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Computer Modeling and Mapping of Ultrasound Intensity in Human Tissues for Gene and Drug Delivery

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Introduction and Purpose

Over the past years ultrasound has been used extensively in medical treatments. It is now being developed and tested in localized drug and gene delivery. One of the main applications for drug delivery is treating cancer. The first step in this process is to encapsulate the drug in micelles and inject them into the body. An ultrasound transducer is placed over the part of the body where the cancer is located and ultrasound is focused through the body to the tumor site. As the encapsulated drugs pass by, the ultrasound causes the capsules to break apart releasing the drug and the ultrasound also aids in the cells uptake of the drug. An important aspect that there is little data on is how the ultrasound will be scattered or concentrated as it goes into the body and crosses layers of skin, fat, and muscle. If hot spots (high ultrasound intensity) are created in other places besides in the cancerous tissues there could be damage to other tissues from the ultrasonic waves and from the release of the drug at an inappropriate spot.

In order to understand better what happens as ultrasound passes through the different layers of body tissue and bones, the finite element package Comsol was used to make computer models. To do this, the default equation in the Comsol acoustics application was slightly modified to include attenuation of acoustic waves. The following is one setup where the effects of different thickness of fat were investigated

The Setup

The geometry used in the Comsol models is based on the transducer setup used to deliver ultrasound into tumors on the back of rat legs. Because a fine mesh is needed to accurately map ultrasonic waves, three dimensional models use more memory than is available on most workstations. For this reason a two dimensional axisymmetrical model is used to cut down on the memory usage and time. The disadvantage is that the geometry has to be simplified. Figure 1 shows the typical setup used in these studies. The dashed line on the left side is the axis that the entire setup would be rotated around. Figure 1b shows a cut out of what the actual analysis would look like in 3D.

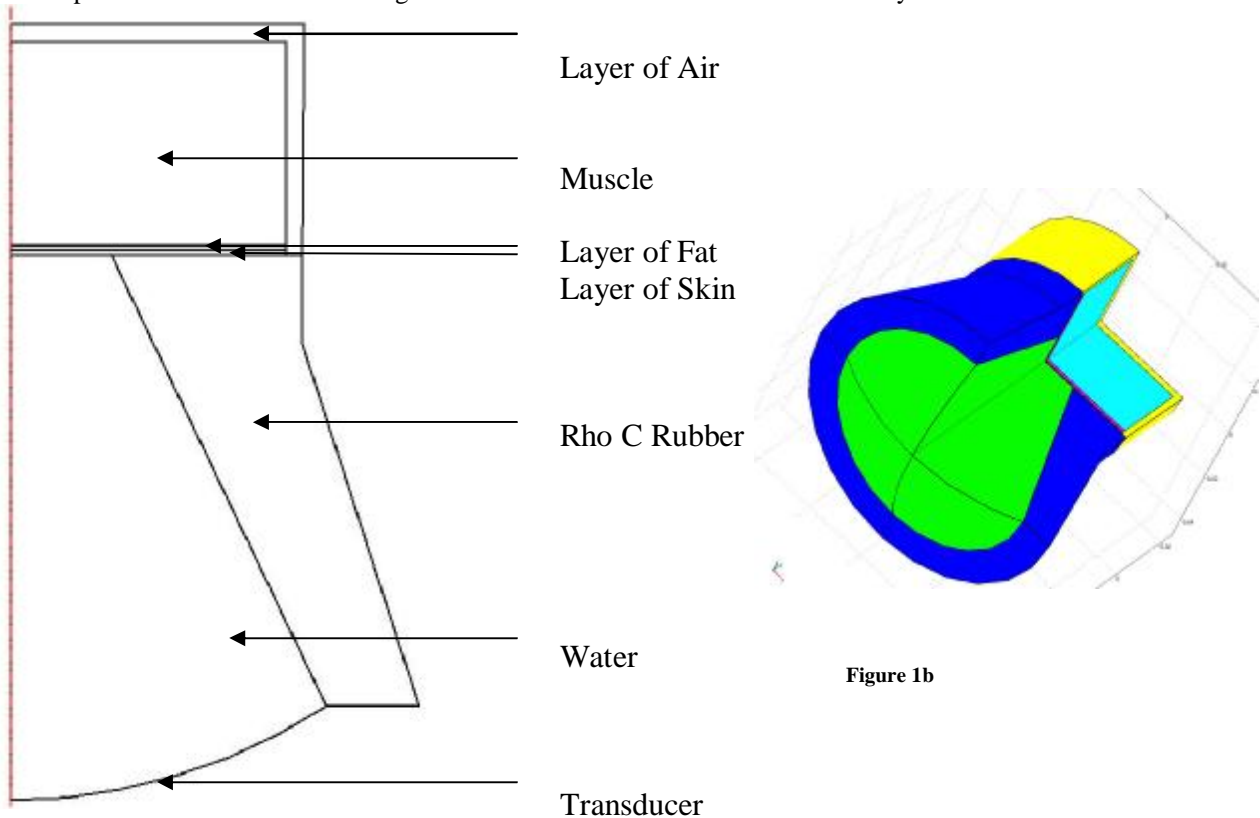


Figure 1a

Results

The geometry was setup to be able to easily change the thickness of the skin and fat then run the FEA analysis. In this study the skin was kept at 0.5mm thick and the fat varied from 0.5mm to 2.5mm. The results are graphed in terms of mechanical index. A mechanical index, an index used to quantify the power of the ultrasound at

that point, of 0.38 was used as the point where cavitation begins to occur and drug release would also begin. The inside area of the plots are areas where the mechanical index is above 0.7 or where tissue damage may begin to occur. This area is represented by the pink area on the inside of the colored area. The outside lavender part is where the mechanical index is above 0.7 but lower than 1.0. Shown in Figure 4a and 4b are two plots, one that shows what the entire geometry looks like with the normal contours of 0.38 and 0.7. The other plot is a surface plot of the mechanical index of the entire area. The results of the finite element analysis in numerical form were used to determine the length and width of the hot spot as well as the maximum mechanical index found. This was done for an area of 2 cm below and above the focal point of the transducer and 1 cm to the side of the focal point. The grid was done with the horizontal and vertical distance between the points of 1.5mm. Chart 1 shows the results of these calculations.

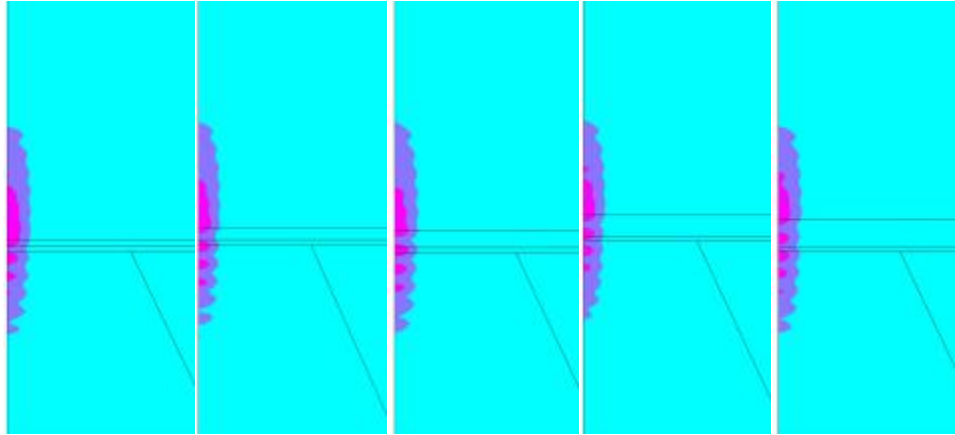


Figure 2 – From left to right, fat thickness of .5mm, 1mm, 1.5mm, 2.0mm, 2.5mm

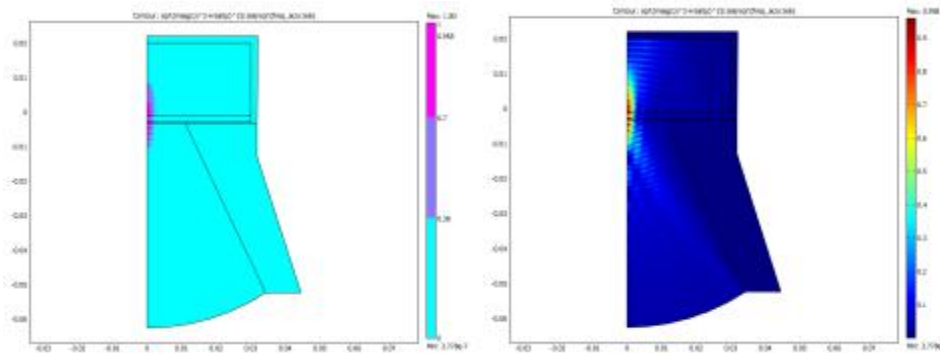


Figure 3 – Contours of mechanical index on left and surface plot on right.

| 0.38 MI and .0005 skin | | | | | | | |
|------------------------|--------|---------------|----------|----------|---------|---------|----------|
| | | fat width (m) | 0.0005 | 0.001 | 0.0015 | 0.002 | 0.0025 |
| hot spot | length | | 18.625 | 19.875 | 18.625 | 18.75 | 19.625 |
| | width | | 4.25 | 4.25 | 4.25 | 4.25 | 4.25 |
| | number | | 2033 | 2025 | 2032 | 2055 | 2053 |
| | max | | 0.946392 | 0.954756 | 0.96753 | 0.92269 | 0.875694 |

Table 1

Conclusions

Overall the changes from one thickness of fat to the other are very small. The 0.38 mechanical index area looks very similar for all of the different fat thicknesses. The 0.7 area changes slightly with thickness. It appears that after going through the skin and fat that the area for the 0.7 mechanical index becomes shorter but is just as wide right afterward passing through the fat. Since the 0.38 mechanical index is the important area for releasing drug, it appears that the thickness of fat has little impact in this setup.

This is an example of some of the comparisons made. For a more complete report email me at spencer_smith@byu.net