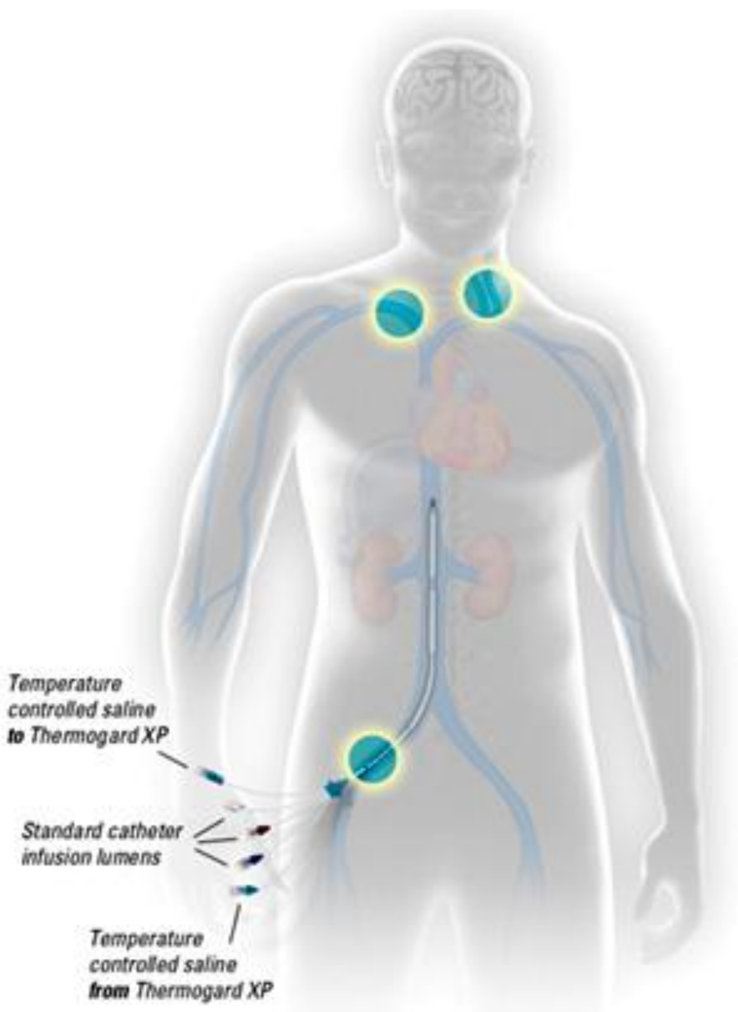
Modeling Therapeutic Hypothermia Using Heat Exchange Catheter to Cool Blood

BEE 4530



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Executive Summary:

Catheter intravenous cooling is a relatively new technique employed to induce hypothermia in patients suffering from neural paralysis or abnormal inflammation. The time it takes to cool the patient's body temperature to the desired level is of particular interest because knowing this time provides an estimate of how long the patient needs to be treated, both in an emergency and in long-term hospitalization. Finding an optimal cooling time for different situations will allow the operators to effectively treat the patient. Thus, the goal of the project is to find the time it takes the catheter to cool the patient's body temperature to the desired level.

In order to achieve this goal, the project modeled a two dimensional, axis-symmetric counter pumps with two domains: the catheter balloon and the vena cava blood vessel. The two domains have opposite flows to depict blood flow and cooling fluid flow. The model measured the temperature flux throughout the vessel with changing catheter length, cooling fluid velocity, and temperature of the cooling fluid to analyze the optimum cooling time.

The results show that whether increasing the length of catheter and decreasing the cooling fluid temperature or decreasing the length of the catheter and increasing the cooling fluid temperature reduces the treatment time significantly. We found that in order to optimally perform intravenous cooling in a vena cava, either of the two methods can be employed to reach the desired temperature. Preferably, in an emergency situation when on-sight surgery is difficult, increasing the cooling fluid velocity is the desired method. On the other hand, when the patient needs to go through long term hospitalization, increasing the number of catheter with low cooling fluid velocity is desirable. In short, the project provides different methods to optimally treat patients with specific needs.

Introduction:

Background

In September 2007, Buffalo Bills tight end, Kevin Everett suffered a complete cervical spinal cord injury after a helmet-to-helmet collision with an opposing player. Everett sustained a C3/C4 fracture dislocation and at his on-field assessment team physicians found that Everett has suffered complete motor paralysis and sensory loss from the clavicles down. Team physicians reduced Everett's body temperature immediately in the ambulance using a chilled saline solution. Upon arrival at the hospital spinal surgery was performed to alleviate the pressure due to the dislocation. After surgery, physicians decided to induce controlled systemic hypothermia to target temperature of 33.5 °C with hopes of regaining some of Everett's motor and sensory function. Surgeons placed an Alsius Cooling catheter in the left femoral vein and advanced it into the inferior *vena cava.* Using this system Everett was kept under careful post-operative observation.

In this example, induced hypothermia played a critical role in maintaining Everett's body temperature. Like such, therapeutic hypothermia is frequently used in hospital intensive care units in the treatment of ischemia, induced by cardiac arrest or stroke, or severe trauma to the nervous system. Several therapeutic modalities exist for hypothermic induction: surface cooling using air, surface cooling using fluids, water-circulating cooling blankets, hydrogel-coated water-circulating pads, water-circulating wrapping garments, water and alcohols sprays, core-cooling using intravascular catheters, infusion of ice-cold (4 °C) fluids, extracorporeal circulation, and antipyretic agents. From these methods, the most effective methods are water-circulating cooling blankets and intravenous catheters in terms of constant thermo-regulation and rapid cooling.

A major advantage of intravenous catheters is prolonged constant thermo-regulation. In fact, some studies have found that the temperature can be maintained in this fashion for up to 2 days (Georgiadis 2001). This system is also used to slowly re-warm the body after the induced hypothermia. The body temperature fluctuates more with the water-circulating blanket system after prolonged periods of time causing this method to be less advantageous than the intravenous catheter. Based on preliminary research and exploration, the series of Alsius Endovascular Core-Cooling catheters worked like a double pump heat exchanger systematically cooling the body by removing heat from the blood as it passes over the catheter.

One important factor to notice about the intravenous cooling method is the time it takes to attain the desired temperature. As in Everett's case, the physicians were faced with time constraints in saving Everett's neurons before it decayed, and were in need of effective design of the catheters. The project attempts to provide this optimal design that will effectively reach the desired temperature in a short time period.

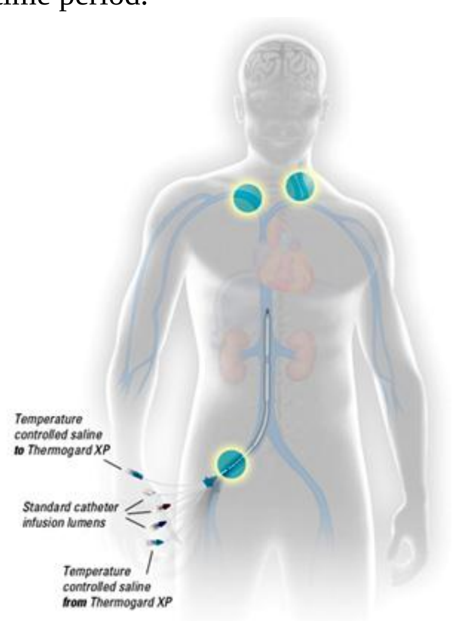


Figure 1: Schematic of catheter inserted in human inferior vena cava.

Design Objectives

Like in the case of Everett's injury, the project will describe induced hypothermia through the inferior *vena cava*. Our project had two major objectives:

- Model and determine how quickly the body can be cooled to the target temperature of 34°C using this endovascular cooling system
- Optimize and design the appropriate coupling of catheter length and initial temperature of cooling solution to create the most efficient thermo-regulation system determined by the time the system took to cool to a desired temperature.

Model Design:

Below is a simplified schematic that was implemented in COMSOL, modeling the intravenous catheter cooling system. We chose to model both the vessel and the catheter as concentric cylindrical tubes for simplicity sake.

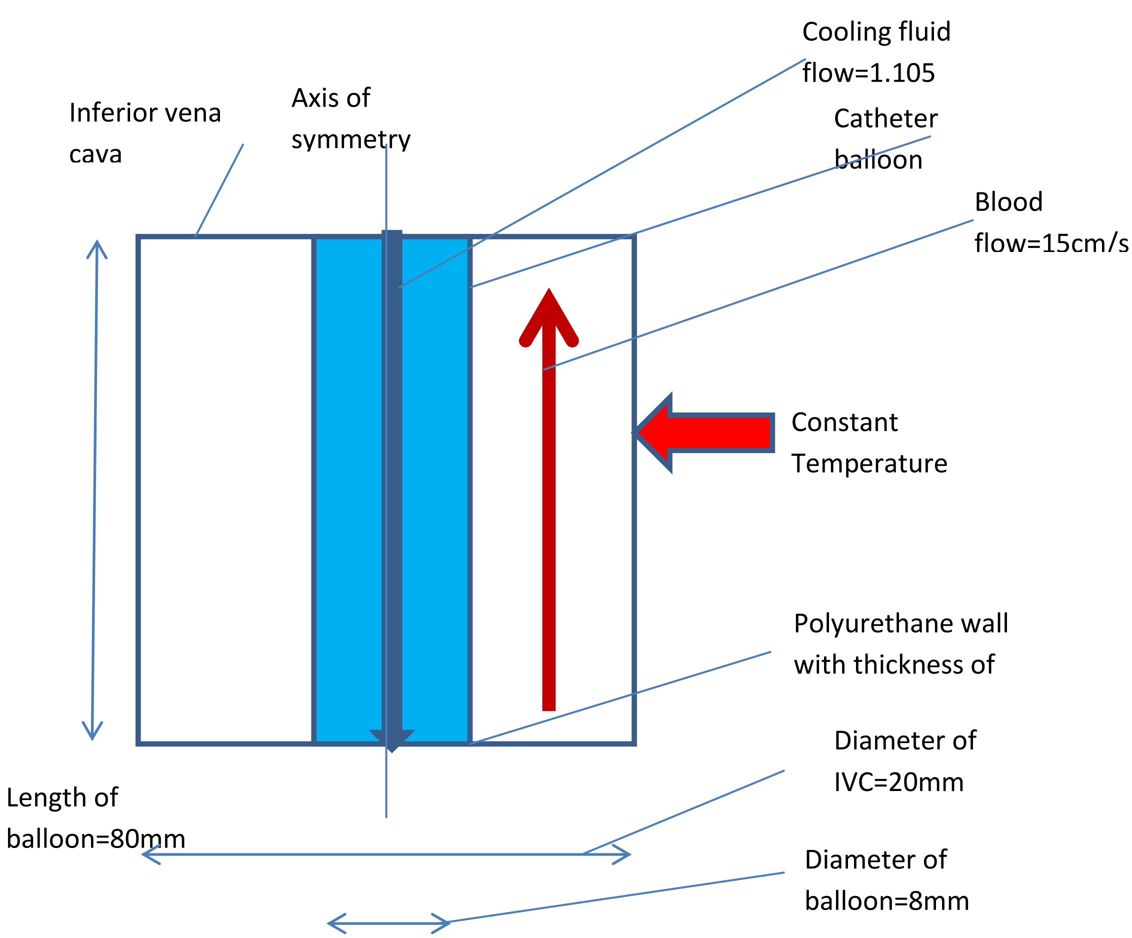


Figure 2: Simplified problem model and its boundary conditions showing catheter balloon inside inferior vena cava that was used in solving the problem.

The most effective insertion point for total body cooling in therapeutic hypothermia is the inferior vena cava because it is the central vessel of the venous system. This was the basis for the location of our model. In our model we described the transfer of heat via conduction and convection from the blood to the catheter cooling fluid inside the inferior vena cava. For the convective term in the heat transfer equation, the countercurrent fluid flow in the catheter-vessel system must be modeled using the incompressible Navier-Stokes equation to determine the appropriate velocity.

We made several valid assumptions in our model. First, it was safe to assume that the cross section of the vessel and catheter balloon remain constant throughout the entire length of the system. Additionally it was safe to assume that the thermal properties of the saline solution were similar to those of water because the solution was only 2 % saline. We modeled blood as an incompressible fluid with constant flow. This assumption had limitations compared to real blood flow because of the pulsating nature of the heart. Also, because the range of temperatures with which the blood and saline experienced in the model was small, the material properties can safely be assumed constant. A steady state model is sufficient for modeling this process because it is at constant laminar flow. The blood flow and cooling fluid flow were in opposite directions as is the case with the catheter.

Complete Solution Method:

To determine the temperature in the inferior vena cava domain, the incoming and outgoing heat flux was modeled against change in temperature over time, represented in the equation below:

$$\rho c_p \frac{dT}{dt} = I - O$$

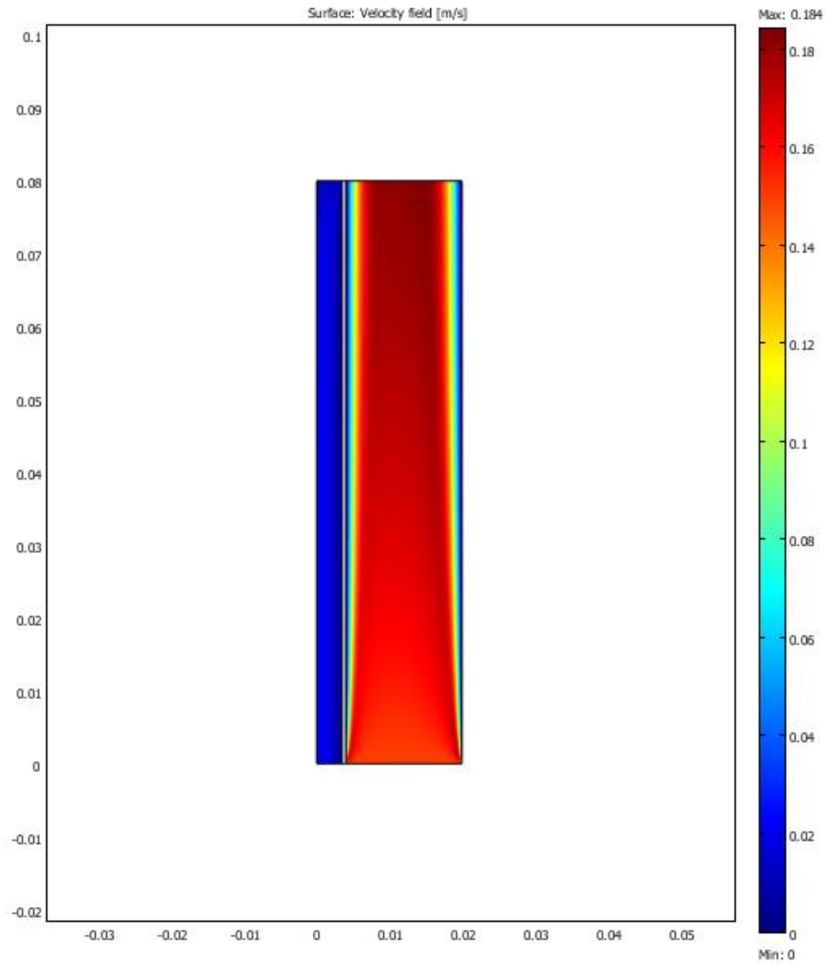
Where I is equal to incoming volumetric heat flux from the blood vessel, and O is equal to outgoing volumetric heat flux due to *n* catheters. The incoming volumetric metabolic heat flux is from the blood vessel.

By integrating the above equation over time, the time to take to cool the blood to the desired temperature can be represented in the equation below:

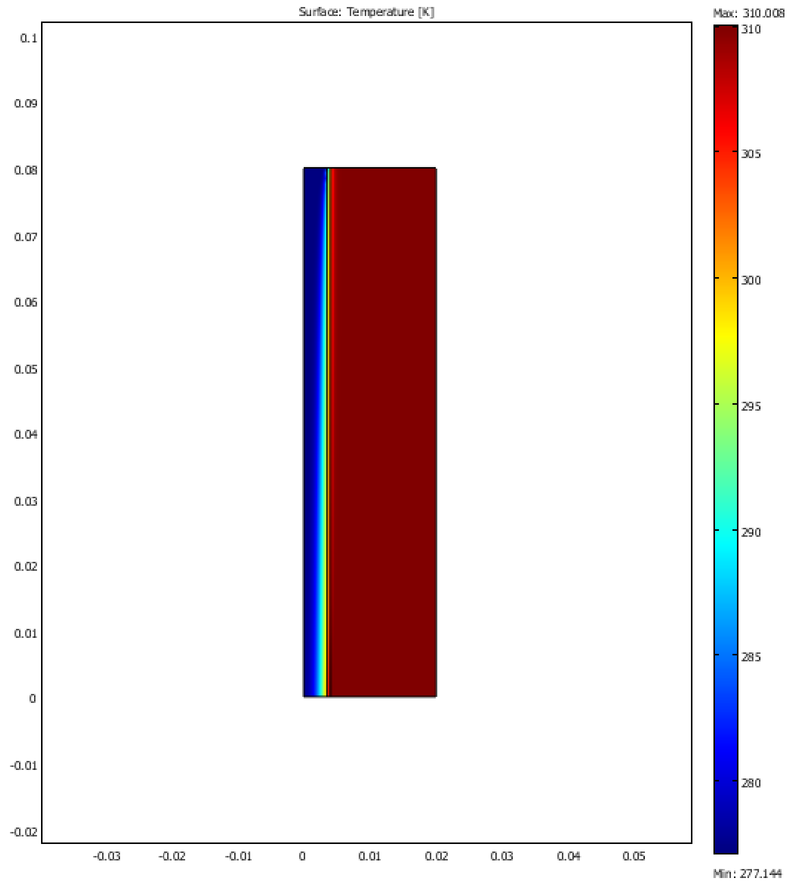
$$t = \frac{\rho c_p \Delta T}{I - O}$$

Results and Discussion:

The first step in our solution was to determine the appropriate velocity profile established by the incompressible Navier Stokes equation. The following plot specified the flow within the blood vessel and the catheter.



The velocity field plot showed the velocity field of the cooling fluid (left) and the blood (right) with no slip boundary conditions on all walls. The cooling fluid was initially at rest and the blood had an initial velocity equal to the average blood velocity in the vena cava. The velocity field was relevant as it provided an idea of how the blood and saline fluid velocity values were derived for convective heat flow equations. From this velocity profile the heat transfer temperature gradient was established.



The temperature plot showed that the cooling fluid warmed up faster than the blood did. There was a larger gradient in the cooling fluid because there was a much smaller volume of fluid. This may also be due to the fact that the cooling fluid had a much lower velocity than the blood so the heat was carried away significantly more slowly than the blood so its temperature appeared to change more. It was expected that there was not much change in blood temperature because the body temperature should not drop more than 2 or 3 degrees. Once this temperature gradient has been established in COMSOL it was used to establish the outgoing heat flux from the blood to the catheter. To determine the out-going heat flux, the boundary integral over the catheter wall-blood vessel interface was taken.

The following outgoing heat flux along with the constant parameters, ρ=1060kg/m^3, c_p=3594J/kgK, ΔT=-3K, I is 0.251 W (average metabolic heat carried past the catheter) and O was 10.751W and both were divided by the volume of the blood (5 L). Through calculation, it was found that it takes around 1.51 hours to cool the blood to 34^{0}C.

Sensitivity Analysis:

For our analysis we changed the following properties: thermal conductivity of catheter, and temperature of cooling fluid. The result yielded almost no changes in our average blood temperature in the vena cava and the catheter-blood interface. In other words, the solution to the model was not sensitive to any of the material properties. Plots of varying parameters against the final solution can be seen below (from Plot 2 to Plot 5). This suggested that none of our material property needs significant accuracy, and thus, it can be said that our model was sufficiently accurate. Because we only expect the temperature of the blood in the whole body to vary across 2-3 ^{0}C, the material properties are unlikely to change significantly, which supports the above conclusion.

Table 1: Sensitivity Analysis of Temperature at Catheter Blood Interface and Entire Vessel

k (of catheter wall) [W/mK]	Tave line integral [K/m^3]	Tave @ catheter blood interface [K]	T of saline [K]	Tave line integral [K/m^3]	Tave @ catheter blood interface [K]
0.2	24.46955	305.8693	273	24.37423	304.6778
0.3	24.42044	305.2555	274	24.38578	304.8223
0.4	24.39082	304.8852	275	24.39733	304.9667
0.5	24.37117	304.6397	276	24.40889	305.1111
0.6	24.35726	304.4657	277	24.42044	305.2555

Table 2: Sensitivity Analysis of Average Heat Flux at Catheter Blood Interface

Length of Catheter [m]	Total Average Heat Flux at the Catheter Blood Interface [W]
0.04	6.787322
0.08	10.91451
0.12	15.24396
0.16	18.08075

The tables indicate the sensitivity of the temperature of the catheter wall-blood vessel interface. The range of temperatures over which the model was tested was very small and the change in the parameters was relatively insignificant.

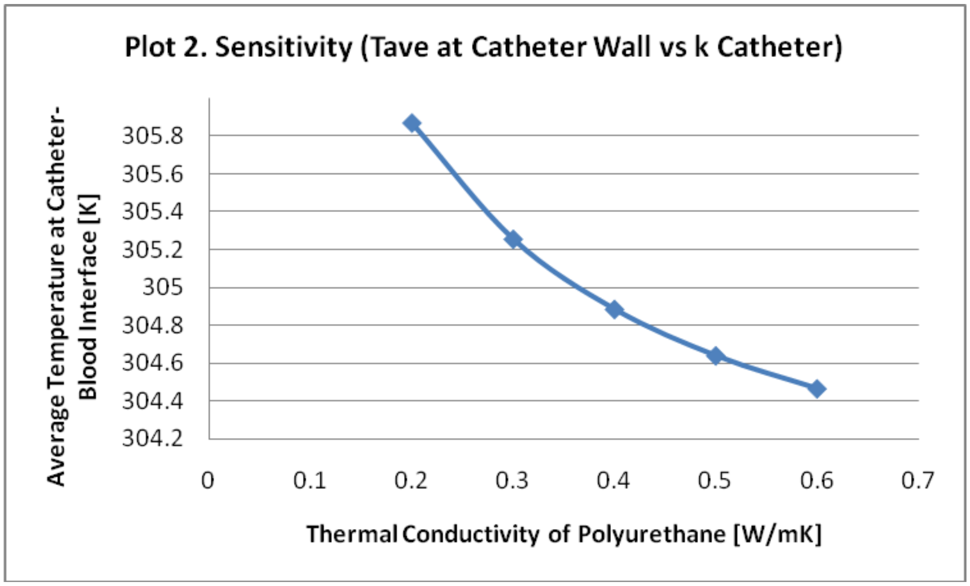


Figure 3: Sensitivity analysis of the average temperature at the catheter wall to the thermal conductivity of catheter wall

There was even less of a difference in the average temperature of the blood vessel as seen below. The range of average temperature was very small and it was relatively insignificant.

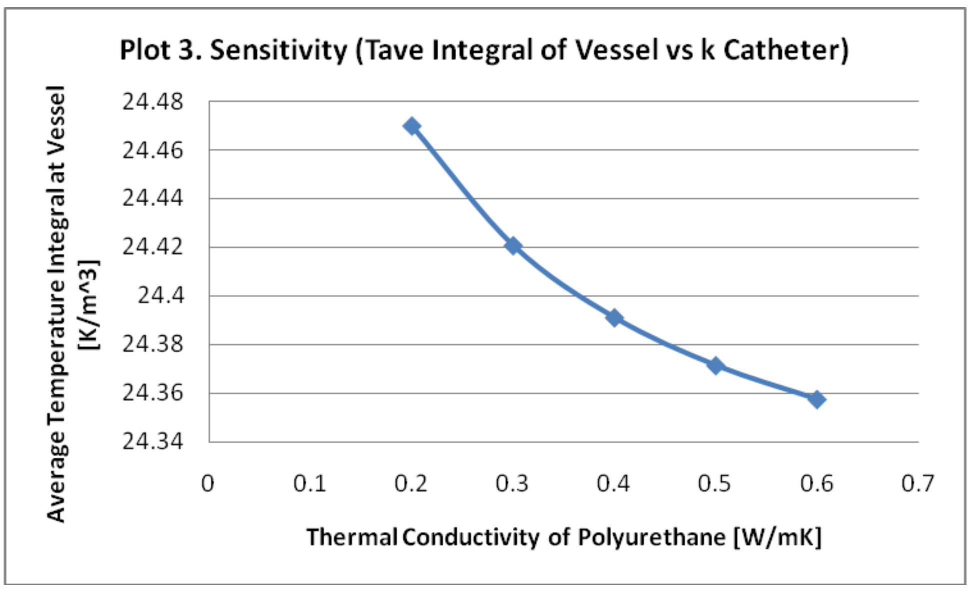


Figure 4: Sensitivity analysis of average temperature of blood in vessel to thermal conducitivty of catheter wall

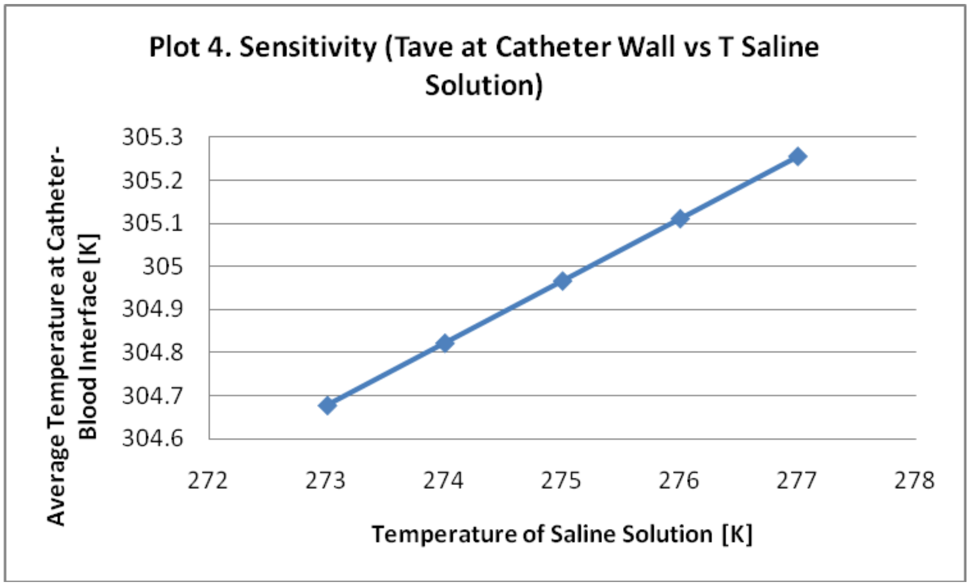


Figure 5: Sensitivity analysis of average temperature at catheter wall-vessel interface with temperature of saline solution

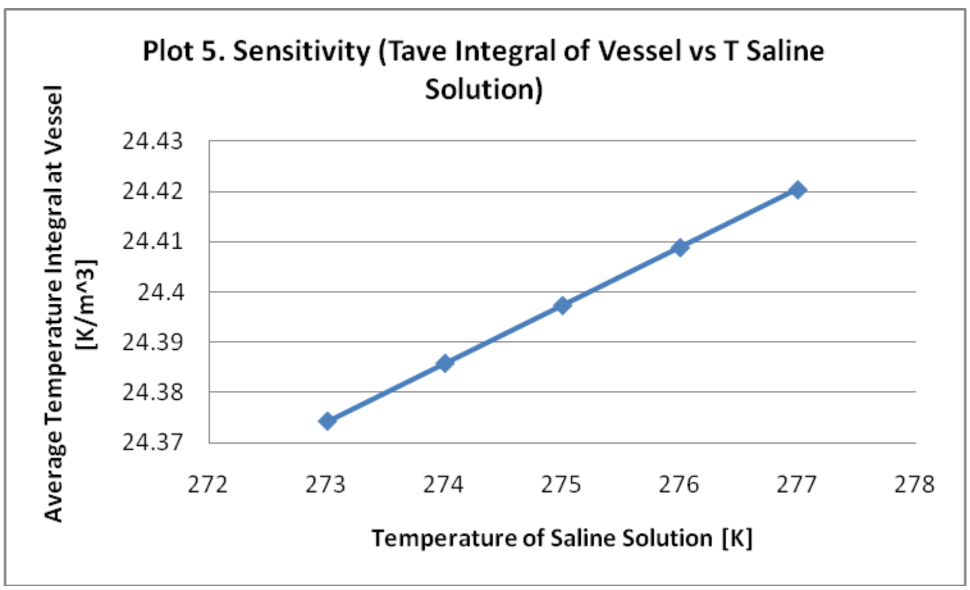


Figure 6: Sensitivity analysis of average temperature in the blood vessel with changing saline solution temperature

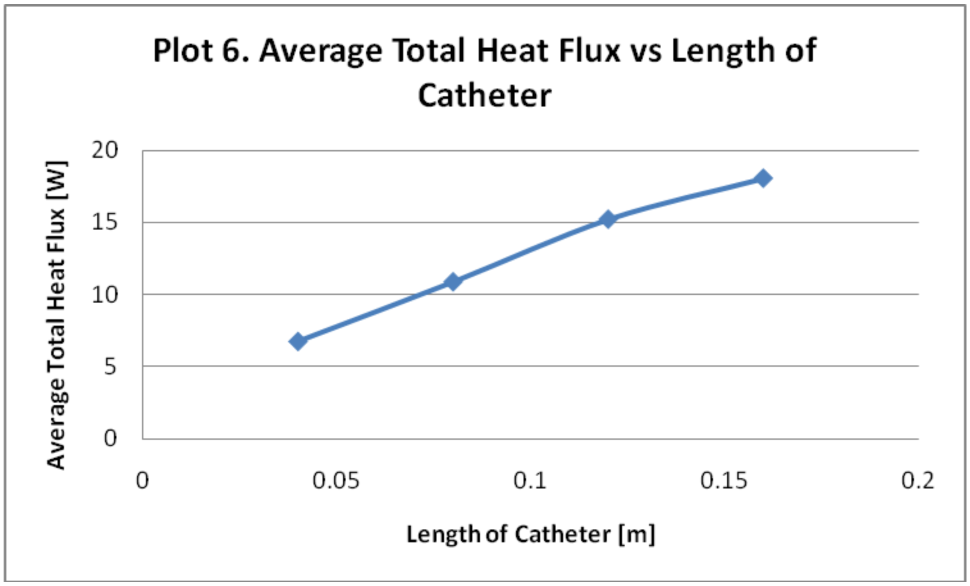


Figure 7: Comparison of average total heat flux to length of catheter

We chose to perform the above sensitivity analysis to determine what parameters our model was sensitive too. The two most practical parameters to vary were the temperature of the incoming cooling fluid and the length of the catheter balloon. From the sensitivity analysis it was evident that as the temperature of the saline solution increased so did the average temperature at the catheter-blood interface. The average temperature at the interface was of particular interest since rapid cooling near the center of the blood vessel was what determined the success of the induced hypothermia. Additionally, as the length of the catheter balloon was increased the average heat flux being removed from the blood in the vena cava increased. Each of the parameters displayed a near perfect linear relationship which was expected. In changing all of the other parameters there was not much variation. This robustness was desired since changing intrinsic material property such as thermal conductivity of the polyurethane was not realistic. Other parameters such as the density, specific heat, and velocity of the blood also were not realistic to vary significantly. Based on the sensitivity analysis it can be said that our model was very robust and fairly accurate.

The time it took to cool the blood was dependent primarily upon the length of the intravenous catheter and the temperature of the cooling fluid (Figure 10).

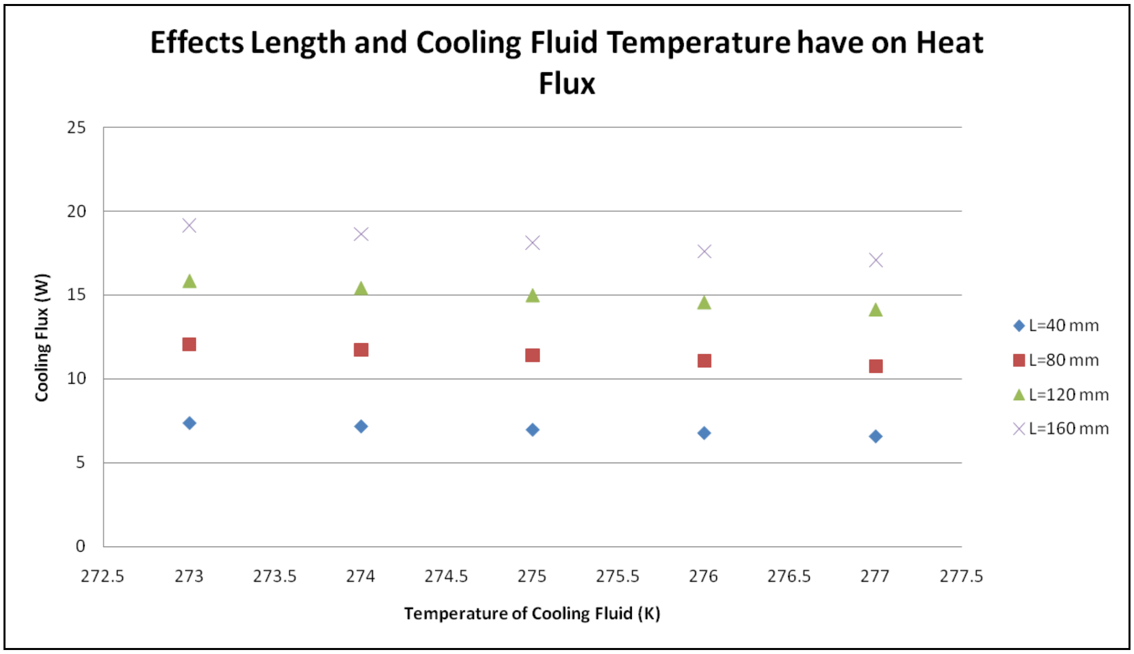


Figure 10: Effects of length and cooling fluid temperature on the cooling flux of the intravenous cooling system. Cooling flux increased as length increased and temperature of cooling fluid decreased.

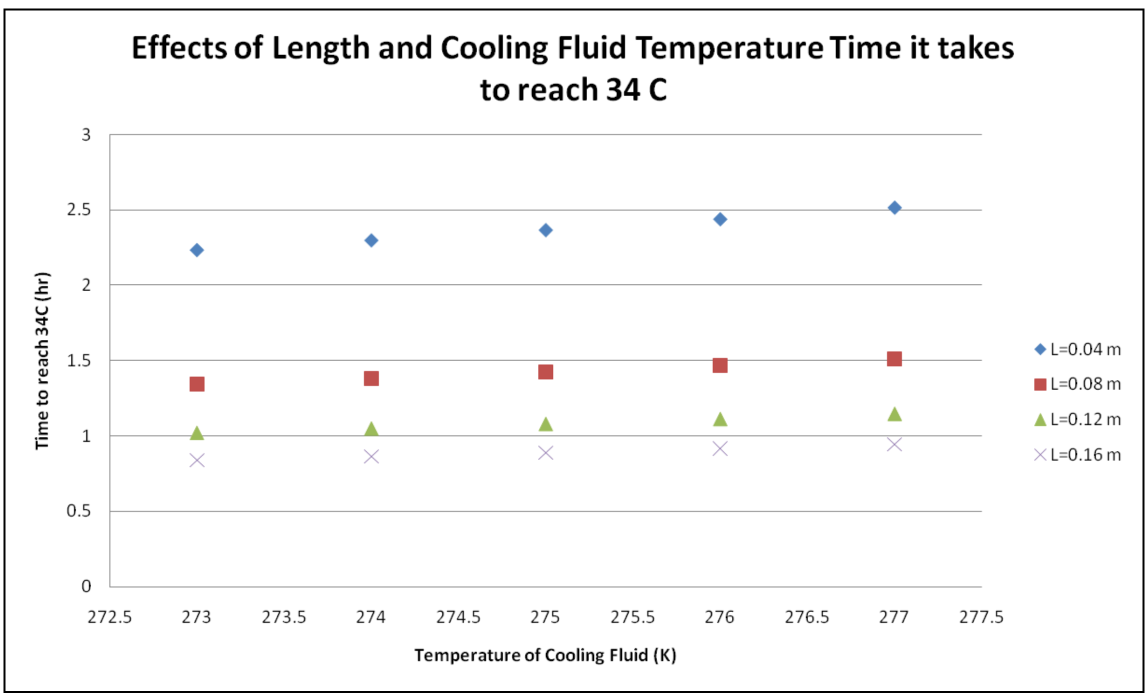


Figure11: Effects of length and cooling fluid temperature on the time it takes to reach target temperature of 34 °C. As length increased and temperature of cooling fluid decreased the time it took to cool decreased.

From this graph it was clear that there was a negative correlation between the total out-going heat flux and the temperature of the cooling fluid. When the temperature of the cooling fluid went up the amount of the heat leaving the blood vessel went up as well. When the length of the catheter increased the heat flux also increased. Immediately following the determination of heat flux the time it took to cool the blood was found as aforementioned.

Accuracy Analysis:

To confirm the accuracy of our results we consulted the literature of actual patient trials with intravenous cooling using an Alsius CoolLine® catheter and CoolGard 3000® active temperature control system. In a preliminary study of six stroke patients, each was cooled using the intravenous method to reduce brain damage for the maximal amount of restored function after recovery. The doctors found that the mean time to cool each patient to the target temperature of 33°C was three hours with an average cooling rate of 1.4°C/hour (Georgiadis, et al., 2001). It should also be noted that the time required to induce hypothermia can vary widely based on protocols such as measures taken to prevent shivering as well as body size, body mass, and initial body temperature (Polderman, 2004). Our model did not take into account all of these variations, but it still had results that were similar to the clinical studies.

Conclusions:

Through the use of COMSOL we were able to find that as the length of the catheter increased so too did the heat flux through the catheter wall. We also found that as the temperature of the saline was decreased, the heat flux through the catheter wall increased. As the heat flux increased, the time required to cool the blood to the desired temperature decreased as well. Based on our sensitivity analysis, the length of the catheter, and surface area by extension, had the greater effect on heat flux and thus times to cool the blood. In short, the longer and colder the catheter was, the efficiency of the treatment increased.

Using this conclusion, one can choose an effective method to treat a patient depending on the situation. In an emergency situation, since insertion of long catheter may be difficult, lowering the saline fluid temperature will increase the efficiency. In a more controlled and prolonged situation, inserting a longer catheter length will increase the efficiency of the treatment.

Design Recommendations:

There are three main controlling factors that determine the efficiency of the treatment. Namely, these include length of the catheter, the diameter of the catheter, and the temperature of the saline fluid. The temperature of the saline fluid may be lowered; however, it can only be cooled to the level where the fluid would not freeze, is harmless, and have high thermal conductivity. The diameter of the catheter is also limiting in that too large of a diameter can lead to blockage of blood flow. Thus, improvements in designs will have to make use of the length of the catheter. Changing the length of the catheter effectively changes the surface area exposed of the catheter.

While there are limitations on how long the catheter can be since it should not exceed the length of the inferior vena cava, there are other ways to increase the surface area of the catheter. One such way is to make the catheter balloon helical in shape. This allows the overall length to stay the same while increasing the surface area of the catheter. This effectively increases the flux of heat loss while maintaining the overall length of the catheter.

Appendix A: Mathematical statement of the problem:

- Geometry:

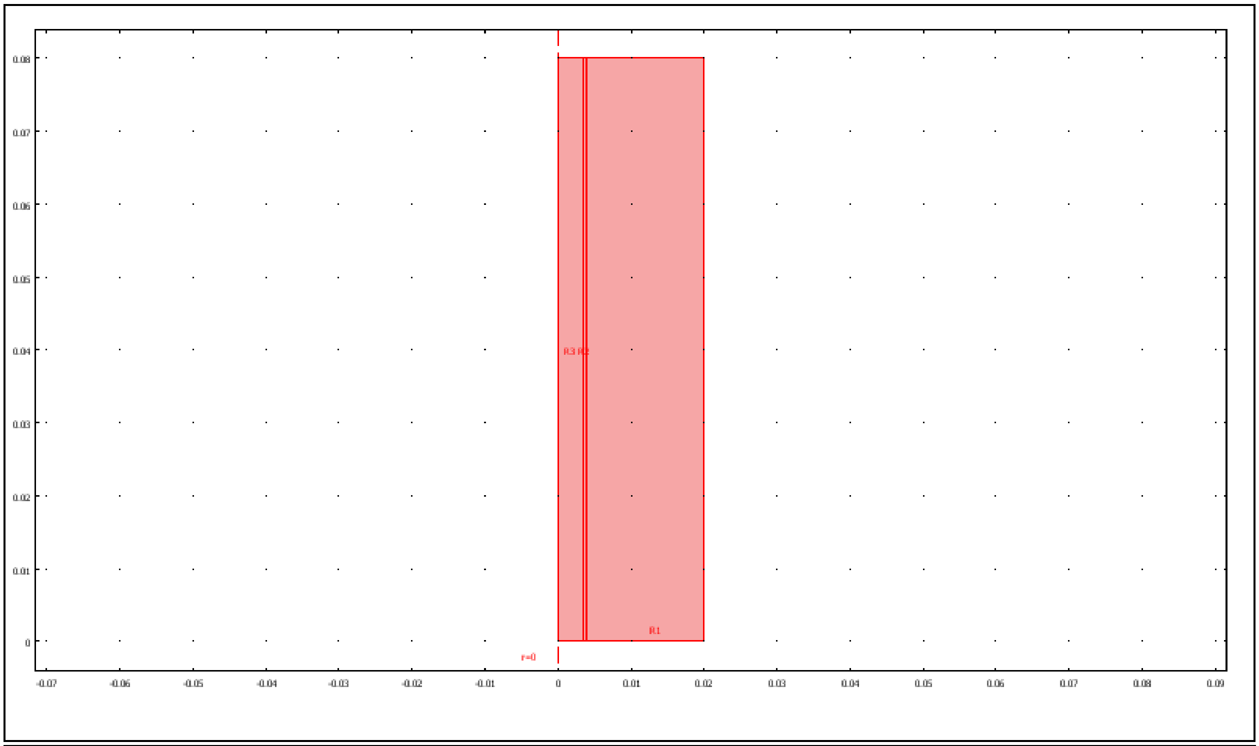


Figure12: COMSOL geometry. Three axis-symmetry domains are shown, namely catheter, catheter wall, and inferior vena cava vessel.

- Governing Equations:
  - Heat transfer:

$$\rho c_p \left(v_x \frac{\delta T}{\delta r} + v_y \frac{\delta T}{\delta z} \right) = \frac{k}{r} \frac{d}{dr} \left(r \frac{dT}{dr} \right) + k \left(\frac{\delta^2 T}{\delta z^2} \right)$$

  - Navier-Stokes

$$\rho(u\nabla)u = \nabla[-pI + \eta(\nabla u + (\nabla u)^T)] + F$$

- Boundary Conditions:
  - Heat flux at blood vessel wall is 0 (insulated).
  - Incoming velocity of blood is 15 cm/s.
  - Incoming velocity of cooling fluid is 1.105 cm/s
  - Heat flux at the middle is 0 (symmetry).
  - Temperature at the inlet of the catheter balloon is 4 ◦C.
  - Temperature of blood entering the system is 37 ◦C.
  - Convective heat flux for both outlets (balloon and vena cava)

- Pressure is 0 Pa at both outlets
- Both ends of catheter are thermally insulated.

- Initial Conditions:
  - Incoming temperature at the bottom of the catheter is body temperature (37◦C).
  - Temperature of cooling fluid is 4◦C.
  - Initial velocity in the vena cava is 15 cm/s
  - Initial velocity in the catheter is 0 cm/s
- Input Parameters:

Table 3: Material Properties and Parameters Used

Parameters/ Constants	Symbol	Value	Units	Reference #
Diameter of catheter bubble	D_B	8	mm	1
Diameter of IVC*	D_I	20	mm	7
Length of catheter bubble	L	80	mm	1
Velocity of blood	V_b	15	cm/s	8
Velocity of cooling fluid	V_c	1.105	cm/s	6
Thermal conductivity of blood	k_b	0.492	W/mK	5
Thermal conductivity of cooling fluid	k_c	0.6	W/mK	5
Thermal conductivity of polyurethane	K_u	0.25	W/mK	5
Heat capacity of blood	C_b	3594	J/kgK	4
Heat capacity of cooling fluid	C_c	4130	J/kgK	4
Heat capacity of polyurethane	C_u	1050	J/kgK	5
Temperature of cooling fluid	T_c	4	◦C	2
Heat generation energy	Q	116	W	4
Density of blood	ρ_b	1060	kg/m^3	4
Viscosity of blood	η_b	$3x10^{-3}$	Pa*s	4
Viscosity of Cooling fluid	η_c	$1.5x10^{-3}$	Pa*s	9
Thermal conductivity of Polyurethane	k_u	0.24	W/mk	10

- *IVC=inferior vena cava

Appendix B: Solution Strategy:

- COMSOL Multiphysics was used as a solver.
- The model assumed steady state. Therefore, no time steps were required.
- Mesh Convergence Analysis:

Average temperature in blood vessel was measured to test the mesh convergence.

Table 4: Mesh Convergence Analysis

Trial	Catheter (Domain 1)	Catheter Wall (Domain 2)	Blood Vessel (Domain 3)	Number of Mesh Elements	Ave Temp-Integral Area at Blood Vessel [m^3K]
1	10x5	10x4	10x10	190	0.029917
2	20x10	20x8	20x20	760	0.029917
3	40x20	40x16	40x40	3040	0.029915
4	80x40	80x32	80x80	12160	0.029915
5	100x80	100x64	100x100	24400	0.029914
6	100x160	100x128	100x100	38800	0.029914
7	100x320	100x256	100x100	67600	0.029914
8	100x320	100x256	100x105	68882	0.029914
9	100x640	100x500	100x105	124500	0.029914
10	100x640	100x500	100x106	124600	0.029914
11	200x640	200x500	200x106	249200	0.029914

*Note: dimensions are written in the form of l*w (or length of domain versus radial elements)

**Note: element number higher than 106 on domain 3 will provide error in COMSOL solving.

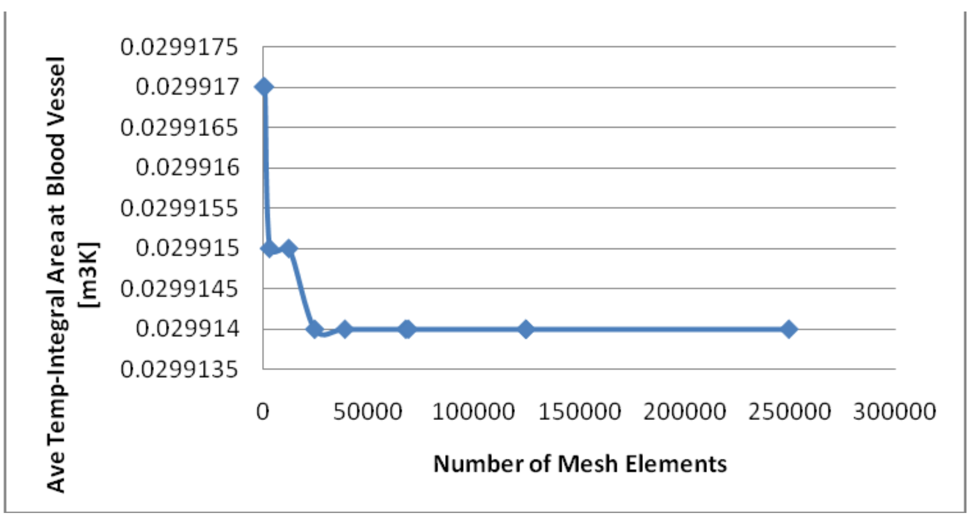


Figure 13. Mesh convergence analysis. Number of elements higher than 50000 did not produce significant change in average temperature at blood vessel

As can be seen above, mesh element number beyond around 50000 will yield same result for average temperature. In other words, mesh converged around element number of 50000 and above. This suggests those mesh dimensions referring to trial 7 and above are appropriate in reducing discretization error from mesh. Actual meshed domain is shown below.

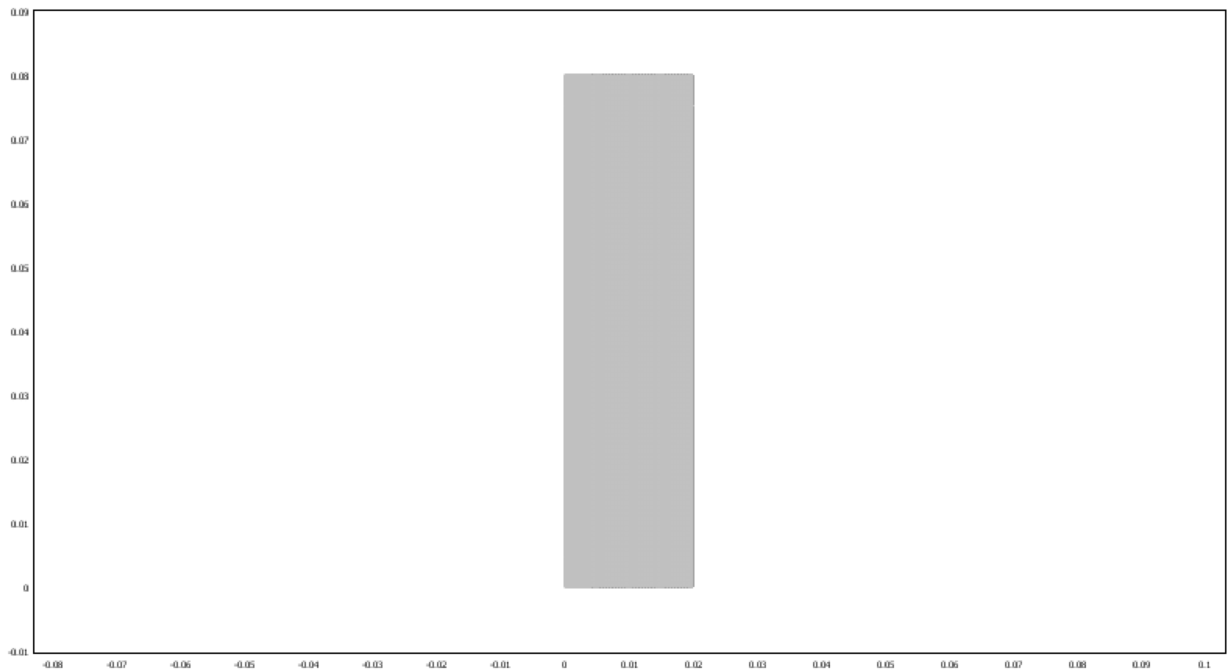


Figure 14. Meshed domain. Optimum mesh settings show very densely meshed domains.

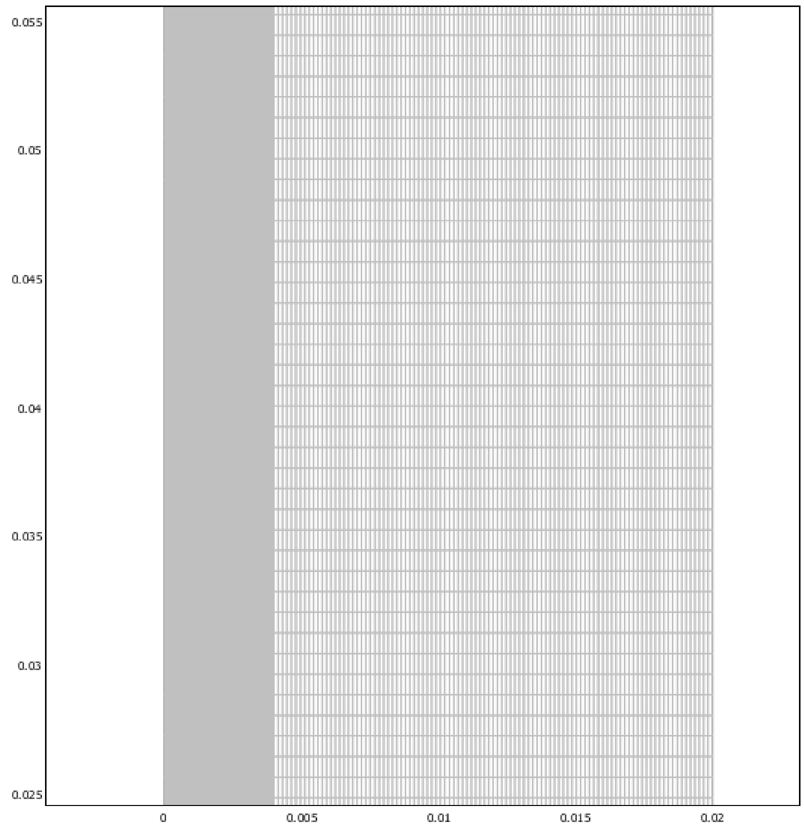


Figure 15. Meshed domain zoomed in. Zoomed in image shows the dense mesh element network in the domain.

Appendix C: References:

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