Laser Interstitial Thermo-Therapy in Hepatic Tissue

Patrick Ahyow
Brian Lee
Kevin Wong

BEE 453: Computer Aided Engineering for Biomedical Processes
Professor Ashim K. Datta

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1.0 Executive Summary

Laser Interstitial ThermoTherapy (LITT) is a well establish surgical method used in the treatment of tumors. This study analyzes the extent of tissue damage when using LITT in a liver. GAMBIT and FIDAP was used to model a spherical tumor with a diameter of 4cm in a 12cm spherical liver. The mesh that was used contained 14326 nodes which were shown to converge using our mesh convergence analysis. From our sensitivity analysis, the optimal time the laser would be on was determined to be 40 seconds, because this was the time where most of the cancerous tissue was destroyed while keeping healthy tissue damage at a minimum. The optimal laser power was determined to be 30W, which provided the correct amount of heating needed to induce necrosis in the most of the tumor, and maintain a safe temperature below 40^{o}C for healthy liver tissue. However, there a small amount of healthy liver was destroyed, but this could not be avoided due to the cylindrical geometry of the laser applicator. In our sensitivity analysis, we determined that varying the thermal conductivity caused very little change in the average tumor temperature. This indicates that thermal conductivity parameter is relatively insensitive to changes and using our values for thermal conductivity would accurately model the process.

2.0 Introduction

Cancer is currently the second leading cause of death in the United States[1]. Cancer develops in the body when cells begin to grow out of control. Instead of dying, cancer cells continue to grow and divide, outliving normal cells and forming new abnormal ones. Depending on the cancer this can lead to the formation of a tumor[1]. There are several different treatments for cancer, with laser therapy being a relatively new method to treat cancer along with other illnesses.

Liver cancer, or hepatocellular carcinoma, is a relatively uncommon cancer in the United States and many Western countries. In this region, liver cancer is usually a secondary result of a hepatitis infection or severe cirrhosis of the liver due to alcoholism. In the Far East, liver cancer is the most common type of cancer. However, incidence resulting in death per hundred thousand lives in the United States has essentially doubled in the last decade alone from 1.4 to 2.5. Outside of the West, the commonly accepted prognosis is a median survival of 3 months from diagnosis[2]. The carcinoma usually appears in either a nodular or infiltrative form. The nodular tumors are usually round to oval in shape. Therefore, our spherical geometry that is used for the tumor is relatively accurate[3].

Laser radiation is now used routinely in surgery to incise, coagulate, or vaporize tissues. Procedures involving lasers are done by converting energy from the laser light into heat directly at the target species. This results in coagulative necrosis, secondary degeneration and atrophy, and tumor shrinkage with minimal damage to the surrounding structures. Lasers in surgery have many advantages to normal surgical methods, such as increased precision, improved hemostasis, and less tissue manipulation[4].

Lasers can be used to shrink or destroy tumors. However, they are most commonly used to only treat superficial cancers (cancer on the surface of the body or lining of internal organ)[5]. One of the most recent developments in laser therapy, laser interstitial thermotherapy (LITT) can be used for tumors in other locations in the body other than the superficial locations. During this procedure, an optical fiber is inserted into interstitial areas (areas between organs) in the body. The laser light at the tip of the fiber raises the temperature of the tumor cells and damages or destroys them[6].

LITT uses the same idea as a cancer treatment called hyperthermia; where body tissue is exposed to high temperatures (up to 113°F). These high temperatures can damage and kill cancer cells, usually with minimal injury to normal tissue, through damaging proteins and structures within cells[7].

LITT has been shown to be able shrink tumors in the liver[5]. Heat treatment against tumors in this area can also be detrimental to the surrounding tissue. Modeling this procedure would be beneficial in determining how long and at what intensity the laser should be run.

3.0 Design Objectives

Using Laser Interstitial ThermoTherapy to incise, vaporize, or coagulate tissue is becoming a common surgical procedure. The light energy in the laser is converted into heat energy, resulting in localized thermal destruction of the desired tissues. The affects of LITT include coagulative necrosis, secondary degeneration and atrophy, and tumor shrinkage.

The main objective of this project is to use Laser Interstitial ThermoTherapy to induce coagulative necrosis and tumor shrinkage. We are modeling the heat transfer from a Nd:YAG laser to a liver tumor and the surrounding healthy tissue. Using the model we aim to determine the extent of tissue damage of the region where the laser is applied. GAMBIT will be used to create the geometry mesh for the tissue and FIDAP will be used to model the thermal characteristics of the surrounding when the laser is applied. Sensitivity of laser intensity is will also be investigated.

Relevant Parameter Values:
Figure 1: Physical Properties of Liver Tissue.

	Normal Tissue	Tumor
Activation Energy, Ea ($J\ mol^{-1}$)	5.064 x 105	-
Frequency Factor, A (s^{-1})	2.984 x 1080	-
Thermal Conductivity, k ($W\ cm^{-1}\ °C^{-1}$)	0.00520	0.00561
Specific Heat, Cp ($J\ g^{-1}\ °C^{-1}$)	3.60	3.60
Tissue Density, ρ ($g\ cm^{-3}$)	1.06	1.06
Optical penetration depth (mm)	3.0	4.2

3.1 Problem Schematic

Our original design for the schematic was to create a three dimensional model, with a cube for the liver, a spherical tumor, and a cylinder representing the laser applicator. However, due to the complexity of modeling this in Gambit, it was changed to an axi-symmetric model as seen in Figure 3. In this new model the same dimensions were utilized, except now both the liver and the tumor are spheres. Although, the schematic is in a 2-dimension form, being an axi-symmetric model will allow FIDAP to model the heating as though it were in 3-dimensions, with a spherical liver, tumor and cylindrical laser applicator.

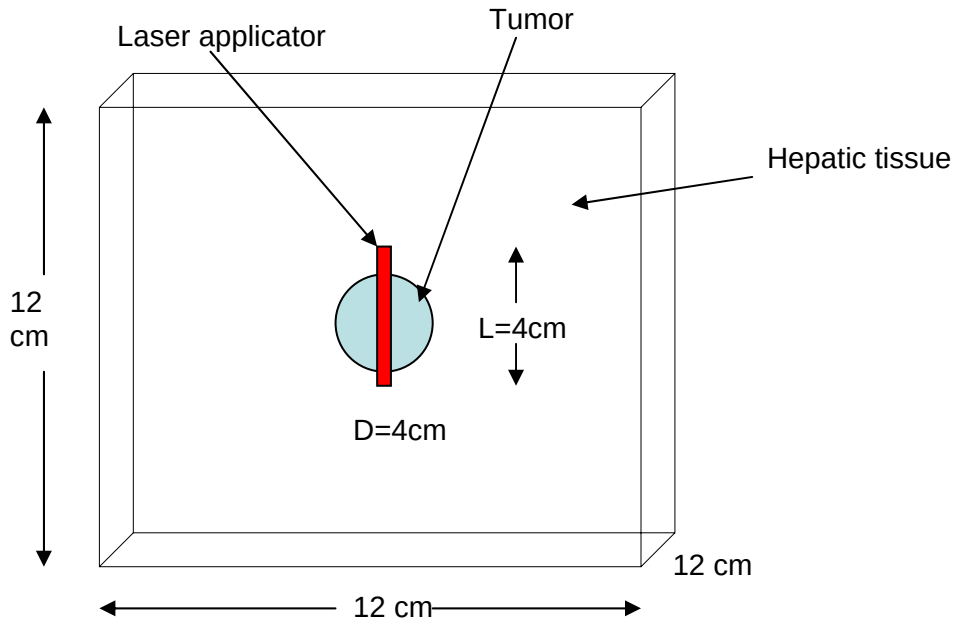


Figure 2. Diagram of 3-D Model with Dimensions.

Laser Applicator dimensions: d=3.0mm, L=4cm, $I = 10^6 \, W/m^2$. Laser power is 30 W.

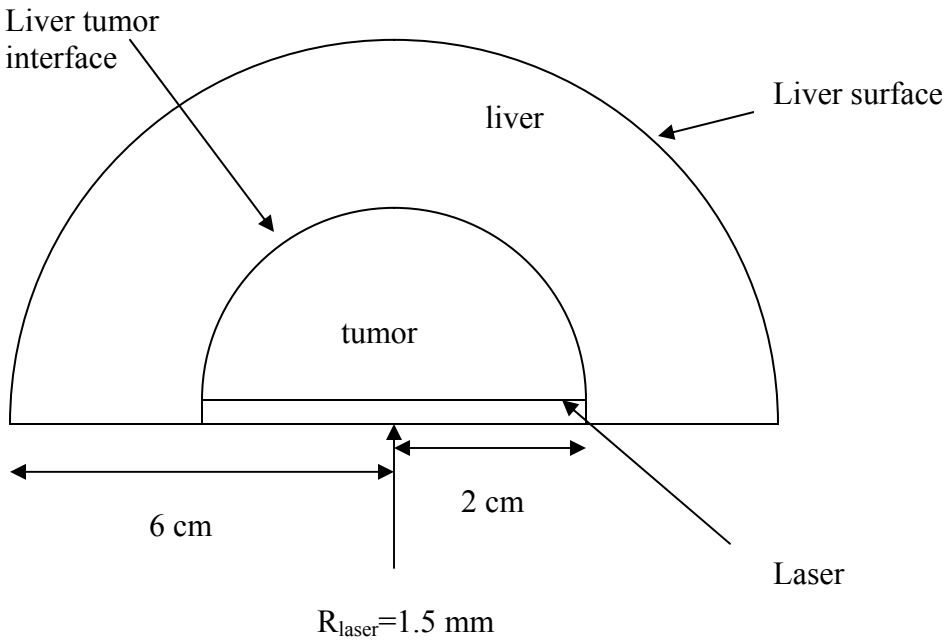


Figure 3. Axi-symmetric Model with Dimensions, using a cylindrical laser applicator that emits radiation radially.

In order to make our model more realistic, we used a subroutine for the heating source term instead of a constant heat flux boundary condition. This helps us in modeling the penetrating effects of a radiative source. A copy of this subroutine can be found in Appendix A.

4.0 Results and Discussion

Our simulation was initially run for 100 seconds. This was decided because the heating from the laser is very rapid, and longer period will be detrimental to the healthy tissue. All properties, boundary conditions, initial conditions, and governing equations are stated in Appendix A. Our goal was to observe the heating of a tumor in hepatic tissue in order to determine the efficacy of LITT for removing tumor tissue. Figure 4 depicts the mesh used for our model containing 14,326 nodes.

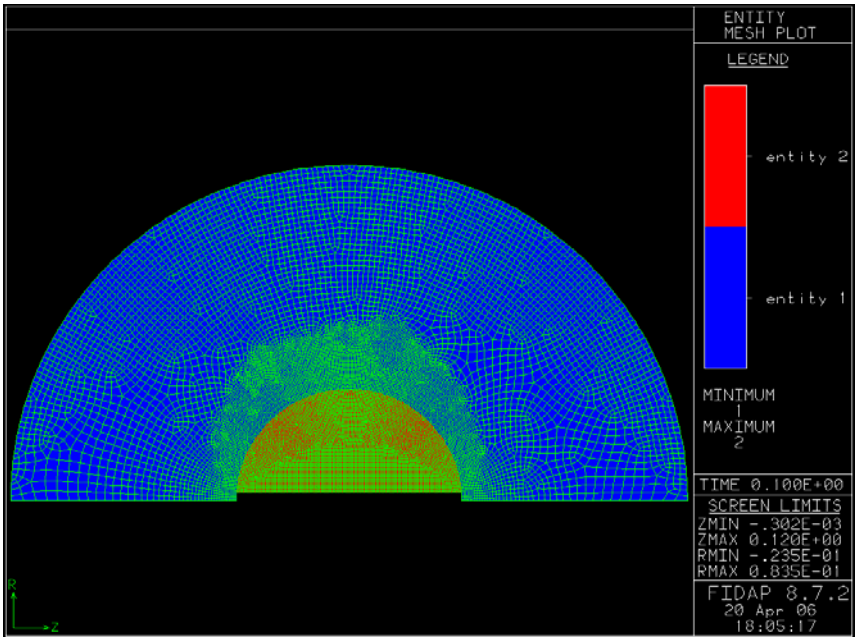


Figure 4. Mesh of Axi-Symmetric Model with the Entites (red=tumor, blue=healthy liver).

The effect from the heating of the laser is shown in Figure 5. This shows temperature contour plot of the two dimensional region after 100 seconds of exposure. The majority of the area of the tumor is heated up by the laser. However, some of the liver tissue is heated as well. Because of the nature of the heating and the geometry of the model this cannot be avoided. However, due to the low thermal diffusivity of the liver, the liver tissue is not greatly affected by the heat source.

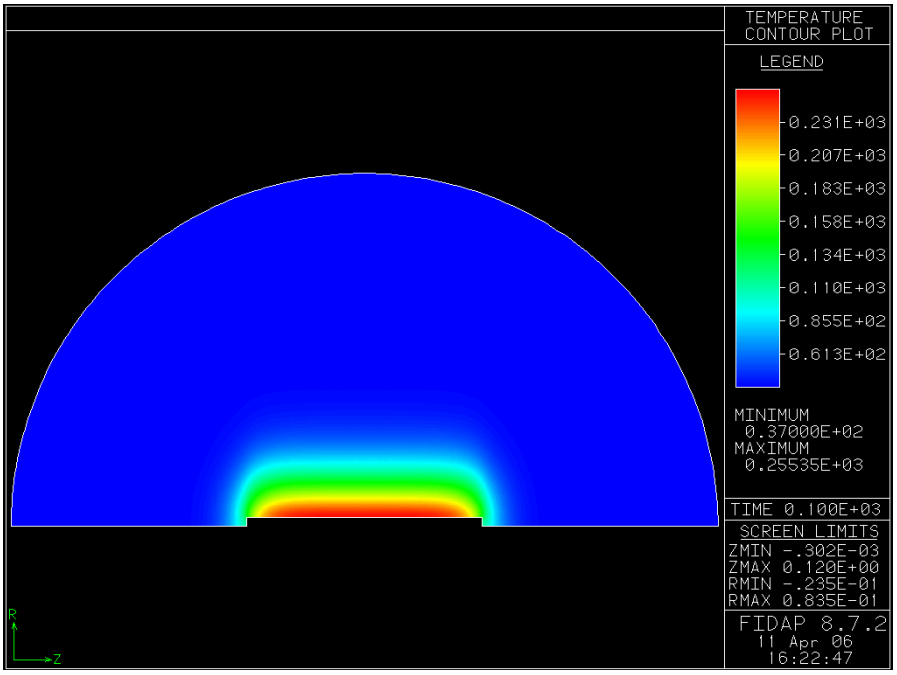


Figure 5. Temperature Contour Plot After 100 Seconds of Heating.

Figures 6 and 7, represent temperature versus time plots at two nodes. One is near the heat source to demonstrate sufficient heating of the tumor tissue for destruction and the second at the interface to show that the heating will not affect much of the healthy liver tissue.

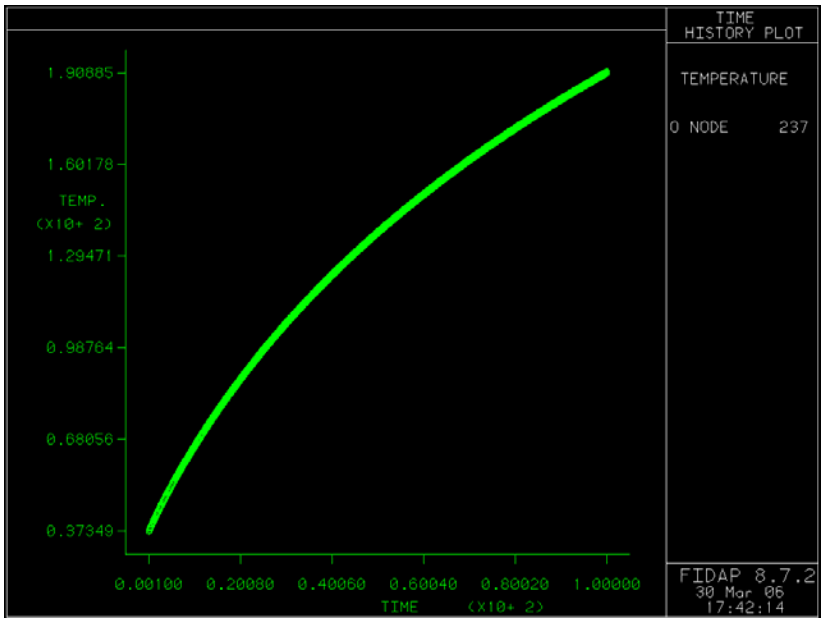


Figure 6. Plot of the temperature of a node near the source of the laser inside the tumor. It is heated up to nearly $200^{\circ}C$ (definitely destroyed).

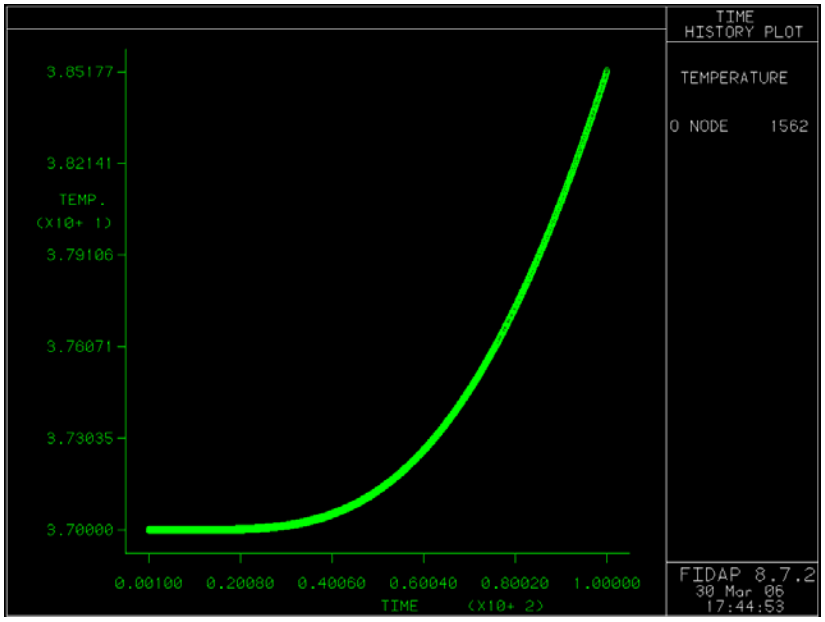


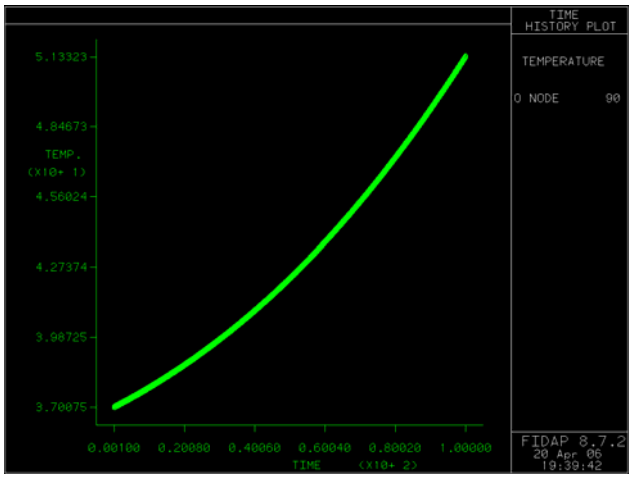
Figure 7. Plot of the temperature of a node near the interface of the tumor and the liver tissue. It is heated up fairly gradually over the 100 seconds about $1.5^{\circ}C$ (tissue intact).

4.1 Sensitivity Analysis

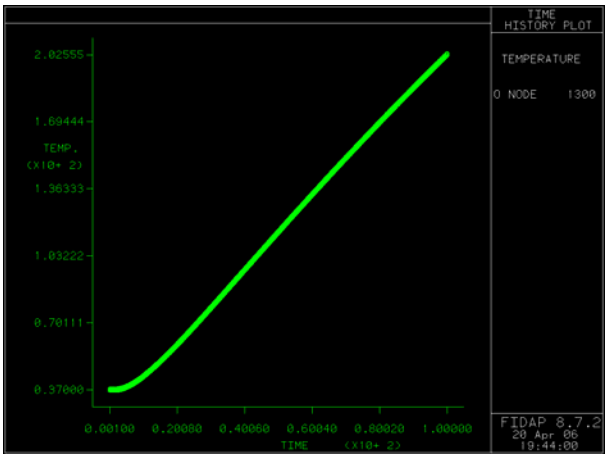
In order to determine the effects of error in our property values and in our solution, the effects of varying time, thermal conductivity of the tumor, and power of the laser were tested.

Time

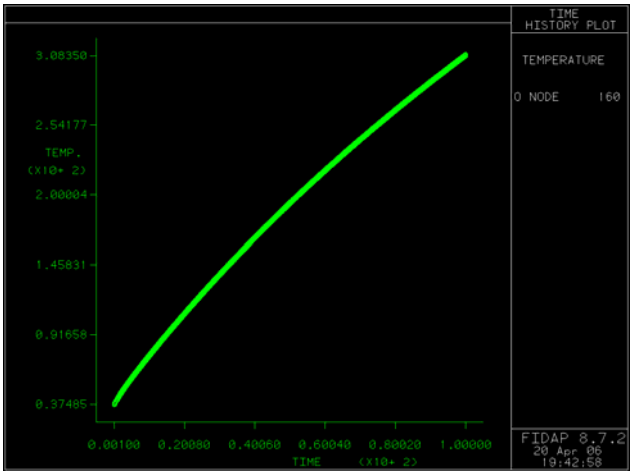
Varying the time is essential in determining the optimal period that the surgery should be performed. To analyze the effect of changing time, temperature versus time plots were mapped at four different nodes, the exact location of the nodes is depicted in Appendix C. As you can see from Figure 8b, much of the tumor tissue is heated to a temperature where it would be destroyed by 40 seconds. However, in Figure 8a, not much of the tumor further away from the heat source will be destroyed even after 100 seconds. This cannot be avoided because if the heating continued further, more healthy tissue would be damaged. A possible solution in real life would be to move the laser around or cycle it on and off to achieve full heating of the tumor while preserving most of the healthy liver. In Figures 8c and 8d, the majority of the healthy tissue is still intact within the 40 seconds. Some good liver tissue is damaged by this time step; however, this is essential if we want to have as much of the tumor removed from the system.



8a.



8c.



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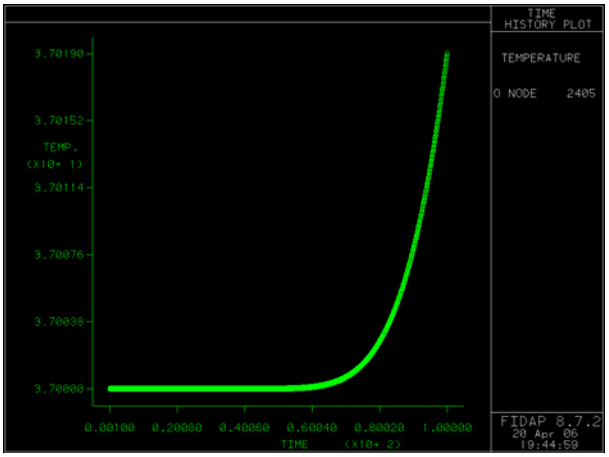


8d.

Figure 8. Temperature Versus Time Plots for (a) node 90, top of the interface between the tumor and liver tissues, (b) node 160, side of the interface between the tumor and liver tissue, (c) node 1300, side of the healthy tissue near the heat source, (d) node 2405, side of the healthy tissue further away from the heat source.

Thermal Conductivity of the Tumor

Varying the thermal conductivity of the tumor between 0.561 W/m/°C, 0.611 W/m/°C, and 0.661 W/m/°C does not appear to have any significant effect in the heating of the tumor. As you can see in the plot below, the three plots for each of the thermal conductivity values overlap each other with very little variation amongst themselves. This clearly displays the extremely small effect of varying the thermal conductivity has on this model. Therefore, any potential error that arises from not knowing the exact thermal conductivity of the tumor tissue (as it may vary in case to case) can be ignored.

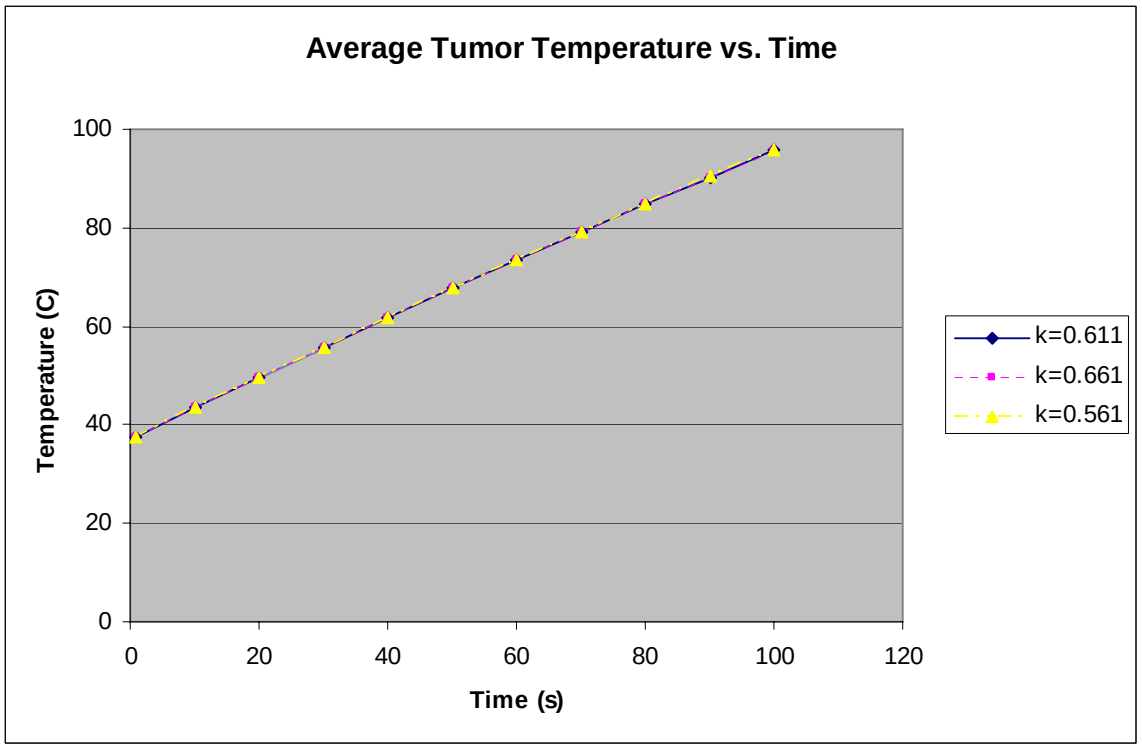


Figure 9. Average Tumor Temperature Versus Time Plot with varying tumor thermal conductivity.

Laser Power

As you can see in the temperature contours (Figure 11), varying the power of the laser between 20W, 30W, 50W, and 100W does not affect the distance the heat spreads, it only affects the level of the heating. As seen in Figure 11, the main effect of changing the laser power is the temperature the tumor is heated to. Anything above the 30W laser is excessive and unnecessary to the heating of the tumor. Therefore, choosing to stay with a 30W laser is the best choice for this model.

Penetration depth (δ) is dependent on laser power. However, when we performed the laser power sensitivity analysis we assumed that the penetration depth remains constant, in order to simplify the model. We should perform sensitivity analysis on one variable at a time.

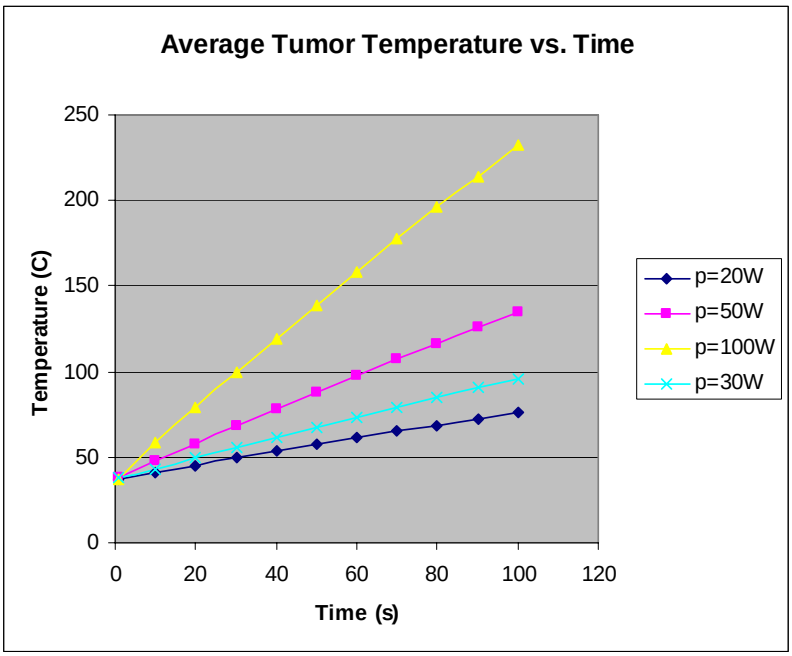
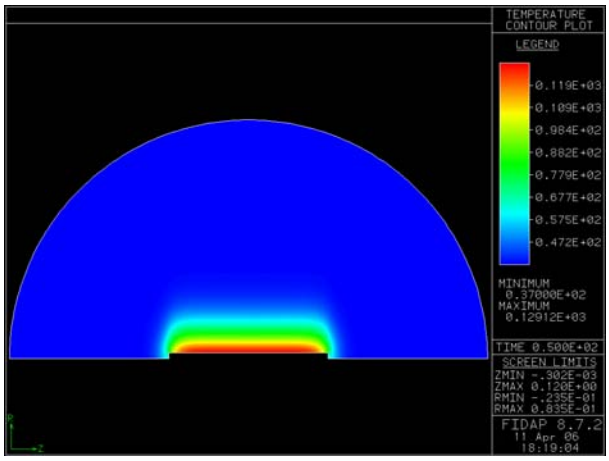
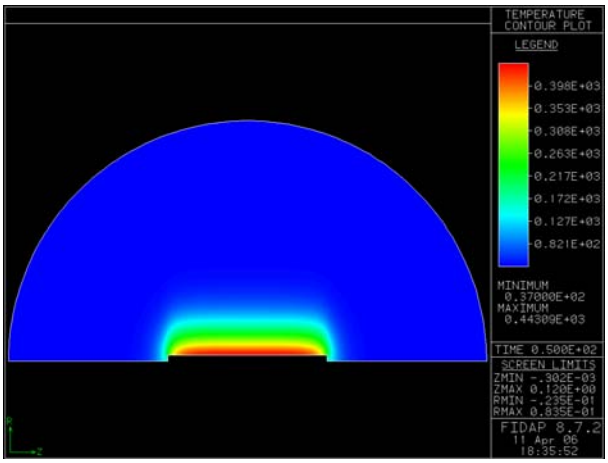


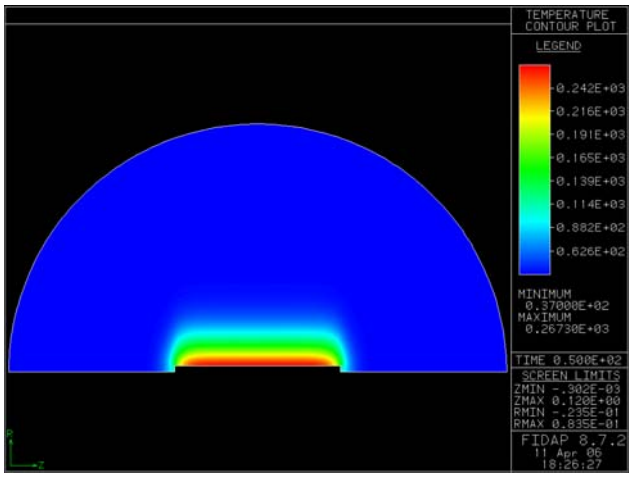
Figure 10. Average Tumor Temperature Versus Time Plot with Varying Laser Power.



11a.



11c.



11b.

Figure 11. Temperature Contour Plots at 50 seconds and powers of (a) 30W, (b) 50W, and (c) 100W.

5.0 Conclusions and Design Recommendations

The goal of Laser Interstitial Thermotherapy is to destroy the majority of a hepatic tumor using heat generated from a laser. From the sensitivity analysis, the time it takes for the laser to destroy most of the tumor is 40 seconds when the laser power is 30 watts. In our sensitivity analysis of the laser power, we used the same amount of time for the varying laser power. Even when the power changed the heat gradient did not seem to change. However, all of the temperatures increased with increasing power. Therefore, we used the same amount of time because a smaller amount of time would result in a smaller penetration of the heat inside the tumor. The optimal power for the laser was determined to be 30 watts since the time length required to destroy most the tumor was short enough so that most of the health tissue remained unharmed. We estimated tissue necrosis due to heating at 80^{o}C and for healthy tissue to remain below 40^{o}C in order to remain unharmed.

Normally, having a higher laser power but a shorter time of exposure is used in heating tissues to destroy tissues locally. However, we wish to heat up most of the tumor. Using our cylindrical laser on a spherical tumor would not result with heating most of the tumor because of the low thermal conductivity of the tumor. Therefore, a lower power and a longer time of exposure were used to help heat a larger portion of the tumor.

Another possible method to isolate the thermal destruction of the cancerous tissue is to cycle the laser on and off. By increasing the average power of the laser and increasing the amount of time between when the laser is on, the overheating of healthy tissue is minimized. In addition, various average power and duty cycles of laser pulses can be tested and optimized for LITT.

Discussion on Realistic Constraints:

Economic

LITT would be a relatively expensive procedure due to the high cost of the equipment involved. The laser applicator has a special applicator that emits the laser radiation radially compared to the convectional laser applicator that focuses a single coherent beam. The physician using the equipment would also have to be professionally trained in order to become a certified user. However, the long term economic effects are beneficial because the equipment can be used multiple times.

Safety and Health

LITT is one of the more safe procedures in tumor removal. Tissue necrosis bought on by LITT has relatively few detrimental effects to the surrounding tissues. The healing time for the healthy tissue after the procedure is less than that of a surgical removal of the tumor. There is also minimal bleeding during the procedure helping with the recovery of patients. We recommend using a low power laser to minimize normal tissue destruction and connecting the laser to a computer that would be able to control and observe the whole process to minimize any human errors. However, damaging a small part of healthy liver is not extremely detrimental because the liver is one of the organs that are able to regenerate.

Appendix A: Mathematical Statement of the Problem

Governing Equations

We use a simple cylindrical coordinate system in modeling the heat transfer the governing equation is,

$$\rho c_p \frac{\partial T}{\partial t} = k\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial T}{\partial r}\right)+\frac{1}{r^2}\left(\frac{\partial^2 T}{\partial \phi^2}\right)+\frac{\partial^2 T}{\partial z^2}\right)+Q, (1)$$

where ρ = density of the tissue

c_p = heat capacity of the tissue

T = temperature

t = time

k = thermal conductivity

r = radial distance

and the z and ϕ terms will be dropped because they do not have any variation.

The heat is generated from the laser's applicator which is 3 mm in diameter. As the laser hits the tissue, absorption and scattering effects take place. However, the intensity of the laser can be simplified to an exponential decay function. Volumetric heat generation can be thought of as the difference between the heat flux into the volume minus the heat flux out of the volume,

$$Q \cdot 2\pi r \cdot \Delta r = q_r" \cdot 2\pi r - q_{r+\Delta r}" \cdot 2\pi(r+\Delta r). (2)$$

This can be simplified to,

$$Q = -\frac{1}{r}\frac{\partial}{\partial r}(r \cdot q_r"). (3)$$

The heat flux due to laser intensity can be modeled by

$$q_r" = I_0 e^{(r_0 - r)/\delta}, (4)$$

where r_0 is the radius of the cylindrical laser and δ is the penetration depth. By combining equations (3) and (4) we obtain

$$Q = -\frac{1}{r}\frac{\partial}{\partial r}\left(I_0 r e^{\frac{r_0 - r}{\delta}}\right), (5)$$

which can be simplified. Therefore, the volumetric heat generation is given by

$$Q = I_0 e^{\left(\frac{r_0 - r}{\delta}\right)}\left(\frac{1}{\delta}-\frac{1}{r}\right). (6)$$

However, from equation (6), we see that when $r < \delta$ there is a negative volumetric generation. Therefore, we determined the maximum heat source generation by the laser in the tumor from equation (6) and set the heat generation at distances less than where the maximum occur to the maximum heat generation to ensure a strictly decreasing exponential decay function.

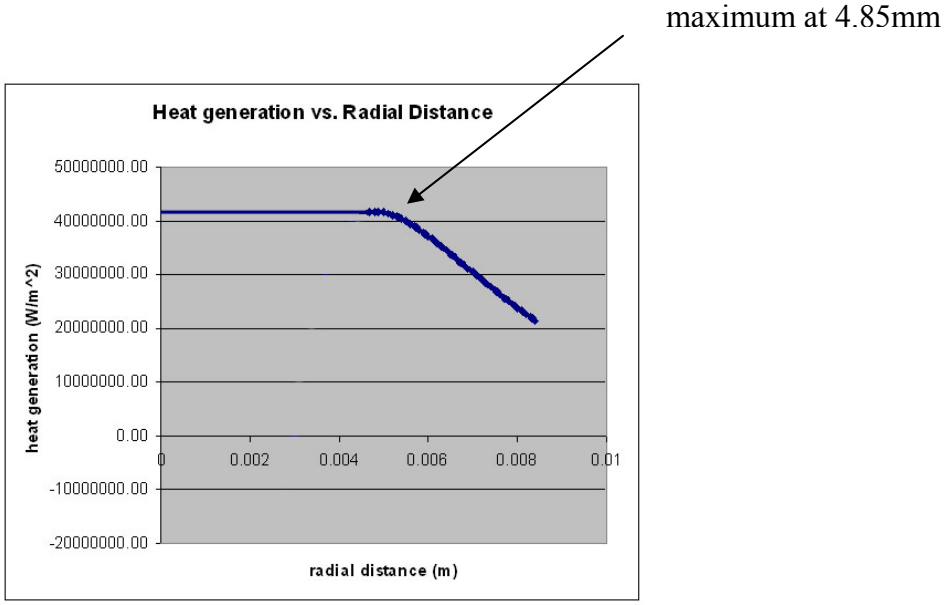


Figure 12. Graphical representation of Q function.

Therefore, we devised a two step function:

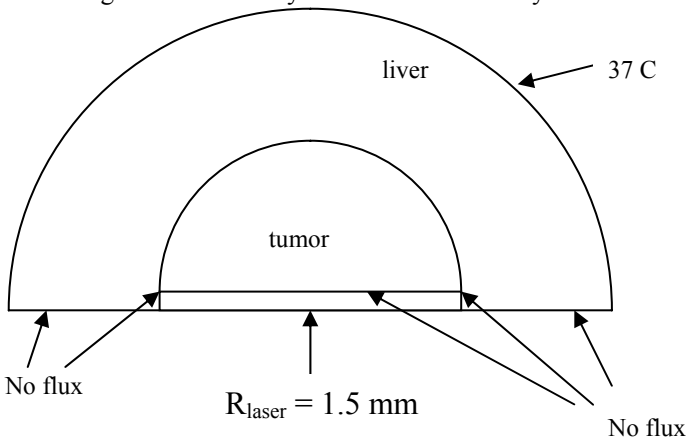
$$0 < r \le 0.00437; Q = 6659882.182 \frac{W}{m^3}$$
$$r > 0.00437; Q = I_o e^{\frac{r_o - r}{\delta}} \left(\frac{1}{\delta} - \frac{1}{r} \right) \quad (7)$$

Boundary Conditions

The laser applicator contains a water jacket to cool the surface. This allows us to assume a no heat flux boundary condition across the applicator boundary. We will also assume a constant temperature boundary condition for all of the edges of the liver.

(For Axisymmetric model)
All boundary conditions are the same with the exception of the outer boundary of the cylindrical tumor has a constant temperature boundary condition. (shown below)

Figure 13. Boundary Conditions for Axi-Symmetric Model.



Initial Condition

The initial temperature of the entire system will be considered to be at the normal body temperature of $37^{\circ}C = 310\,K$.

Initial Parameters

Input Parameters	
Liver Density	1060 kg/m^3
Liver Thermal Conductivity	0.52 W/m/°C
Liver Specific Heat	3600 J/kg°C
Tumor Density	1060 kg/m^3
Tumor Thermal Conductivity	0.561 W/m/°C
Tumor Specific Heat	3600 J/kg°C
Liver Surface Constant Temperature	37 °C
Laser Bottom Heat Flux	0 W/m^2°C
Laser Sides Heat Flux	0 W/m^2°C
Liver Initial Temperature	37 °C
Tumor Initial Temperature	37 °C
δ (penetration depth)	0.00437

Figure 14. Table of Input Parameters for FIDAP.

```
BCNO (TEMP, CONS = 37.0, ENTI = "liversurface")
 BCFL (HEAT, CONS = 0.000000000000E+00, ENTI = "laser")
 BCFL (HEAT, CONS = 0.000000000000E+00, ENTI = "laserend")
 ICNO (TEMP, CONS = 37.0, ENTI = "liver")
 ICNO (TEMP, CONS = 37.0, ENTI = "tumor")
```

Subroutine

```
do n = 1,NPTS
        r = XYZL(N,2)
        f = exp(-(r-0.0015)/0.003)
        if (XYZL(N,1).LT.(0.04).OR.XYZL(N,1).GT.(0.08)) then
                SORCE(n) = 0
        else if (r.LT.(0.00473)) then
                r = 0.00473
                f = exp(-(r-0.0015)/0.003)
                SORCE(n) = -(1/r)*1.6e5*f+(1.6e5/0.003)*f
        else
                SORCE(n) = -(1/r)*1.6e5*f+(1.6e5/0.003)*f
        endif
ENDDO
```

Appendix B: Problem Statement

Problem Statement

Below is a table representing the settings for the problem that was designed for this model.

```
PROB (AXI-, BUOY, NOMO, TRAN, LINE, FIXE, NEWT, INCO)
```

Descriptor	Value	Explanation
Geometry Type	AXISYMMETRIC	System is symmetric about an axis
Temperature Dependence	ENERGY	We are interested in temperature changes
Flow Type	NO MOMENTUM	There is no flow in our model
Simulation Type	TRANSIENT	Solution is time dependent
Convective Term	LINEAR	There is no flow in our model
Surface Type	FIXED	Surface is fixed

Figure 15. Table of Problem Settings used in FIDAP.

Time Integration Statement

For our analysis of Laser Interstitial Thermo-Therapy (LITT) to induce coagulative necrosis and tumor shrinkage, we used a relatively short time period of 100 seconds. Since LITT very rapid tissue damage, a longer time period is not needed. Because our time period is short and our geometry is relatively simple, we used a small time step of 0.1.

```
TIME (BACK, FIXE, TSTA = 0.000000000000E+00, TEND = 10.0, DT = 0.1,
NSTE = 100)
```

Descriptor	Variable	Value
No. of Time Steps	Nsteps	1000
Starting time	Tstart	0
Ending time	Tend	100
Time Step	Dt	0.1
Time stepping algorithm	Fixed	

Figure 16. Table with Settings for Time Integration for FIDAP.

Element Mesh

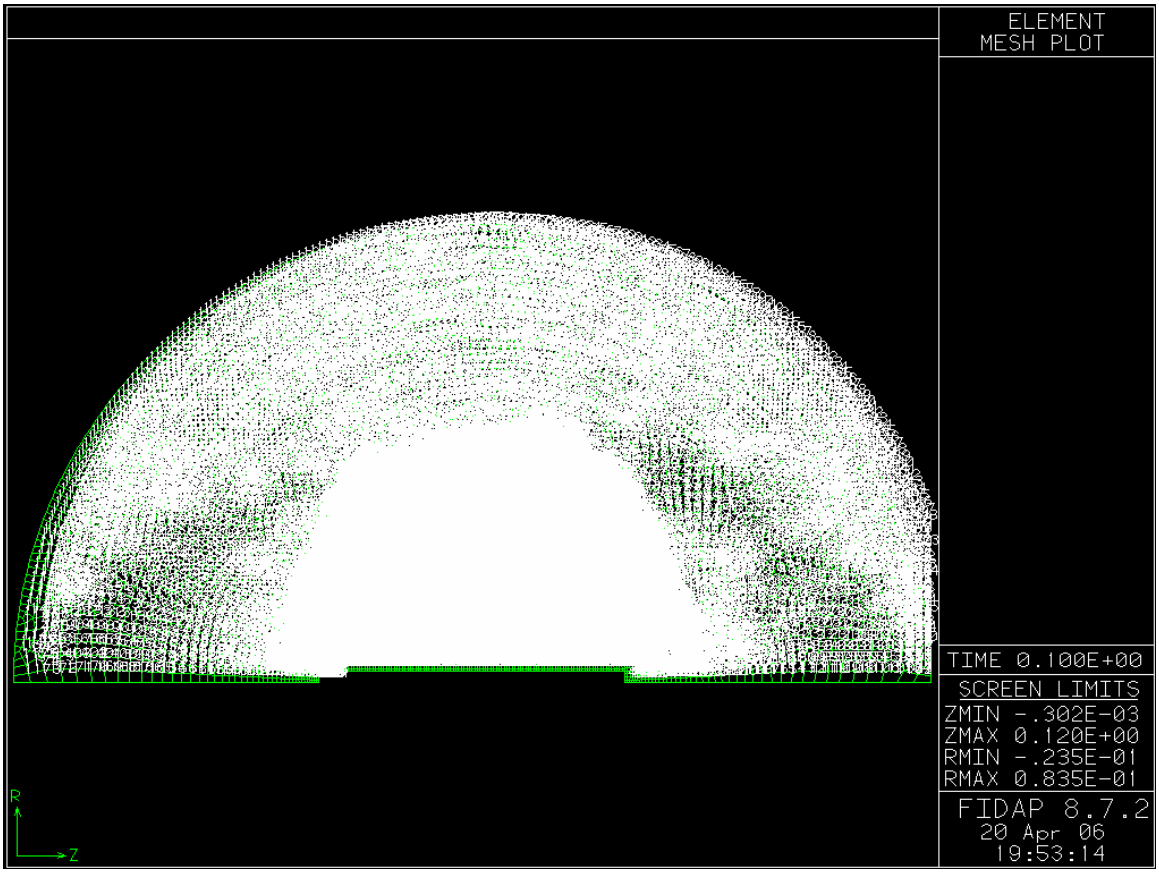


Figure 17. Element Mesh of Model.

Mesh Convergence

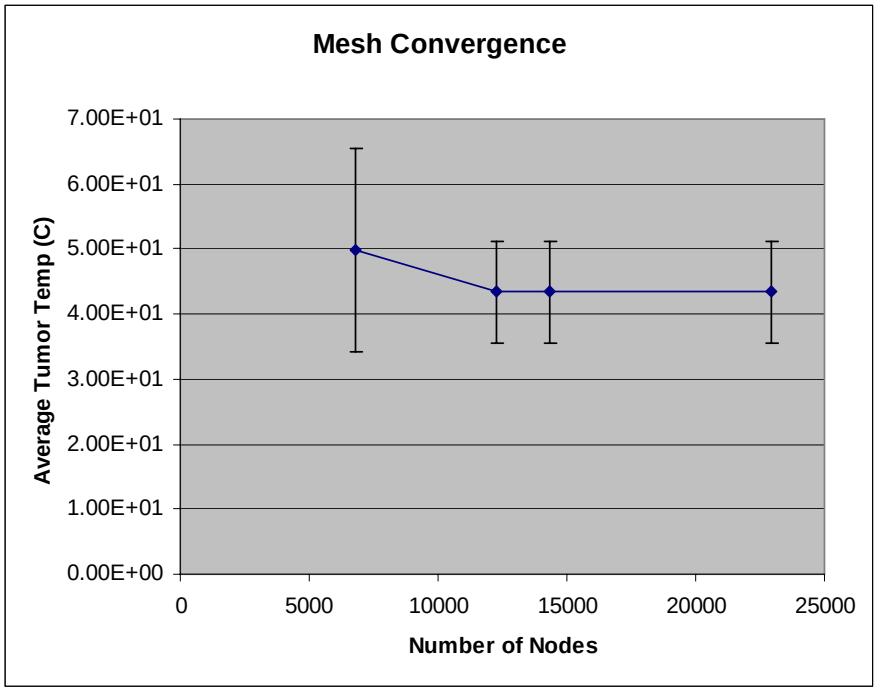


Figure 18. Plot of Average Tumor Temperature Versus Number of Nodes for Mesh Convergence.

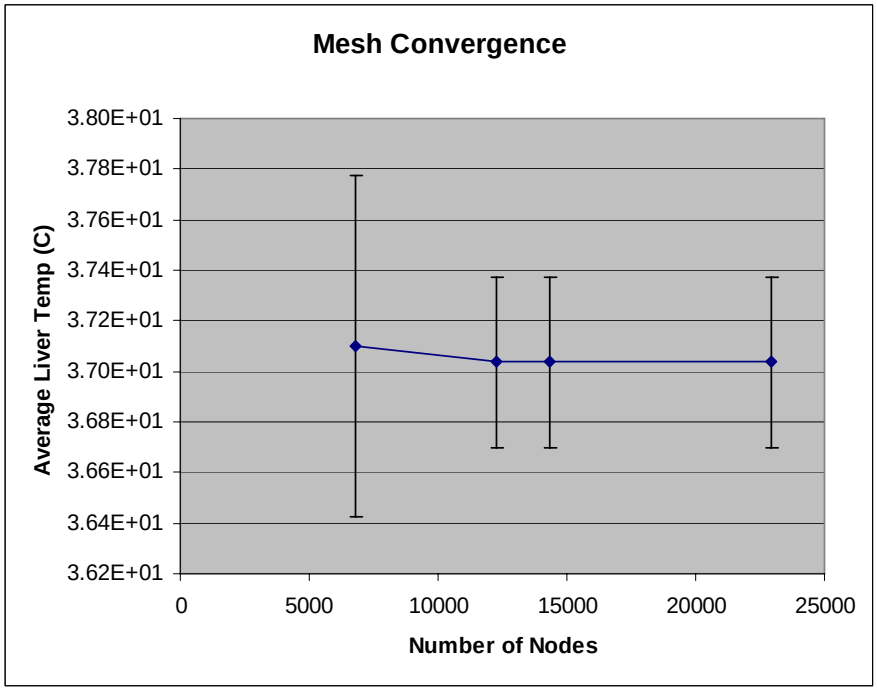


Figure 19. Plot of Average Liver Temperature Versus Number of Nodes for Mesh Convergence.

Appendix C: Data.

Mesh Convergence

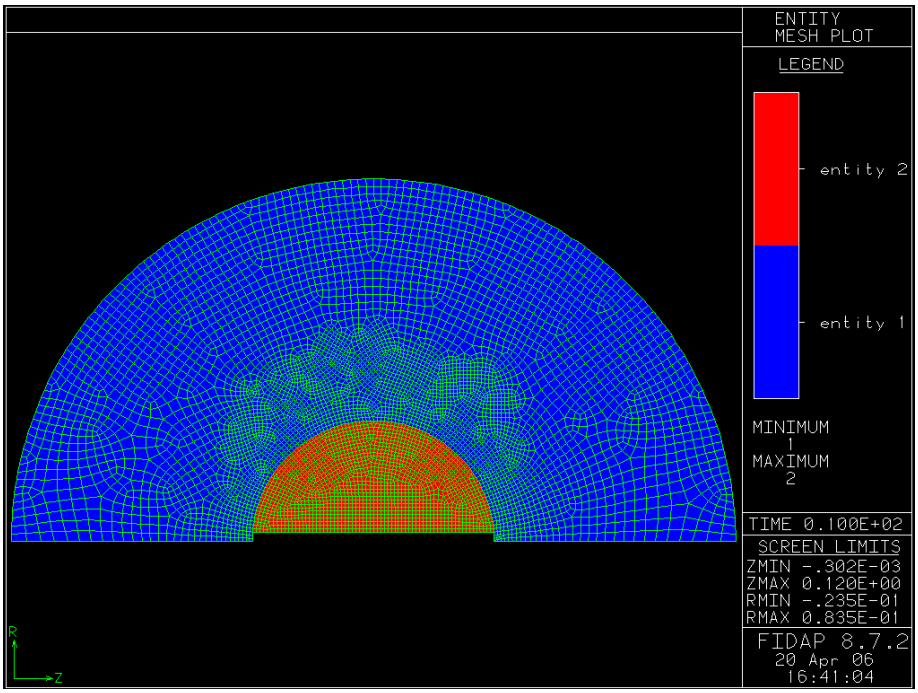


Figure 20. Mesh with 6797 Nodes.

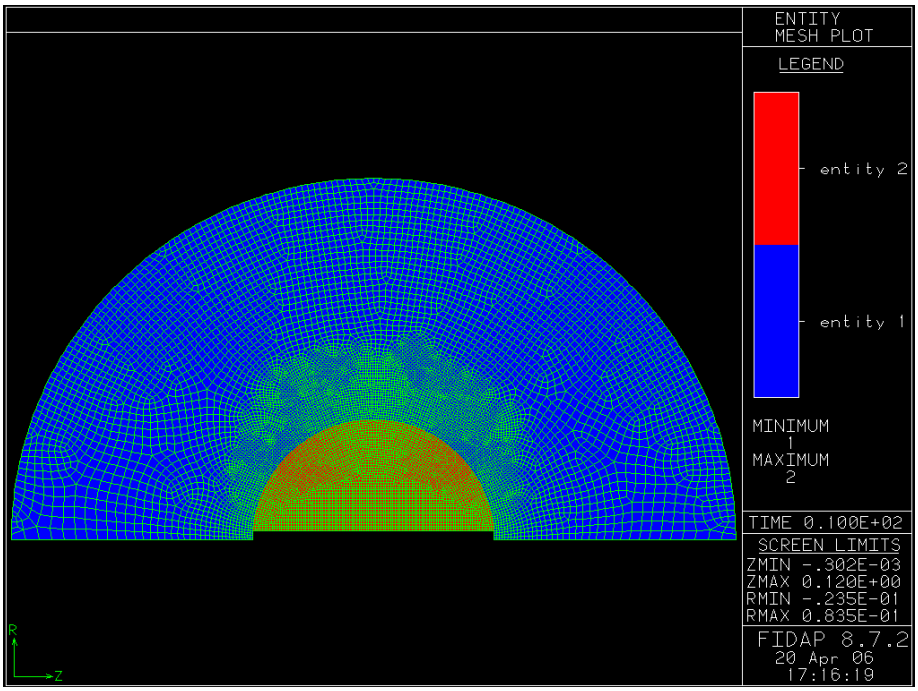


Figure 21. Mesh with 12289Nodes.

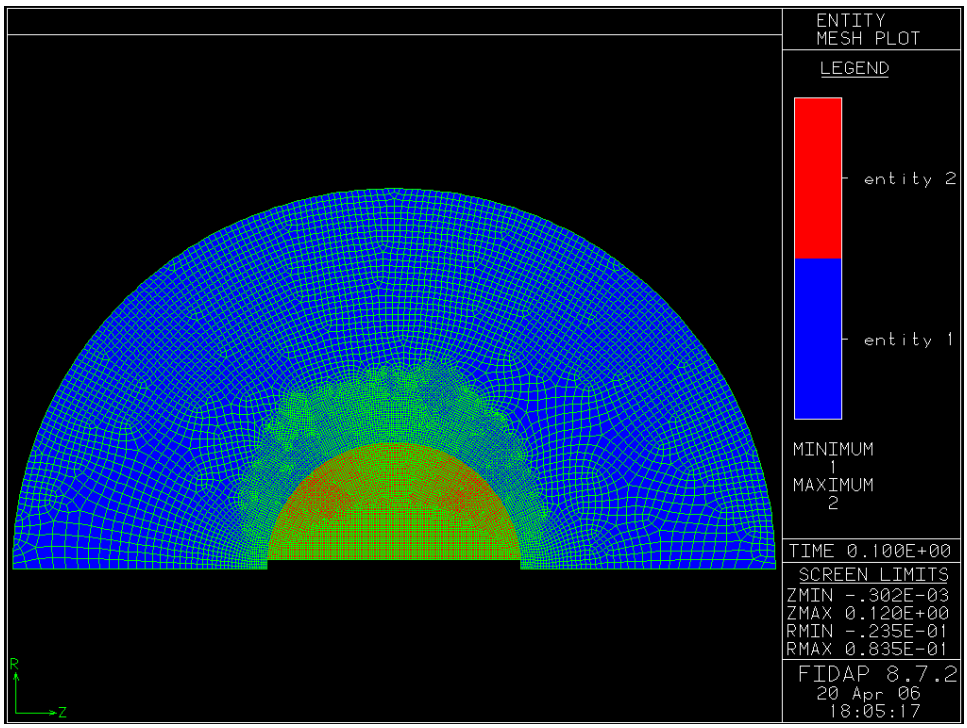


Figure 22. Mesh with 14326 Nodes.

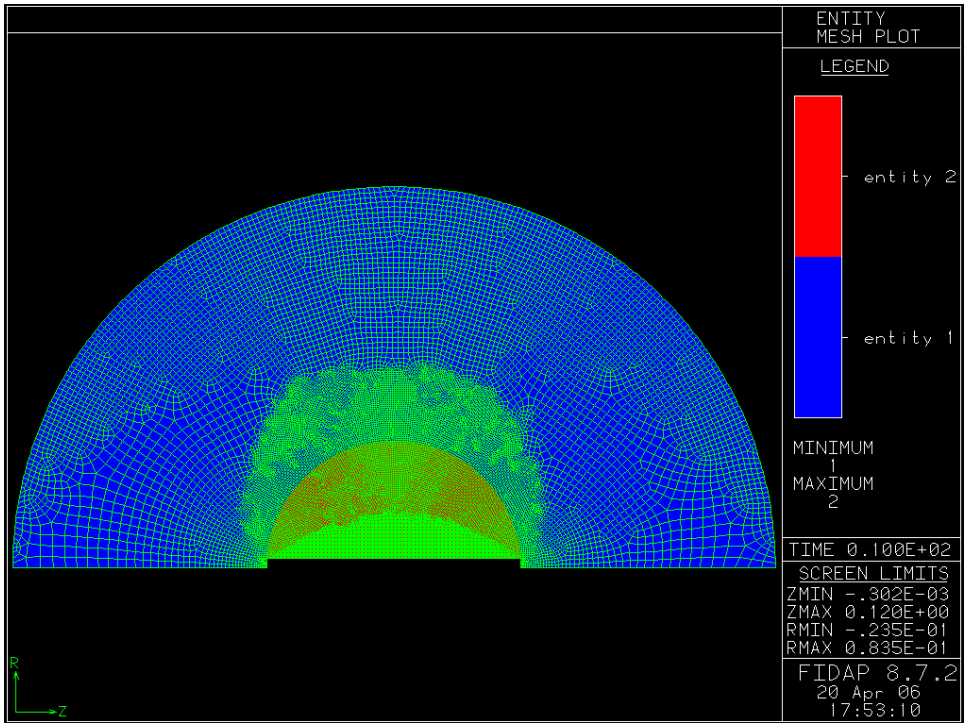


Figure 23. Mesh with 22923 Nodes.

Location of nodes used for time sensitivity analysis.

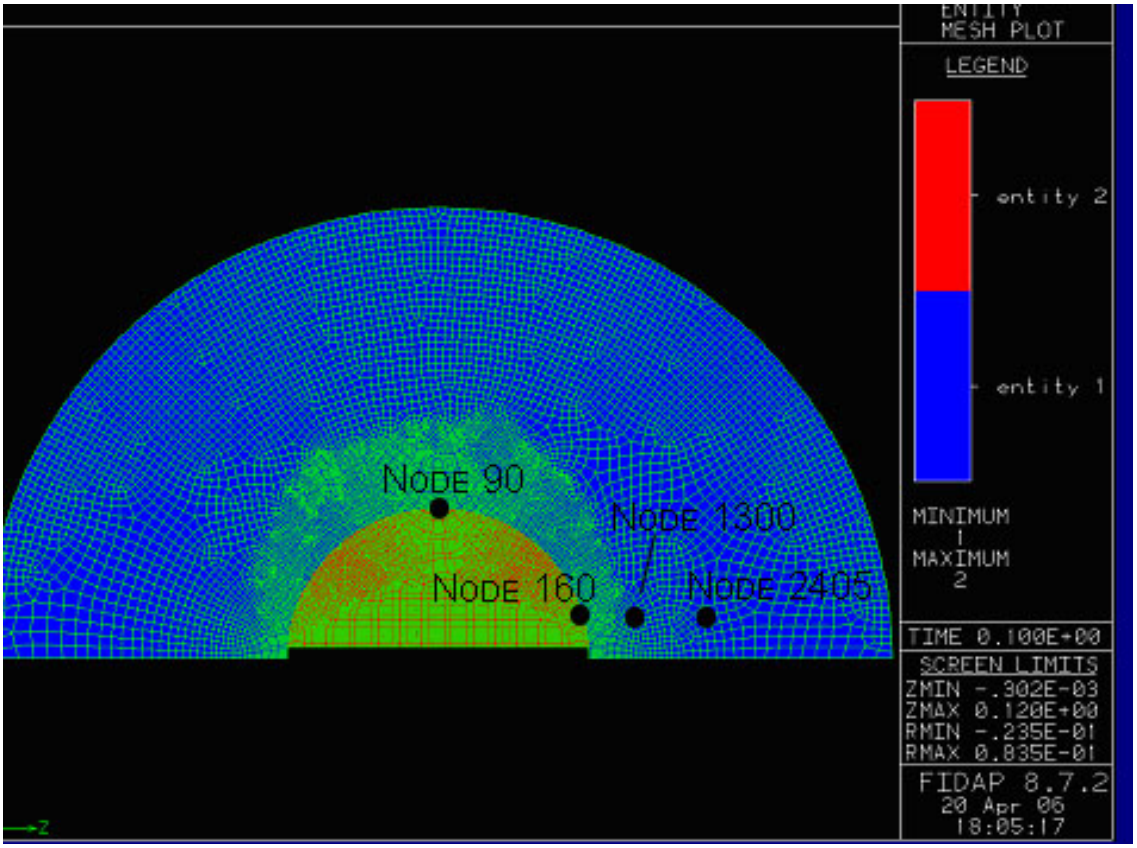


Figure 24. Location of Nodes for Figure 8.

Fidap Input File

```
/  INPUT FILE CREATED ON 05 Apr 06 AT  16:28:56
/
/ ***  FICONV Conversion Commands ***
/ ***  Remove / to uncomment as needed
/
/  FICONV(NEUTRAL,NORESULTS,INPUT)
/  INPUT(FILE= "laserV3.FDNEUT")
/  END
/  *** of FICONV Conversion Commands
/
TITLE

/
/ ***  FIPREP  Commands ***
/
FIPREP
 PROB (AXI-, BUOY, NOMO, TRAN, LINE, FIXE, NEWT, INCO)
 PRES (MIXE = 0.100000000000E-08, DISC)
 EXEC (NEWJ)
 SOLU (S.S. = 50, VELC = 0.100000000000E-02, RESC = 0.100000000000E-01,
       SCHA = 0.000000000000E+00, ACCF = 0.000000000000E+00)
 TIME (BACK, FIXE, TSTA = 0.000000000000E+00, TEND = 10.0, DT = 0.1,
NSTE = 100)
 OPTI (SIDE)
 DATA (CONT)
 GRAV (MAGN = 0.000000000000E+00, THET = 0.000000000000E+00,
       PHI = 0.000000000000E+00)
 PRIN (NONE)
 POST (RESU)
 SCAL (VALU = 1.0)
 ENTI (NAME = "liver", SOLI, PROP = "mat1")
 ENTI (NAME = "tumor", SOLI, PROP = "mat2")
 ENTI (NAME = "liversurface", PLOT)
 ENTI (NAME = "interface", PLOT)
 ENTI (NAME = "liveraxis", PLOT)
 ENTI (NAME = "laser", PLOT)
 ENTI (NAME = "laserend", PLOT)
 DENS (SET = "mat1", CONS = 1060.0)
 DENS (SET = "mat2", CONS = 1060.0)
 SPEC (SET = "mat1", CONS = 3600.0)
 SPEC (SET = "mat2", CONS = 3600.0)
 COND (SET = "mat1", CONS = 0.52)
 COND (SET = "mat2", CONS = 0.561)
 BCNO (TEMP, CONS = 37.0, ENTI = "liversurface")
 BCFL (HEAT, CONS = 0.000000000000E+00, ENTI = "laser")
 BCFL (HEAT, CONS = 0.000000000000E+00, ENTI = "laserend")
 ICNO (TEMP, CONS = 37.0, ENTI = "liver")
 ICNO (TEMP, CONS = 37.0, ENTI = "tumor")
 EXTR (ON, AFTE = 5, EVER = 5, ORDE = 3, NOKE, NOFR)
END
/  *** of FIPREP Commands
CREATE(FIPREP,DELE)
CREATE(FISOLV)
PARAMETER(LIST)
```

Appendix D: References

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2. "Deaths from Liver Cancer" Wrong Diagnosis. 5 May 2006 http://www.wrongdiagnosis.com/l/liver_cancer/deaths.htm
3. "Hepatocellular carcinoma." Wikipedia, The Free Encyclopedia. 16 Apr 2006. 5 May 2006 <http://en.wikipedia.org/w/index.php?title=Hepatocellular_carcinoma&oldid=48707429>.
4. Mohammed, Yassene; Verhey, Janko F. A finite element method model to simulate laser interstitial thermotherapy in anatomical inhomogeneous regions. *BioMedical Engineering Online.* 04 January 2005.
5. "Lasers in Cancer Treatment." National Cancer Institute. 5 May 2006 http://www.cancer.gov/cancertopics/factsheet/Therapy/lasers
6. "Lasers in Cancer Treatment." CancerMail from the National Cancer Institute. 5 May 2006 https://www.meb.uni-bonn.de/cancernet/600078.html
7. "Hyperthermia in Cancer Treatment." National Cancer Institute. 5 May 2006 http://www.cancer.gov/cancertopics/factsheet/Therapy/hyperthermia