, M. Ibrahin Gutierrez, A. V. Hernandez, C. Alther Negreira Casares, A. R. Fernandez, and L. Leija Salas, "Acoustic cavitation detection produced by ultrasound in an agarose-gel phantom analyzed with frequencies spectrogram," *I2MTC 2020 - Int. Instrum. Meas. Technol. Conf. Proc.*, pp. 3–7, 2020, doi: 10.1109/I2MTC43012.2020.9129484.