Mechanical and Thermal Effects of Focused Ultrasound on a Biological Tissue using COMSOL Multiphysics®, Three Different Approaches

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1. Introduction

The young crystalline lens is flexible and soft, able to deform in order to achieve a wide range of focus, from far to near objects. Unfortunately, while aging, a vision disorder called presbyopia affects us. It is characterized by the stiffening of the crystalline lens, causing a progressive loss of the visual accommodation amplitude. Finding a procedure to soften out the tissues of the crystalline lens, is the aim of future ophthalmological anti-aging treatment. Ultrasounds have a great advantage in the medical field: They can reach a targeted volume inside a human organ, or biological tissue, without any harm effect occurring in the path taken by the transmitted signal. In other words, only the targeted zone is treated with good accuracy, while keeping the risk of damage of the surrounding tissues very low. Ultrasound is generated using piezoelectric crystals, which vibrate when subjected to an electric field. There are various methods for focusing the ultrasound waves. The simplest method may be the shelf-focusing (using a curved ultrasound source), where the beam focus is fixed at the position determined by the geometrical specifications of the transducer and this method has been selected to do the following simulations. Now, if we want to use focused ultrasound as a treatment, we need to quantify the resulting bioeffects. In order to do that, the simulation of this treatment using COMSOL Multiphysics® is the first step to take before starting the experimental phase. Accordingly, the acoustic, thermal, and mechanical properties of the different part of the eye are gathered and introduced into the materials section of the software, to predict the behavior of the ultrasound propagation, and quantify the induced effects [1-4].

2. Model Definition

Figure 1 shows the 2D axisymmetric geometry simulated in this model. A geometric transducer is constructed and whose radius of curvature is approximately equal to the desired focal distance [5]. Then, a normal displacement boundary condition will be defined on this curvature. The resulting focal region has mostly the shape of an ellipse, and its dimensions depend on the transducer frequency and focusing geometry [6].

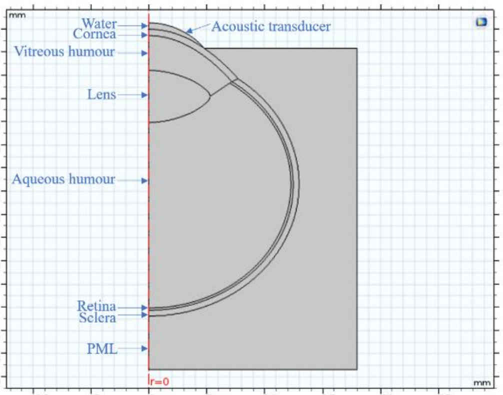

Figure 1. Model geometry. The different domains of the human eye are shown in addition to the PML (Perfectly Matched Layer).

In this work, three physics have been employed and coupled using different approaches, to obtain the required results. Another aspect that is considered after selecting the physics we want to solve, is the study type selection. It must be selected appropriately. So, for the pressure acoustics physics, a frequency domain study is chosen to compute and solve the model, because the structure is being subjected to a harmonic excitation for a specific frequency of 5 MHz. Concerning the bioheat transfer physics, a time-dependent study is chosen because the field variable (temperature) is changing with time, and the structure is subjected to some load over a certain period of time (one second). Finally, for the solid mechanics physics, the frequency-domain equation form will always be solved at each time step.

3. Theoretical Background

3.1 Pressure Acoustics, Frequency Domain Interface

It is used to compute pressure variations for the propagation of acoustic waves in fluids at quiescent background conditions (no flow). The "Linear Elastic with Attenuation" fluid model has been chosen since the attenuation coefficients of ocular tissues are found in the literature as experimental values that takes account for the actual viscoelastic properties of the tissue and how they attenuate the pressure waves. The purpose of this fluid model is to mimic a behavior of damping by solving the Helmholtz equation (1) [7]:

$$\nabla.\left(\frac{-1}{\rho_c}(\nabla p)\right)-\left(\frac{\omega}{c_c}\right)^2\frac{p}{\rho_c}=0 \qquad (1)$$

Where, the acoustic pressure p is a harmonic quantity, ρ_c is the density, c_c is the speed of sound, and ω is the angular frequency.

There will be a significant heat generation in the focal zone due to the absorbed ultrasound energy by attenuation. This heat is obtained in COMSOL Multiphysics® as a derived variable called plane wave total power dissipation energy (acpr.Q_pw). So, the heat source (Q) is given by equation (2):

$$Q=2\alpha I=2\alpha\left|Re(\frac{1}{2}pv)\right| \qquad (2)$$

Where α is the acoustic attenuation coefficient, I is the acoustic intensity magnitude, p is the acoustic pressure, and v is the acoustic particle velocity vector.

3.2 Bioheat Transfer Interface

It describes heat transfer by conduction in living tissues. So, the thermal conductivity, heat capacity and density of each part of the eye are gathered and introduced in the materials section. Then, equation (3) is solved in "Bioheat Transfer" interface:

$$\rho C_p\frac{\partial T}{\partial t}=\nabla.(k\nabla T)+Q \qquad (3)$$

Where T is the temperature, ρ is the density, C_p is the specific heat, k is the thermal conductivity, Q is the heat source. The assumption associated with the use of equation (3) is that the tissue properties do not change when the temperature rises [3], [4].

3.3 Solid Mechanics Interface

Thermal expansion has been defined to say that there is an additional strain caused by the variation in temperature. Using the secant coefficient of thermal expansion (α), the thermal strain (ε_{th}) is given by:

$$\varepsilon_{th}=\alpha\left(T-T_{ref}\right) \qquad (4)$$

Where the temperature T is a model input, that will be the existing temperature variable from the "Bioheat Transfer" interface. As for the reference temperature T_{ref} it will be the initial temperature of the tissues.

Knowing that, when a structure is subjected to high frequency vibrations, a significant amount of heat is generated due to the mechanical losses in the hyperelastic material. Then, the acoustic wave generated in the fluid (at a frequency of 5 MHz) transforms into an elastic wave in the solid. So, accordingly to the above paragraph, an analysis in the frequency domain is done, in which the stress-strain analysis is combined with the heat equation to compute the thermoelastic response for the vibrating structures. The temperature rise is given by solving the heat-transfer equation (5):

$$\rho C_p\frac{\partial T}{\partial t}=\nabla.(k\nabla T)+Q_h \qquad (5)$$

Where k is the thermal conductivity, C_p the specific heat, ρ is the density, and T is the temperature averaged over the time period. The heat source Q_h, is the internal work of the non-elastic forces (viscous forces) over the period, and it is obtained in COMSOL Multiphysics® as a derived variable called total power dissipation density (solid.Qh) [5].

3.4 Events Interface

Since we are dealing with a pulsed heat load, in order to model accurately and efficiently such situation, Events interface has been utilized instead of tightening the tolerances. Accordingly, the solver will take smaller time steps around this point to catch the change in the solution accurately. Noting that we use Explicit Event feature, because we know at which times our load is turning ON and OFF [10].

4. Approaches investigated to solve the model

In the following simulations, the transducer is driven at the frequency of 5 MHz that is turned on for one second and then turned off to let the tissues cool down. The general assumptions made for the three approaches are as follow:

a. Nonlinear effects are neglected.
b. Shear waves are neglected (excluding for the second approach).
c. The thermal properties of the ocular tissues are constant and don’t depend on temperature (i.e. the tissue properties do not change when the temperature rises).
d. The mechanical properties of the ocular tissues are constant and don’t depend on temperature.

4.1 First Approach

The first approach gives us information about the pattern of the focalized pressure field. In other words, we can quickly visualize and modify it by varying the transducer parameters like frequency and normal displacement. Knowing that increasing the frequency decreases the area of focal zone and increasing the normal displacement increases the amplitude of pressure. As shown in Figure 2, the equivalent fluid model “Linear Elastic with Attenuation” has been employed to define all the domains of the eye. Figure 3 summarizes the interfaces used in this approach and their corresponding inputs/outputs. In this model, the “Pressure Acoustics, Frequency Domain” interface is used to simulate the pressure field created by the transducer. Then, the heat (Q), a derived value, is calculated and multiplied by our step function, to specify the exposure time of our procedure. This heat will be taken as a heat source for the thermal problem. The “Bioheat Transfer” interface is then used to simulate the induced temperature field. This manual multiphysics coupling give us valuable information even with the according assumptions.

In Table 1, the number of degrees of freedom and the computation time for each study are presented. Knowing that, the mesh created for the “Bioheat Transfer” interface is different, since only the lens domain and its surrounding are the most important. Therefore, not all the domains where selected for the mesh to reduce computation time.

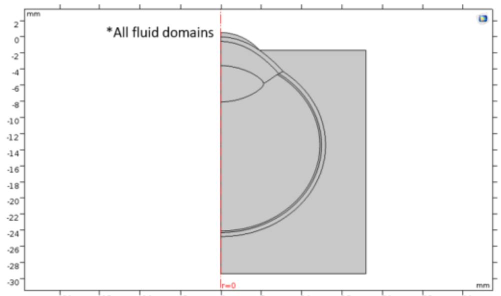

Figure 2. “Fluid equivalent” domains defined in this model.

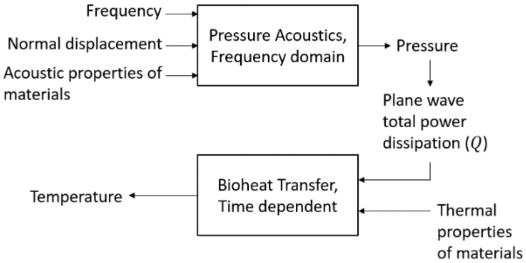

Figure 3. Schematic representing the first approach implemented in COMSOL Multiphysics®.

Study	No. of degrees of freedom	Computation Time (min)
Frequency Domain	5'450’000 (Mesh 1)	8
Time Dependent (5 s)	265'000 (Mesh 2)	10

Table 1. Number of degrees of freedom and computation time associated to each study.

4.2 Second Approach

In this approach, the main goal is to quantify the induced mechanical bioeffects mainly in the lens region. Therefore, some domains are defined using mechanical properties instead of acoustic properties. Accordingly, the pressure acoustics physics interface models fluid domains and the solid mechanics physics interface models solid domains (using “Hyperelastic Neo-Hookean” material model), as shown in Figure 4. Therefore, the pressure waves emitted in the fluid domain transform into elastic waves in the solid domain. To be able to simulate that, the built-in multiphysics coupling “acoustic-structure boundary” is defined at every fluid-structure boundary.

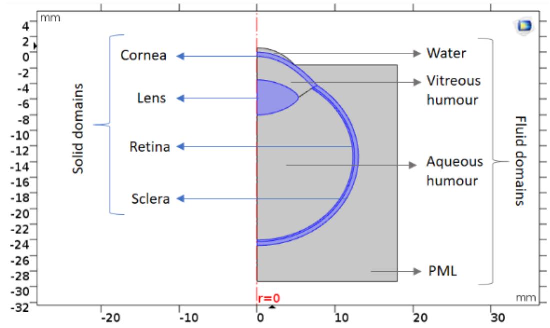

Figure 4. The “hyperelastic solid” and “fluid equivalent” domains defined in this model.

As shown in Figure 5, the solid mechanics interface is implemented to calculate the displacement field (Displacement 1) in the solid domains. Then, the heat (Q2), a derived value, is taken as the second heat source in the thermal problem in addition to the heat (Q1) that is obtained from the pressure acoustics interface, as explained before. Additionally, a thermal expansion node is created for each hyperelastic material, which take as a model input, the temperature field at each time step, to quantify the amount of total displacements (Displacement 2) induced due to the thermal expansion process.

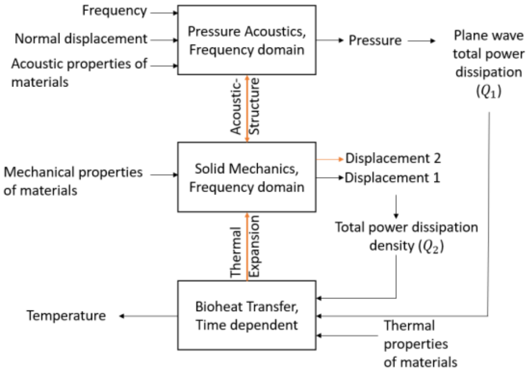

Figure 5. Schematic representing the second approach implemented in COMSOL Multiphysics®.

However, by executing this approach, it has been shown that at 5 MHz, the number of mesh elements starts to be extremely high and so as the number of DOF (Degree of Freedom). This multiphysics model has been successfully tested at lower frequencies (however, it is not a sufficient frequency to focalize energy), but when the frequency used is 5 MHz (really small wavelength), the maximum element size of the mesh needs to be really small. Accordingly, the memory required is really high, as a result this approach has been discarded. In Table 2, the number of degrees of freedom and the computation time for the first study are presented.

Study	No. of degrees of freedom	Computation time
Frequency Domain	14'000’000	Fail after 9 hrs
Time Dependent	Not performed	Not performed

Table 2. Number of degrees of freedom and computation time associated to each study.

4.3 Third Approach

In this approach, the simulation starts exactly the same way as explained in the first approach. Then, the solid mechanics interface is added to perform a thermal expansion analysis on a hyperelastic lens as shown in Figure 6.

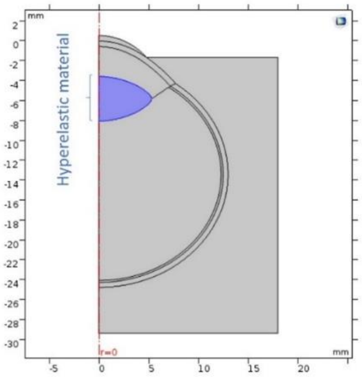

Figure 6. The model used for the solid mechanics interface only, where the lens is defined as a hyperelastic material.

As shown in Figure 7, the pressure field and the corresponding temperature field are simulated in the defined fluid equivalent model of Figure 2.

Then, the temperature field as function of time is introduced as an input for the defined model of Figure 6 to evaluate the thermal expansion effect on the hyperelastic solid lens due to the ultrasound exposure. Therefore, at every time step the temperature is evaluated, as well as the corresponding thermal expansion.

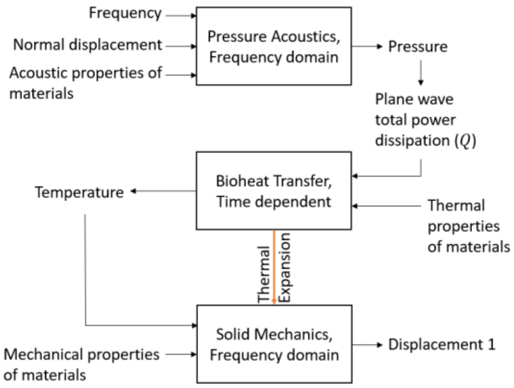

Figure 7. Schematic representing the third approach implemented in COMSOL Multiphysics®.

In Table 3, the number of degrees of freedom and the computation time for each study are presented.

Study	No. of degrees of freedom	Computation time
Frequency Domain	7'251'000 (Mesh 1)	8 min
Time Dependent (60 s)	202'000 (Mesh 2)	10 hrs

Table 3. Number of degrees of freedom and computation time associated to each study.

5. Simulation results

In this section, the simulation results of the third approach are presented. Figure 8 illustrates the acoustic pressure field. As we can see the beam converges into a focal zone where the pressure amplitude reaches as high as 3.24 MPa at the focal point. Figure 9 shows the sound pressure level plot (in the acoustics domain as well as in the PML region). We can easily see the diffraction that occurs in the PML region, which is a domain added to damp the pressure field, in other words to absorb all the outgoing waves.

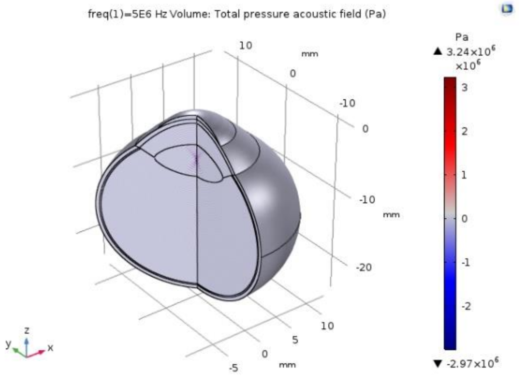

Figure 8. Acoustic pressure field in the eye without PML in 3D, where $p_{max} = 3.268\ MPa$ at (0,5.6322)

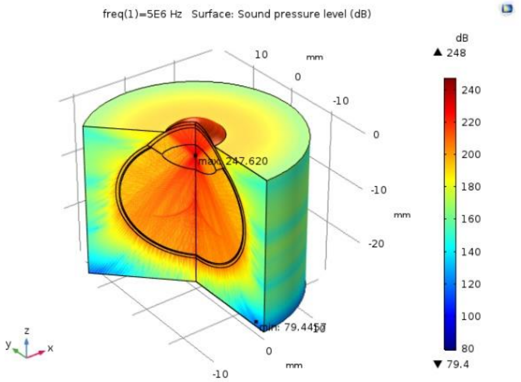

Figure 9. The 3D plot shows the sound pressure level (SPL) in the acoustics domain and the PML region, where $SPL_{max} = 247.6$ and $SPL_{min} = 79.4$.

An illustration of the acoustic intensity magnitude is given in Figure 10. This plot shows more clearly how the acoustic energy is well focused and distributed in the oval-shaped focal zone which is about 1.2 mm long and 0.2 mm wide. Figure 11 shows the acoustic pressure amplitude profile along the z-axis (r=0). As we can see, the amplitude is the highest in the focal zone and oscillates at much lower amplitude in the remaining domains. Figure 12 shows the acoustic pressure amplitude profile along the radial direction in the focal plane (z =5.6322 mm). We can also see that other than the focal zone, the amplitude in the radial direction is oscillating at very low amplitudes.

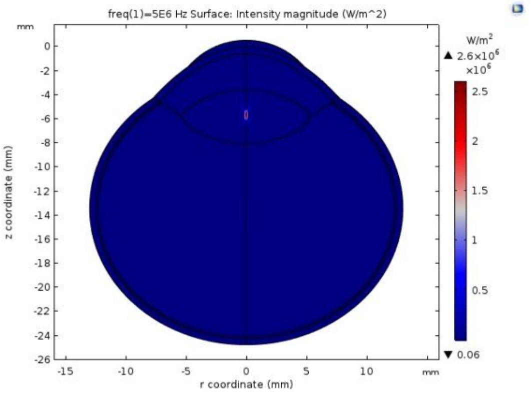

Figure 10. The intensity field in the eye in 2D, where $I_{max} = 2.6 * 10^6 \, {W}/{m^2} = 260 \, {W}/{cm^2}$ at (0,-5.6224)

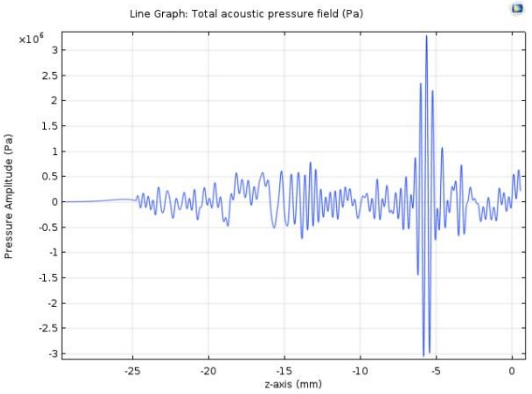

Figure 11. Acoustic pressure amplitude profile along the symmetry axis (r=0)

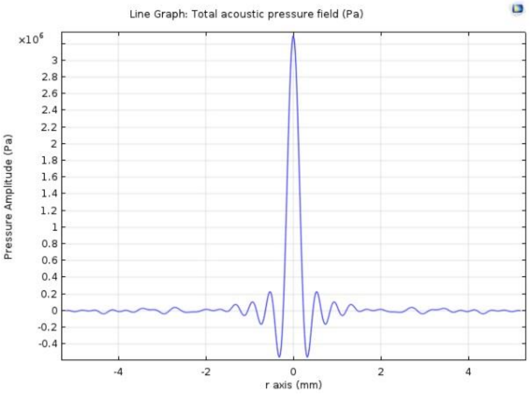

Figure 12. Acoustic pressure amplitude profile along the radial direction in the focal plane

Figure 13 shows the maximum temperature rise at t=1 s, where $\Delta T_{max} = 10.5 \, K$ occurs at (0,-5.6224). The oval-shaped heated zone is about the same size as that of the acoustic focal zone.

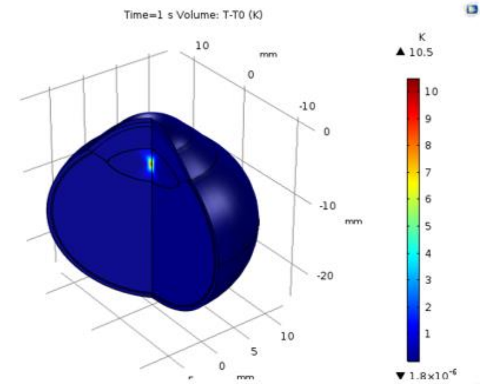

Figure 13. 3D plot of the temperature rise ($\Delta T = T - T0$) in the eye at t=1 s.

Figure 14 plots the heating and cooling curves at acoustic focus and 0.2 mm off in r-direction. As expected, the temperature increases during the exposure of focused ultrasound, from t=0 to t=1 s, hence the events interface has worked perfectly because the maximum temperature rise is exactly at t=1 s. Then, the ocular tissues start to cool down through natural conduction. Also, the temperature reaches a value near zero starting from t=30 s.

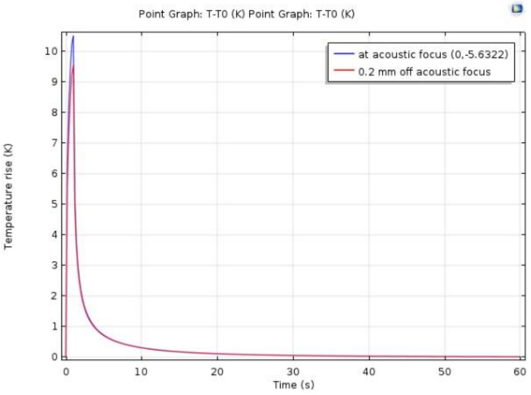

Figure 14. Heating and cooling curve during one minute at acoustic focus and 0.2 mm off in the r-direction.

Figure 15 shows the total displacement field in the lens at t=1s. It is a valuable information to have in order to check that the medical procedure will not change the lens geometry while heating up the focal zone. As we can see the range of values are very small near to zero (the maximum displacement, is equal to 4.6E-10 mm at the focal zone).

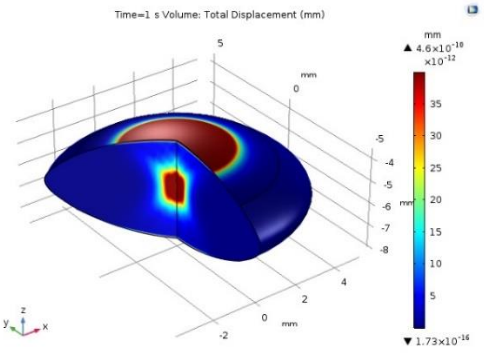

Figure 15. Total displacement field in the lens region due to thermal expansion at t=1 s

6. Conclusions

In order to model focused ultrasound in the eye, four different interfaces of COMSOL Multiphysics® have been used in this work, through the three following approaches. The first approach considered the material properties of the eye parts, as an equivalent fluid, allowing to see the wave propagation and focusing through the eye. This method proved to be simple and easy to set up while providing relatively accurate information, especially regarding the amount of time needed for computation. Then, the second approach, focusing on the acoustic-solid interaction, would have provided new information compared to the first approach: as solids were considered, elastic wave propagation and resulting stresses would have been computed. However, this approach required tremendous amount of computational power, so it has been discarded.   Finally, the third approach proved to be the most efficient of all: first the thermal field has been computed similarly as the first approach, but it was then injected in a separate mechanical study to compute the resulting thermal stresses on a hyperelastic lens. The results obtained for the amount of time needed, were the most effective in comparison with the second approach. There is still some way of improvement for building a more accurate model: first, mechanical and thermal properties as function of temperature may be implemented, so that a bidirectional multiphysics coupling can be set up. Finally, the other remaining parts of the eye like the iris, ciliary body, zonular fibers, and choroid could be integrated, to evaluate the global behavior and the side effects of doing the treatment, on them.

7. References

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