EXECUTIVE SUMMARY

Coronary artery disease involves the buildup of plaque (from cholesterol) on the inside of the arteries, which limits the flow of blood through the vessel. Occlusion of these vessels leads to angina and ultimately to heart attacks. Several common treatments exist to reopen the arteries including angioplasty (with or without a stent), atherectomy, and laser ablation. However, surgical procedures are sometimes necessary and the available options are bypass surgery and transmyocardial laser revascularization, TMR.

TMR is a procedure in which ten to forty 1mm channels are created in ischemic heart tissues, where the number of channels made varies from patient to patient based on their individual cases[i]. This procedure allows for oxygenated blood to flow into the heart and will also result in revascularization the deoxygenated heart tissues[i]. This procedure was modeled using Gambit to create the mesh and FIDAP to model the diffusivity of oxygenated blood into deoxygenated heart tissue. The governing equations used to model the flow of oxygenated blood through the channel and diffusion of the oxygen into the deoxygenated tissue layer were the species and momentum equations. No reaction term was used in the species equation because it was assumed there was no elimination of oxygen by the tissue. A fully developed parabolic velocity profile was assumed in conjunction with the momentum equation. The initial conditions included an oxygen concentration of 0.2 ml 0_2 / ml blood at the intake and 0.1 ml 0_2 / ml blood in the deoxygenated muscle. The boundary conditions consisted of a constant zero flux at the top, left wall, right wall, and axis. The exit of the channel is free as is the blood / muscle interface because FIDAP will solve for the 0_2 concentration based on the other parameters that were specified.

Based on this model, it is evident that oxygenated blood in the newly created channels does diffuse into the deoxygenated heart tissue. Although there is diffusion throughout the entire sample, the diffusion nearest the inlet is greatest and decreases along the length of the channel and radially outward from the channel as expected. In addition, the desired oxygen concentration, 80% saturation[vii], was achieved at the channel-tissue boundary but not within the tissue layer. These results could be attributed to some of the assumptions that we were forced to make in modeling the procedure due to the limitations of the software in handling a two-phase model. However, with the optimal diameter found, 1.4 mm, and a closer channel spacing, a more optimal diffusion profile may be achieved.

DESIGN OBJECTIVES

Coronary artery disease (CAD) is the most common heart disease today. CAD most often results from a condition known as atherosclerosis, which happens when a waxy substance forms inside the arteries that supply blood to your heart[ii]. Just like other organs, the heart needs a constant supply of oxygenated blood. The coronary arteries supply the heart muscle with the fresh blood nourishment it needs to pump the blood throughout the body. When the heart's own need for oxygen rich blood rises, occlusions (obstructions) in coronary arteries prevent it from receiving the necessary amount. This insufficient supply of blood results in oxygen deprivation, a condition called myocardial (heart) ischemia. An ischemic heart reacts by giving off a sensation of pain, called angina, in which patients can suffer chronic chest pain, pressure or discomfort[iii]. Furthermore, as the blockage within the arteries thickens, it puts the patient at an even greater risk for a heart attack[iv]. Traditional treatments for CAD are bypass surgery or balloon angioplasty with coronary stenting, however, some severely diseased patients may be too weak or ill to undergo these common procedures[v]. Fortunately, a new approach in treating CAD offers an alternative to these patients.

Transmyocardial Revascularization (TMR) is a laser surgery that opens tiny new channels in the heart muscle to supplement the function of the coronary arteries. Therefore, instead of the heart using its coronary arteries to obtain fresh blood, the heart feeds itself by taking blood from within its own chambers (through the new perfusion channel in the heart muscle). The procedure begins with a CO_2 laser being fired between heartbeats to make very small passages through the left ventricle[ii]. The surgeon makes between 10 to 40 channels, applying finger pressure to help close the opening on the outer part of the heart[vi]. The channel seals at the surface, but the interior remains open, bringing oxygen-rich blood through the heart muscle[vii].

Using Gambit and FIDAP we have constructed a model to represent how an area of the heart suffering from ischemia (lack of oxygenated blood) would gradually get oxygenated again after the TMR surgery has been performed. As shown below in figure 1, we have modeled the 1mm diameter channel, produced by the CO_2 laser, next to a region of deoxygenated heart tissue. Our objective is to see how effective TMR surgery can be at introducing oxygen back into the heart. We hope to see the extent at which oxygen gets absorbed into the tissue and if it can absorb enough to reach a healthy oxygen concentration level in the heart.

Oxygenated blood typically has an oxygen saturation of 98%, whereas deoxygenated muscle is saturated with oxygen at a level of about 50%. In our model, we used an intake concentration value of 0.2 ml O_2 / ml-blood which was for oxygenated blood and 0.1 ml_{O2} / ml_{blood} in the deoxygenated muscle that was to be treated with TMR. The desired oxygen concentration to be achieved in the treated tissue was intended to be approximately 80% of the intake

concentration[viii]. Our model has shown that the desired oxygen concentration level of 80% was reached at locations near the blood-muscle border, but at locations further from the channel, the diffusion was not as effective.

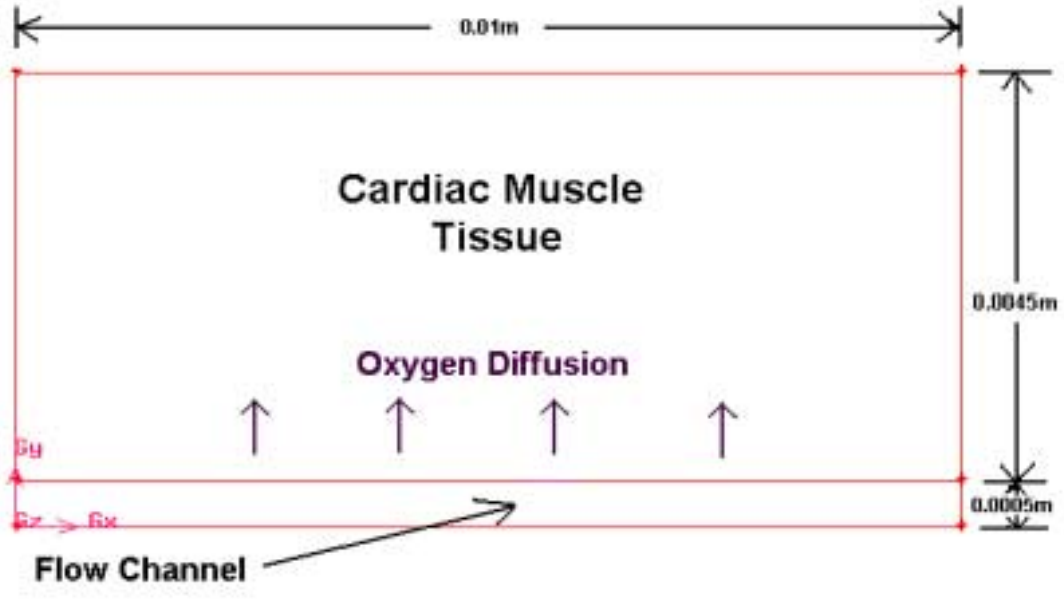

Figure 1: Schematic of the blood flow channel and the surrounding tissue through which oxygen will diffuse.

Results and Discussion

Assumptions

In order to evaluate the effectiveness of TMR, we monitored oxygen diffusion from the channel to the surrounding heart tissue. In the process of solving this problem, it was necessary to make several simplifying assumptions due to the limited capabilities of FIDAP. The simplifying assumptions made were:

1) Material properties are constant and homogeneous.
2) An infinite supply of oxygen was available at the channel intake in the form of dissolved gas in the blood.
3) The parabolic blood velocity profile was fully developed prior to oxygen diffusion.
4) Oxygen concentration in the blood is equal to the oxygen concentration in the heart tissue at the channel-tissue border. (Ordinarily this is not true, but the

FIDAP program does not offer a sub-routine to calculate the concentration gradient across a barrier that separates two phases of matter)

5) The species reaction term in the tissue is ignored, so elimination of oxygen is not taken into consideration.
6) The oxygen flux at the channel entrance is constant.
7) Initially, before the well is drilled, the concentration of all points is uniform.
8) The oxygenated blood entering the intake is at 98% saturation[vii].
9) The deoxygenated tissue has a percent saturation of 50% oxygen[vii].
10) Desired oxygen concentration in the tissue from TMR is to ~80% of the intake oxygen concentration for successful results[vii].

Geometry and Material Properties

Using GAMBIT, an axi-symmetric mesh was created which consisted of two entities, the blood flow channel and a heart muscle layer, with the bottom border being the axis of symmetry of the channel. With the axi-symmetric geometry, the problem is geometrically reduced from a 3-D problem to a 2-D problem; however, FIDAP still calculates the solution as if it were a 3-D problem. The mesh was graded by taking into account the oxygen concentration gradient in the blood and also in the heart tissue. Since the largest gradient occurs around the channel-tissue boundary, both in the blood and the heart tissue, the greatest number of nodes is located in this region. The mesh that was created can be found below in Figure 2.

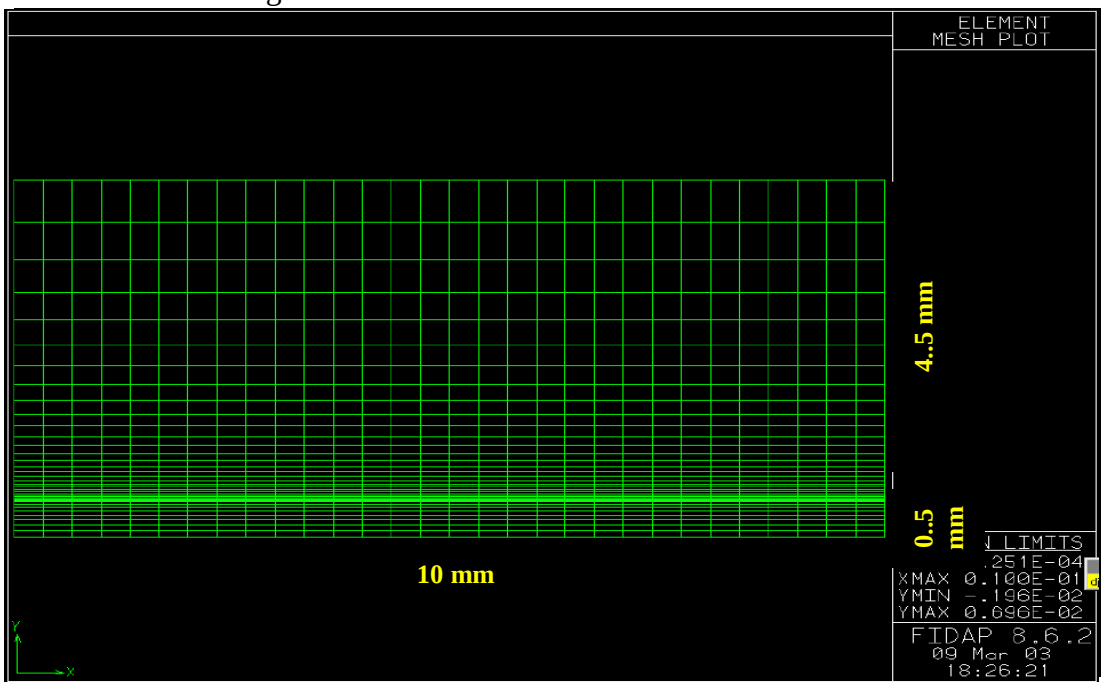

Figure 2: Axi-Symmetric Mesh of Channel and Surrounding Muscle Tissue

The dimensions of the mesh including channel radius, channel depth and tissue width are located on the mesh in Figure 2. The tissue width used was determined by taking into account the channel placement typically used in TMR surgery. With a typical placement of 1 channel per cubic centimeter, the tissue width was determined by calculating the radial distance between two placed channels, also taking into account channel radius.[viii] Channel radius and depth were obtained from a surgeon involved in TMR.[viii]

Since modeling TMR turned out to be a fairly complex physical problem, several mechanisms of species and momentum transfer were at work and many material properties were used in order to accurately arrive at a solution. Since the model included both blood and muscle, physical properties for both phases of matter were used. Table 1, shown below, lists the properties used and their values for the respective material.

Table 1: Material Properties

Material Property	**Blood**	**Muscle**
Diffusivity (m^2/s)	0.704×10^{-6}	0.106×10^{-8}
Density (kg/m^3)	1061.0	1500.0
Viscosity ($kg/m\text{-}s$)	0.200×10^{-2}	-------
Oxygen conc. (% saturated)	98	50

Governing Equations

There are several types of transport occurring during TMR. Since we chose to only model the mass transfer of oxygen, and not the actual drilling of the well with the CO_2 laser, the model does not take into account energy transfer in the form of heat. So the energy equation is not necessary.

When considering the mass transfer of oxygen through the blood in the flow channel and then through the muscle tissue, the concentration, or Species equation, in cylindrical coordinates, is used. The reaction term, which accounts for elimination of the species, is not taken into account as stated in the assumptions, but the oxygen concentration in the channel and tissue is changing with time. The Species equation calculates the oxygen concentration at each node and the oxygen diffusion gradient is shown in the diffusion contour plots discussed later in this section.

The flow of blood in the channel is described using the Momentum, or Navier-Stokes equations for fluid transport. A parabolic velocity profile develops as a

result of the no-slip, zero velocity boundary layer at the channel walls, and the maximum velocity at the axial midline of the channel. Values at each node are calculated using the Momentum equation in cylindrical coordinates. Mathematical representations for the Species and Momentum equations, with cancelled terms, are shown in Appendix A.

Boundary and Initial Conditions

The FIDAP program needs to have defined boundary and initial conditions at all bounds and surfaces of the model's geometry in order to make accurate calculations for diffusion gradients. At the intake of the flow channel, a constant flux of oxygenated blood enters the channel at 0.1 x 10^{-2} ml_{O2}/s and there is a nodal oxygen boundary value of 0.2 $ml_{O2}/ml_{blood.}$ The exit of the channel is said to be "Free," and the program makes internal calculations there, depending on the diffusion mechanisms taking place earlier on in the channel. The boundary conditions at the top, left wall, right wall, and bottom all have zero flux conditions. The flux is set to zero at the walls and top because there is no diffusion of oxygen through these boundaries. The bottom channel axis has zero flux because the geometry is axi-symmetric and this border is treated as the midline of the cylinder through which there is no flux. The blood-muscle border does not have a boundary condition assigned because this is the border that the program is making mass transfer calculations across, depending on the differing constants of the materials, such as density and diffusivity. The velocity of blood coming into the channel through the intake is constant. The average value used is 0.0005 m/s, and is used in the calculation to determine the parabolic velocity profile in the channel.[2] The maximum velocity is given by :

$$V_{MAX} = 2\ V_{AVG}$$

The profile is input into the program as constant, to eliminate any accumulations at the intake and exit of the channel due to a developing or lagging profile. The relation for V_{Max} is:

$$V_{MAX} = V_{AVG}\left(1 - \frac{r^2}{R^2}\right)$$

Where R is the radius of the channel and r is the variable distance along the radius.

Initially, the entire mesh, both blood and muscle, is set to have a uniform oxygen concentration of 0.1 ml O_2/ml-blood. This is because at t = 0, the channel has not yet been drilled, and so the entire mesh represents the deoxygenated muscle tissue, which is at 50% oxygen saturation.[3,4] Immediately following the start of

the process, the oxygen gradient forms because of the incoming flux at the intake, and the concentration increases throughout the channel and the tissue. In addition, since the material properties of both the blood and muscle are said to be constant and homogeneous throughout the process, there is no change in their values.

Contour Plots of Time Dependant Oxygen Gradients

Contour plots of oxygen diffusion at different times throughout the TMR procedure can be found in Figures 1 through 5 in Appendix C. The images were generated using the FIDAP software, and have color coordinated specified values of oxygen shown on each plot. Measurements were taken at 5 time-steps, starting with a time just after the initial condition, TS = 5, and progressively for the values of TS = 10, 100, 200 and 500.

In addition to contour plots developed for the entire geometry, changes in oxygen concentration with time were plotted for selected nodes, one at the channel-tissue boundary and one at the tissue interior. From the graphs in Figures 6 and 7 in Appendix C, it can be seen that there is an exponential increase in oxygen concentration with time. However, the increasing trend seen in the graphs will eventually level off at a constant oxygen concentration as suggested by the plots. From the figures, it is also observed that there is a significant increase in oxygen concentration at the boundary node, however, the interior node shows little change in concentration. This result indicates that the suggested distance between channels is too large since desired oxygen levels are not being achieved within the tissue.

Sensitivity Analysis

A sensitivity analysis was done by modifying the mesh, the initial oxygen concentration in the blood, and selected material properties including tissue density and oxygen diffusivity. For each modification, the oxygen concentration at two selected nodes, one at the channel-tissue boundary and one in the tissue interior, was recorded in order to determine how the changes affected the problem solution.

Two modifications were made on the mesh used, the first dealing with the dimensions of the channel. The change was made to determine the channel size that optimizes oxygen diffusion to the surrounding tissue. Two additional meshes were created one with a channel radius of 0.7mm and the other with a channel radius of 0.9mm. The overall height of the mesh was not changed

(channel radius + tissue width), only the location of the channel-tissue interface. The change in oxygen concentration with channel diameter for the border node and the internal node can be found in Figures 3 and 4 respectively.

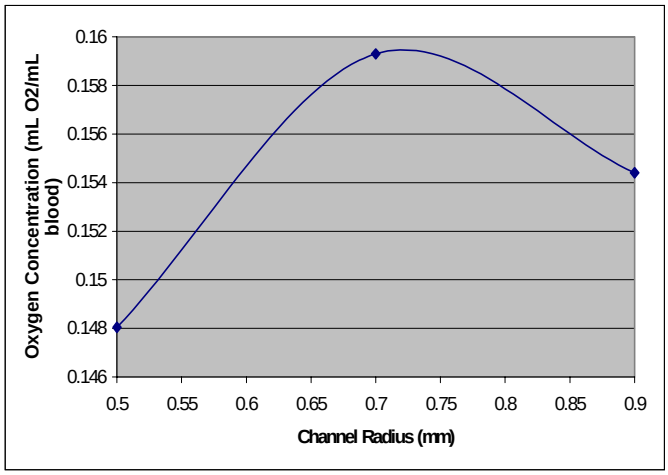

Figure 3: Tissue Oxygen Concentration versus Channel Radius at a Border Node

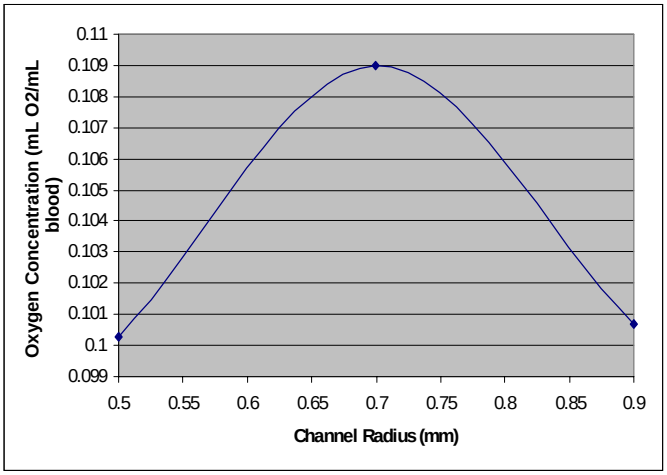

Figure 4: Oxygen Concentration versus Channel Radius for an Internal Tissue Node

From the results found in Figures 3 and 4, it can be concluded that an optimal channel radius is 0.7 mm. With a change in channel radius from the originally modeled 0.5mm to 0.7 mm, there is a 7.6% increase in oxygen concentration at the channel-tissue boundary and an 8.6% increase in oxygen concentration within the heart tissue layer.

A second modification to the mesh was done by increasing the number of nodes in the mesh. The new mesh created can be found in Figure 8 in Appendix C.

A comparison of tissue oxygen concentrations from the original mesh to the refined mesh illustrates a 2% change in oxygen concentration at the border node, and less than a 0.1% change at the internal node. These changes in oxygen concentration are insignificant, therefore we can conclude that a more refined mesh is not necessary.

In addition to changes in the mesh, changes were made to initial oxygen concentration in the blood, tissue density, and oxygen diffusivity. These are all parameters that are likely to vary in actual cases; therefore, it is necessary to determine how much of an effect any changes in value will have on the solution. Figures 5, 6 and 7 below show how changes in these parameters affect the tissue oxygen concentration at a border and internal node.

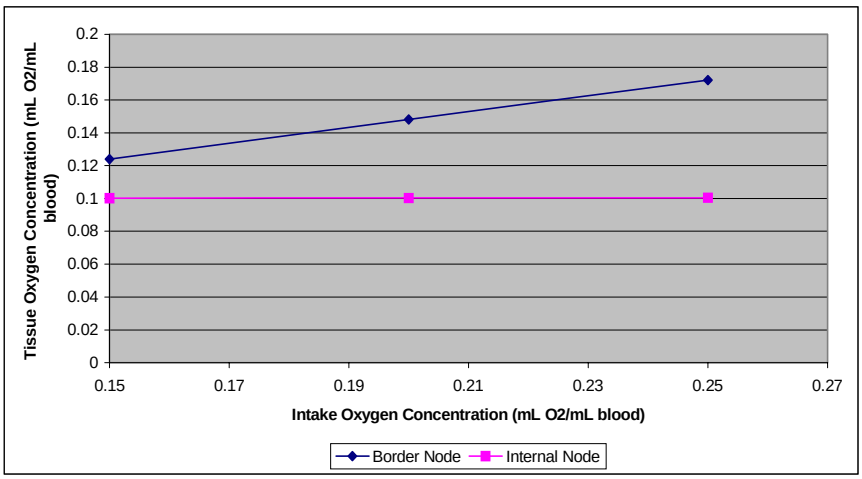

Figure 5: Intake Blood Oxygen Concentration versus Tissue Oxygen Concentration for a Border and an Internal Node

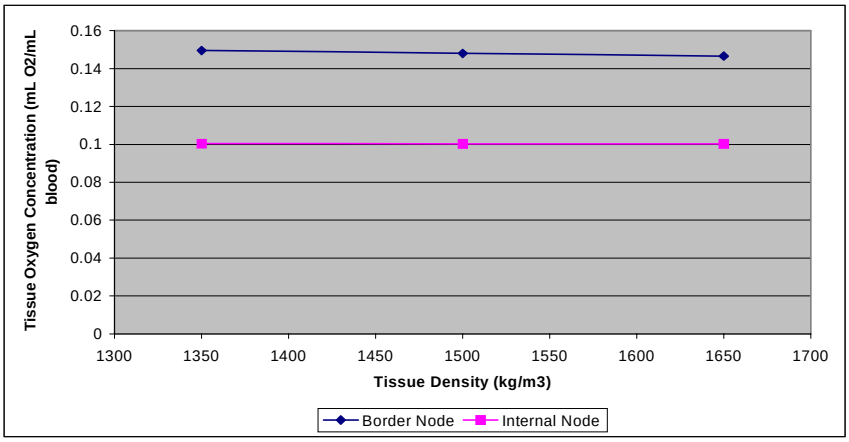

Figure 6: Tissue Density versus Tissue Oxygen Concentration for a Border and an Internal Node

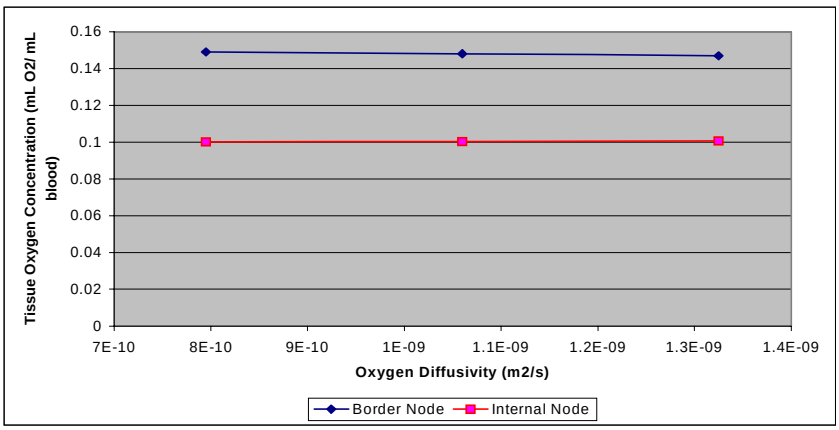

Figure 7: Oxygen Diffusivity versus Tissue Oxygen Concentration for a Border and an Internal Node

As would be expected with an increase in initial oxygen concentration in the blood, an increasing trend was seen with respect to oxygen concentration in the heart tissue. The variation in the original value used resulted in a ± 16.0% change in the original tissue oxygen concentration at the border node and a ± 0.15% change in the original tissue oxygen concentration at the internal node. Variation in this initial value significantly affects the oxygen concentration at the channel-tissue boundary, however, shows little affect on the internal oxygen concentration. This reaffirms the previous observation that channel placement is too far apart due to the fact that the internal heart tissue does not receive enough oxygen even with a 25% increase in the original blood oxygen concentration. In addition, it is observed that any decrease in blood oxygen concentration from our initial value also prevents the boundary tissue from achieving the desired oxygen concentration (80% of intake oxygen concentration[viii]). This may present a problem in our model, and additionally adds to the complications involved in TMR as currently practiced.

The sensitivity analysis done on the tissue density parameter showed a decreasing trend with increasing tissue density. The variation on this value resulted in a ± 1% change in tissue oxygen concentration at the border node and a ± 0.02% change in oxygen concentration at the internal node. Changes in this parameter show little affect on the problem solution, therefore, it is not necessary to be concerned about variations in patients with respect to this value.

Variations in the oxygen diffusivity value resulted in different trends depending on location within the tissue layer. Changes in diffusivity resulted in a decreasing trend in tissue oxygen concentration at the tissue-channel boundary and an increasing trend within the tissue layer. This may be attributed to the fact that an increase in diffusivity would allow the oxygen to diffuse further into the tissue layer, resulting in an increase in oxygen concentration further in the layer at the expense of the boundary concentration. Despite these differing trends, variations in the diffusivity showed little affect on the problem solution. At the border node, a ± 0.7% change was observed and at the internal node, a ± 0.25% change occurred. These results indicate that it is not necessary to be concerned about variations in this parameter.

Conclusions and Design Recommendations

The objective of transmyocardial laser revascularization (TMR) is to re-perfuse oxygen deprived heart tissue with oxygenated blood from the surrounding capillaries by drilling several channels into the heart tissue. We modeled the diffusion of oxygen from blood in a capillary to a section of heart tissue through a single channel. The problem solution showed that the desired oxygen concentration (~80% saturation) is achieved at the channel-tissue border, but not within the tissue layer. As the blood flowed through the channel, most diffusion occurred at the channel intake, and decreased throughout the length of the channel as seen in Figures 1 through 5 in Appendix C. Although minimal

compared to tissue perfusion close to the channel, oxygen diffusion also occurred at further distances from the channel. This fact is not obvious by looking at our contour plots, due to the inability of FIDAP's color scheme to represent the small variations in diffusion.

Design Recommendations

We created meshes with varying channel diameters to see if this parameter would have a significant effect on oxygen diffusion. As evident in Figures 3 and 4, a channel radius of 0.7 mm resulted in the greatest level of oxygen at both the channel-tissue interface and within the tissue layer. Although the normal channel radius used by surgeons in TMR surgery is 0.5 mm, our data concludes that it may be beneficial to optimize the channel radius at 0.7 mm. However, even with a change in channel radius to the optimal value, the desired oxygen concentration is not achieved within the tissue layer, leading to the previous conclusion that channels need to placed closer together. Grouping the channels closer together could further optimize the process, ideally increasing the overall concentration of oxygen throughout larger regions of tissue. Further studies are recommended to determine the optimal placement of channels with considerations of specific design requirements that may vary with individual patients depending on age, extent of tissue death, extent of blocked blood vessels, etc.

Software Limitations

Many of the assumptions we were forced to make in our model were due to limited capabilities of the software. One of the largest problems we encountered was the inability of FIDAP to calculate diffusion of a species through different phases, in our case, the phases being blood (fluid) and tissue (solid). To effectively model mass transport, Henry's Law is needed to convert mass transfer from two different phases, which FIDAP was not capable of. Due to this limitation, we made the assumption that initially the oxygen concentration in the blood was equal to the oxygen concentration in the heart tissue at the channel-tissue border. This simplified our model greatly, but could have introduced error into our calculations. We also had to assume there was a fully developed parabolic velocity profile in the channel, which physiologically is not correct, but again because of FIDAP's limitation, we were forced to make this assumption.

Benefits of Modeling

Overall, the benefits of modeling are extremely important in analyzing any complex engineering problem. The benefits can be especially important in modeling a surgical procedure such as TMR. In many instances, computer modeling is effective in saving production costs and labor time when developing a product or protocol. This is true in our model as well, but more importantly modeling can improve the safety of the TMR procedure and the overall health of a patient. There are always risks associated with any surgical procedure, and it is extremely important for scientists and researchers to minimize these risks to create a safe and effective process. In TMR surgery, it is extremely important to thoroughly model the process before the surgery is done to assure maximum safety. By modeling TMR before ever performing it on a patient, the efficiency and safety of the procedure are greatly enhanced, as well as researchers understanding of the physiological mechanisms taking place.

Conclusion

Transmyocardial laser revascularization (TMR) has potential as a less invasive alternative to open heart bypass surgery for coronary artery disease, however, the procedure needs to be refined in order to achieve more successful results. As shown in our model, drilling a channel in heart tissue can effectively transport oxygen from saturated blood to deoxygenated heart tissue, but modifications to the procedure may allow oxygen to diffuse further into the tissue layer. Although some simplifications had to be made to our model due to physiological complications and software limitations, our model does effectively illustrate the mechanisms involved in the surgery and may provide a starting point for further studies in improving the effectiveness of TMR as an alternative treatment for coronary artery disease.

Appendix C

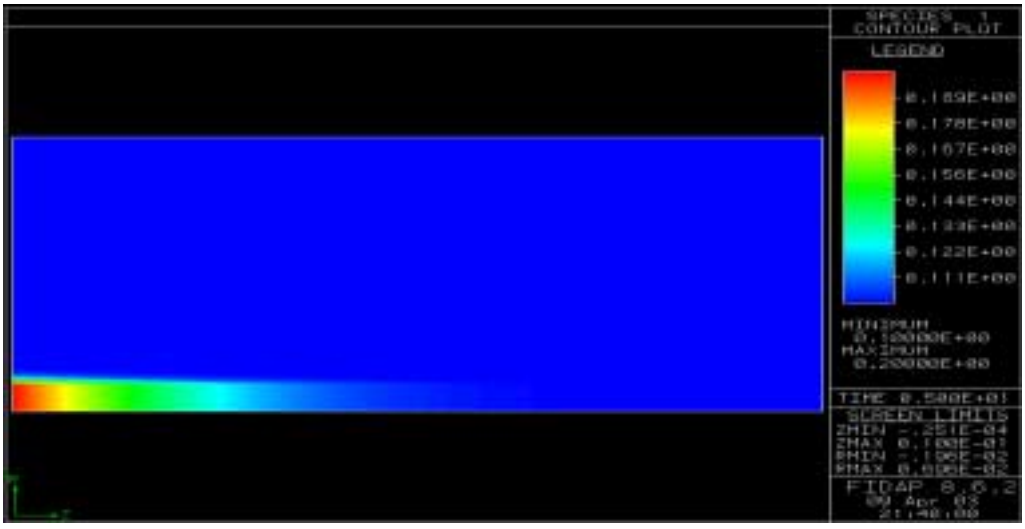

Figure 1: TS = 5; The flow is just entering the channel, no appreciable diffusion has occurred.

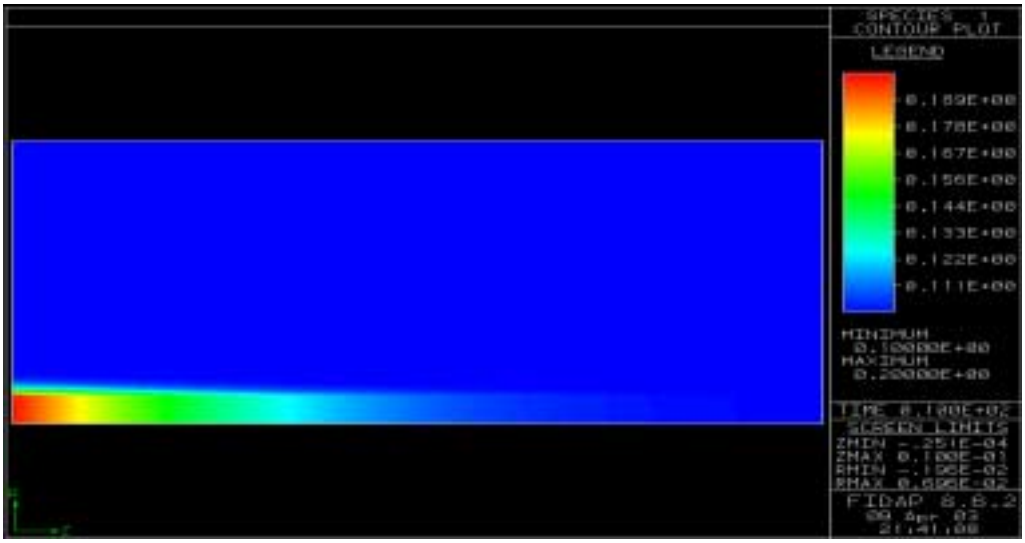

Figure 2: TS = 10; The blood flow has moved along the channel slightly further and although there is still no appreciable oxygen diffusion into the tissue, there clearly is an increase from TS = 5.

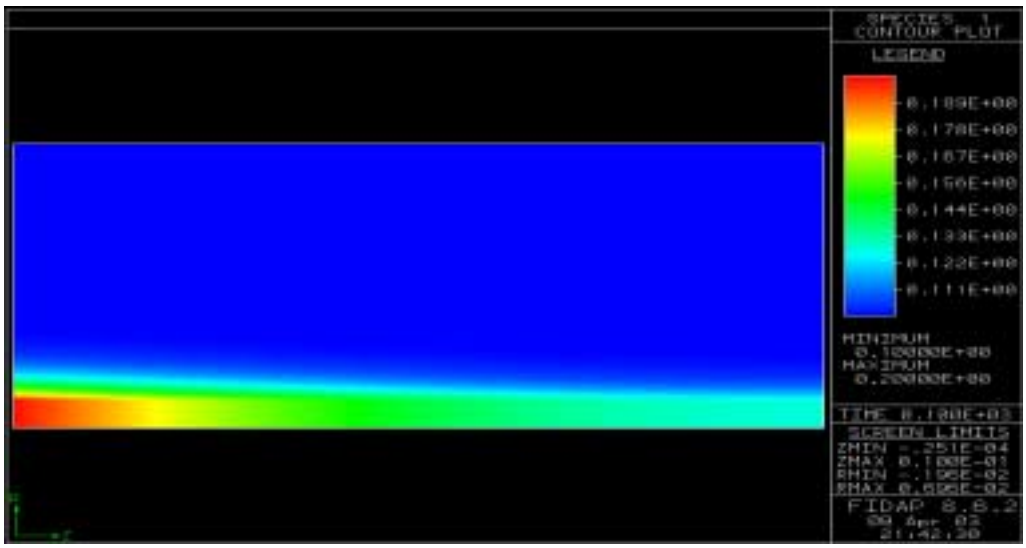

Figure 3: TS = 100; The blood has now achieved flow throughout the entire length of the channel. A diffusion gradient is clearly visible now, as oxygen is diffusing within the blood inside the channel and making it's way out of the channel, radially into the muscle.

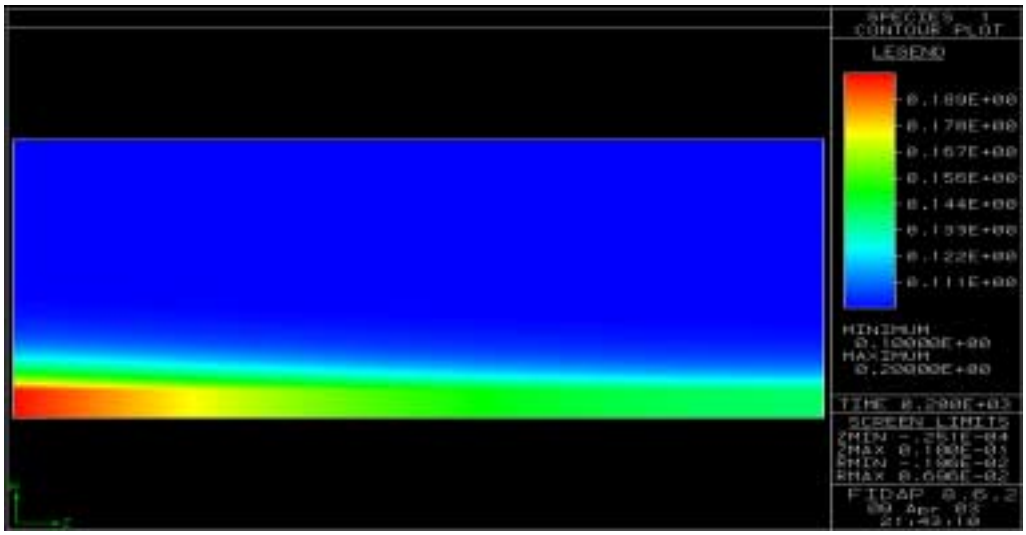

Figure 4: TS = 200; A more prominent diffusion gradient is shown here as there is an increase in oxygen concentration in the tissue between this time frame and the previous time. The gradient is larger at the beginning of the channel because there is a high influx of oxygen there.

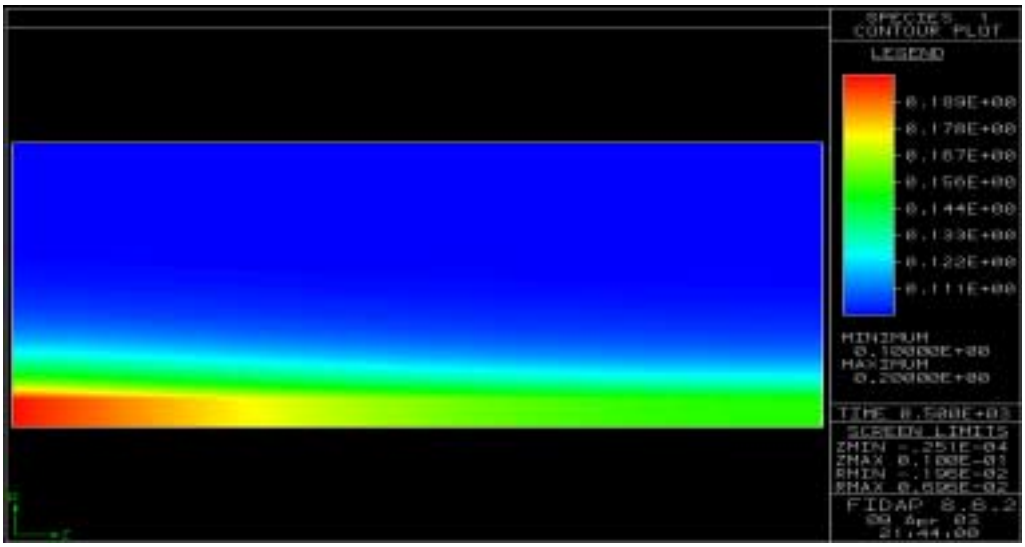

Figure 5: TS = 500; At the final time measured in the process, the oxygen gradient has increased, but shows no appreciable difference proceeding this time.

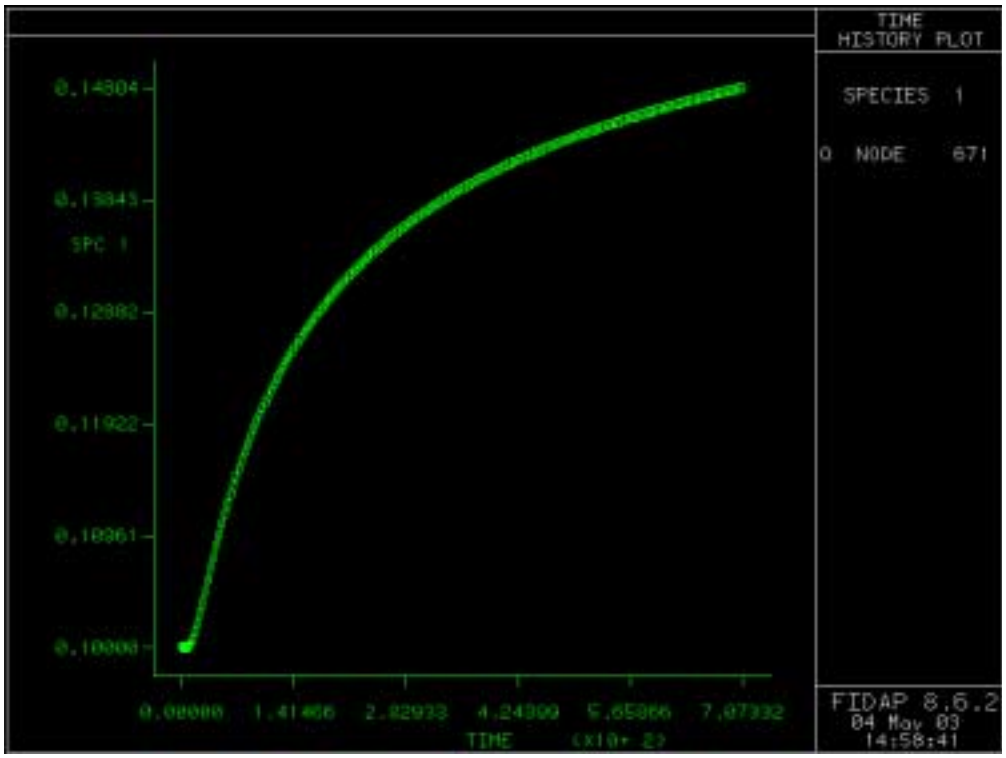

Figure 6: Tissue Oxygen Concentration vs. Time at a Border Node

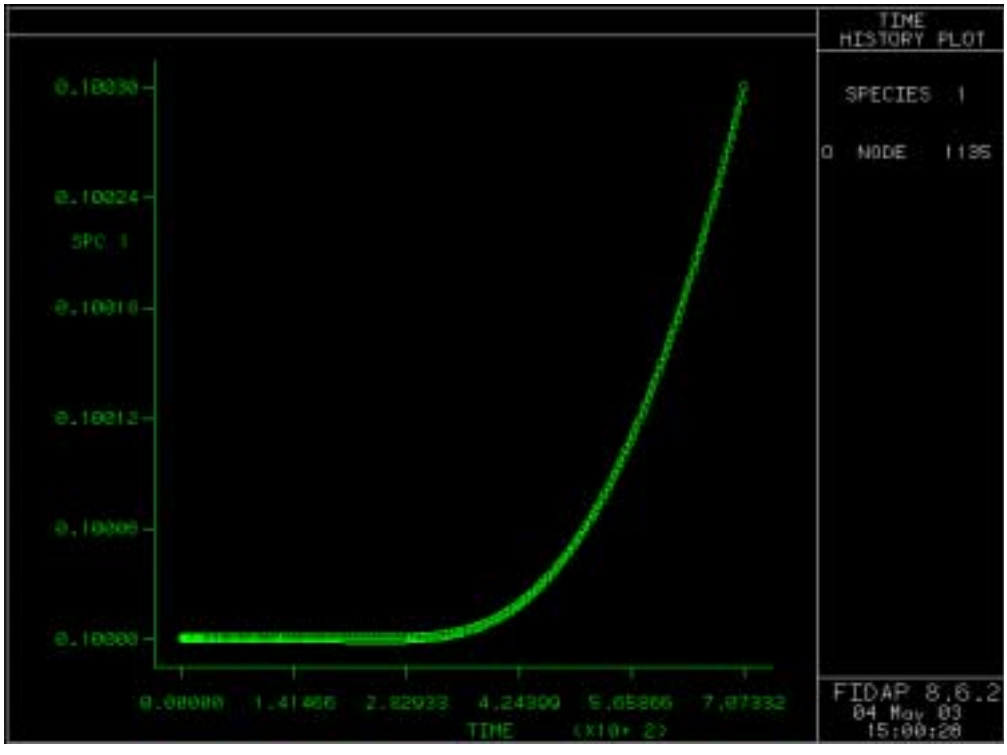

Figure 7: Tissue Oxygen Concentration vs. Time at an Internal Node

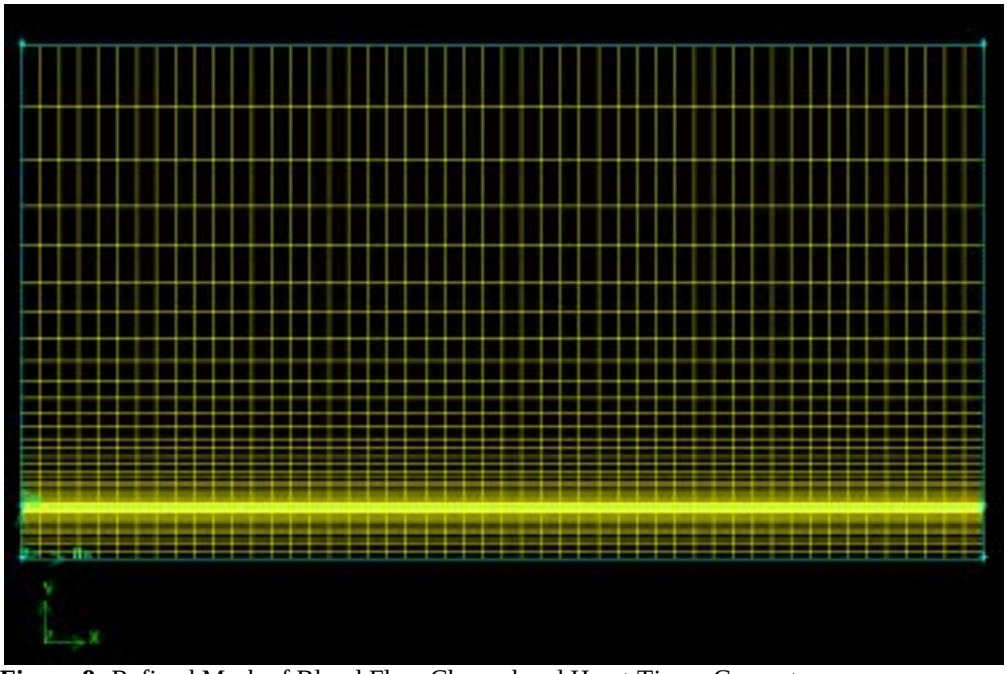

Figure 8: Refined Mesh of Blood Flow Channel and Heart Tissue Geometry

Appendix D

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Northwestern University,The Feinberg School of Medicine, Department of Surgery