Ice Ice Baby: Determining Optimum Cooling Parameters for Neonatal Asphyxia Hypothermia Therapy

Final Honors Capstone Report
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1.0 Introduction

Before getting into the description of this capstone project, it is important to understand what neonatal asphyxia is, why it happens, and what efforts are being made to combat it.

1.1. Problem Definition

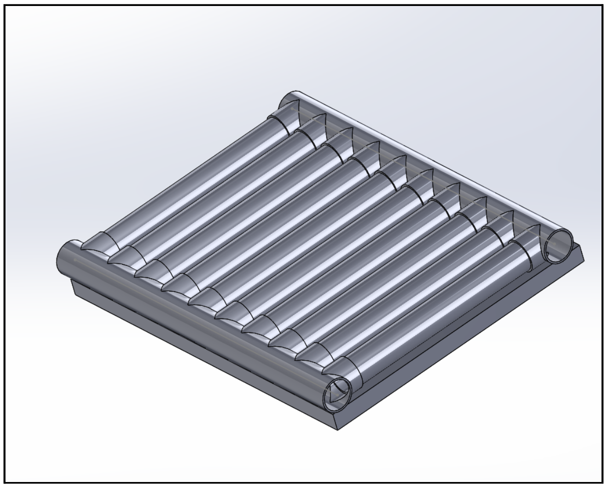
Neonatal asphyxia is a leading cause of neonatal death in India. Approximately 3.6 million neonates around the world are affected by asphyxia annually, and in India specifically, neonatal asphyxia is responsible for 25% of newborn deaths. The condition is caused by oxygen deprivation during or shortly after birth that can be caused by several issues such as knotting of the umbilical cord around the infant's neck, prolonged delivery, maternal preeclampsia, infant heart or lung malformations, or inadequate oxygenation of maternal blood. This can lead to symptoms including seizures, pale skin, diminished respiratory and heart rates, and an overall state of shock. When the obstacle to oxygenation is removed (i.e. umbilical cord is unwrapped from infant's neck), blood can dangerously rush into the head and overwhelm the neural tissue, putting survivors at risk for developmental delays, disabilities, cerebral palsy, motor disorders, and other physical maladies. As a result, hypothermia therapy is the standard treatment for asphyxiated infants, as it helps slow cell metabolism and reduce neurological damage.

The current method for hypothermia therapy in India is through the use of makeshift cold packs made from surgical gloves as they lay in a specialized bed (Figure 1). These surgical gloves are filled with water, tied at the heel, and put into a freezer overnight for next-day use. However, this method is unable to provide a consistent cooling temperature and is thus difficult to administer and regulate. There are commercially available products (i.e. Tecotherm Neo) that are able to continuously monitor infant's temperature and apply a reliable cooling therapy. However, these devices are marketed at thousands of dollars, which is not economically feasible in low-resource communities such as those in India. **Therefore, there is a need for a cost-effective (< $750) device to effectively mitigate the brain injury caused by neonatal asphyxia in low-resource communities.**

Figure 1. Current method of hypothermia therapy for asphyxiated infants involves the use of a makeshift cold pack using a surgical glove (circled in red).

1.2. The Neonatal Asphyxia Project

The Neonatal Asphyxia Project (NAP) team has partnered with Dr. Heena Patel and Dr. Vaibhav Patel at the Hasya Newborn Care Centre to design a device that uses hypothermia therapy to mitigate the effects of neonatal asphyxia. The Hasya Newborn Care Centre is the first comprehensive neonatal hospital in the rural area of northern Gujarat, India. As such, they have specified the cooling requirements for the device to be that it must cool the neonate to 33-34℃ within a period of 60-120 minutes as well as keep the neonate's body temperature stable at 33-34℃ for 72 hours unless manually adjusted. Currently, NAP is prototyping and testing components for a device that applies hypothermia therapy to the neonate through water flow. The team has developed two major prototypes: a tube bed design and a waterbed concept (Figure 2).



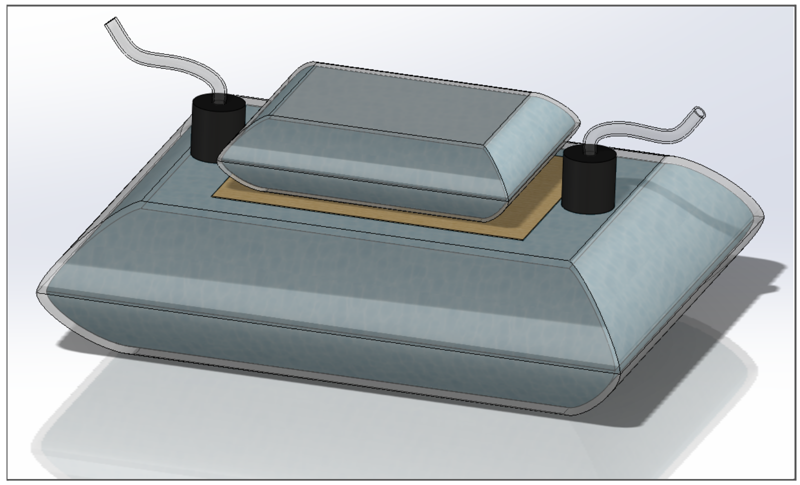


Figure 2. NAP's current major prototypes include a tube bed design (left) and a waterbed concept (right) that both utilize water flow to provide hypothermia therapy

Both of these solutions involve the neonate laying on a cold plate and body heat being transferred to water that passes through a radiator to dissipate the heat to the environment. This water must be cooled to a predetermined temperature before reaching the neonate in order to provide an effective and safe cooling. As such, care must be taken to determine this optimum cooling temperature before these prototypes are implemented in the clinical setting to ensure the safety of the neonates.

2.0 Questions and Problems Addressed by this Capstone Project

During my time as a member of NAP in the 2020-2021 school year, I was a part of the build, or design, sub-team that is currently working on optimizing the cooling regulation as well as developing a realistic prototype of the device. As stated previously, the device will ultimately have to be set to a specific cooling temperature, which had yet to be determined, so I wanted to use computational simulations to determine the optimum temperature for cooling the infants. I initially planned to focus on in-person prototyping and testing, but due to the uncertainty of prototyping during the COVID-19 pandemic, I chose to adjust my project to focus on modeling and simulations.

The major goal of this capstone project was to develop a detailed model of the neonate and tube bed prototype assembly. I initially considered modeling the waterbed assembly, but due to its complex geometry and flow patterns associated with the waterbed, I decided to start with the simpler tube bed design. With this focus in mind, I broke the project down into three major steps: first modeling heat transfer and temperature distribution throughout the infant's head separately, then modeling fluid flow throughout the tube bed apparatus separately, and then finally coupling the heat transfer and fluid flow physics together to obtain a complete model of the entire assembly. Once this model was complete, I hoped to optimize the cooling parameters applied to the neonate for hypothermia therapy. Specifically, I wanted to determine the optimum temperature applied to the neonate for cooling, the radius of the tubes in the prototype assembly, and the velocity of water flowing through the tubes in the prototype assembly. This plan provided me with a strong foundation to guide me through the project and keep track of my progress along the way.

3.0 Methods

As stated previously, the simulations were broken down into a separate heat transfer simulation and a separate fluid flow simulation, which were then combined to create the overall model of hypothermia therapy being applied to a neonate. Heat transfer and fluid flow were modeled using the bioheat transfer and laminar flow modules in COMSOL. The multiphysics coupling feature in COMSOL was used to combine the two simulations.

3.1. Heat Transfer Methods

Heat transfer was modeled using the bioheat transfer equations and boundary conditions shown in Figures 3 and 4.

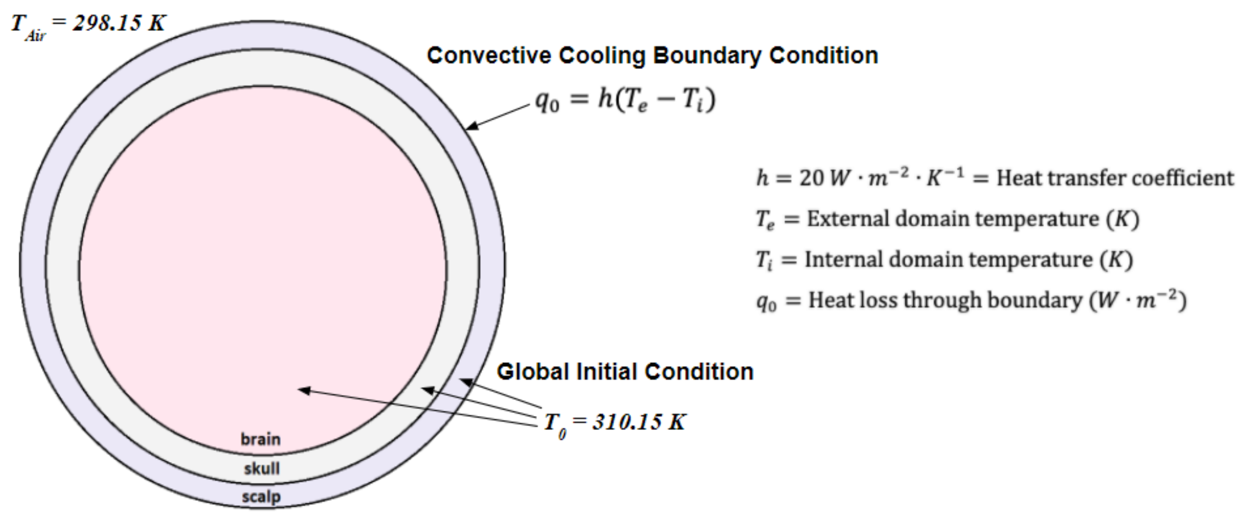


Figure 3. Boundary conditions used for bioheat transfer simulations in COMSOL. A convective cooling boundary condition was utilized with a standard ambient temperature of 298.15 K and an initial body temperature of 310.15 K.

Heat Transfer in Tissue

$$\boxed{\rho C_p \frac{\partial T}{\partial t}} = \boxed{\nabla(k\nabla T)} + \cancelto{0}{Q_s} + \cancelto{0}{Q_p} + \boxed{Q_m}$$

Bioheat transfer — Heat Diffusion Rate of Tissue — Metabolic Heat Source

$$\rho = \textit{Density of tissue} = 1100\ (kg \cdot m^{-3})$$
$$C_p = \textit{Tissue heat capacitance} = 4450\ (J \cdot kg^{-1} \cdot K^{-1})$$
$$k = \textit{Tissue thermal conductivity} = 0.53\ (W \cdot m^{-1} \cdot K^{-1})$$
$$T = \textit{Temperature}\ (K)$$
$$Q_s = \textit{Heat source within the medium} = 0\ (W \cdot m^{-3})$$
$$Q_p = \textit{Heat change due to blood perfusion} = 0\ (W \cdot m^{-3})$$
$$Q_m = \textit{Heat source due to metabolic activity} = 10010\ (W \cdot m^{-3})$$

Figure 4. Thermodynamic equation used for bioheat transfer simulations. Heat source within the medium and heat change due to blood perfusion were considered to be negligible. The heat source due to metabolic activity was determined to be 10010 W/m^3 (Figure 5).

A significant amount of time and thought went into determining the heat source settings used in the simulation. At first, I discovered that setting all biologic heat generated to zero did not work extremely well because it still caused the body temperature to drop by 3 K even when the external temperature was room temperature. I then tried adjusting the parameters in the bioheat transfer equation. Of course, I could not change the arterial blood temperature, specific heat, and density values since those are accepted everywhere to be true, but I was not extremely confident in the perfusion rate and metabolic heat source values obtained from literature. I found that when the biologic heat was not set to zero, the heat generated by perfusion dominated everything, and the temperature of the head hardly changed even when a freezing cold temperature was applied. I realized that COMSOL does not slow the perfusion rate even when the temperature is super cold, and the (Tb-T) in the cooling boundary equation actually causes the heat generated to increase when the temperature gets colder. In other words, COMSOL does not actually model the main hypothermia therapy effect of reduced blood flow on the head. Because of this, I just set the perfusion rate equal to zero and focused solely on the metabolic heat source Qmet.

For the metabolic heat setting (Q_m), I performed multiple parametric sweeps of the Q_m value to determine what value maintains a body temperature of 310.15 K when exposed to an external temperature of 298.15 K for two hours. From this, I found that a constant metabolic heat source setting of 10010 W/m^3 maintained a stable temperature of 310.15 K for two hours (Figure 5). Of course, this is still not the most accurate model of metabolic heat generation, as metabolism is influenced by numerous factors and is rarely a constant value, and this will be discussed in the limitations section.

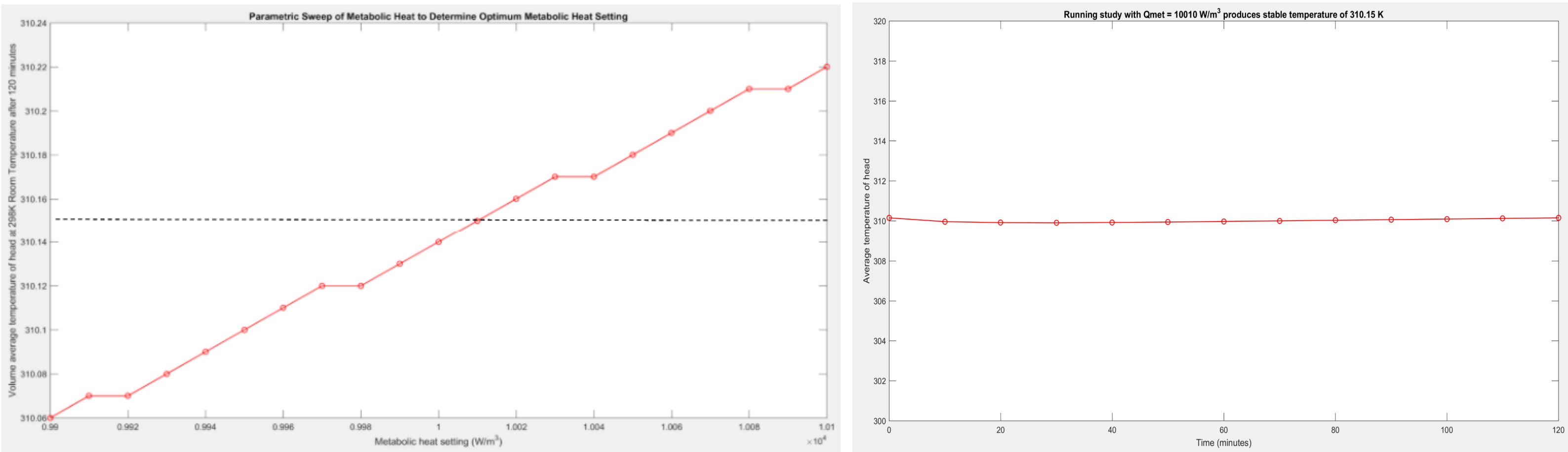


Figure 5. Parametric sweep of metabolic heat source setting (left) reveals an optimum value of 10010 maintains a stable temperature of 310.15 K over a period of two hours (right).

Before modeling heat transfer through a complex head model, I utilized a simplified spherical model (Figure 6) with multiple layers to imitate the various layers of the brain, skull, and scalp with each layer having different thermal properties such as specific heat and conductance. This sphere had the same average radius of that of a neonate, but it obviously did not have the same extent of curvature and complexity.

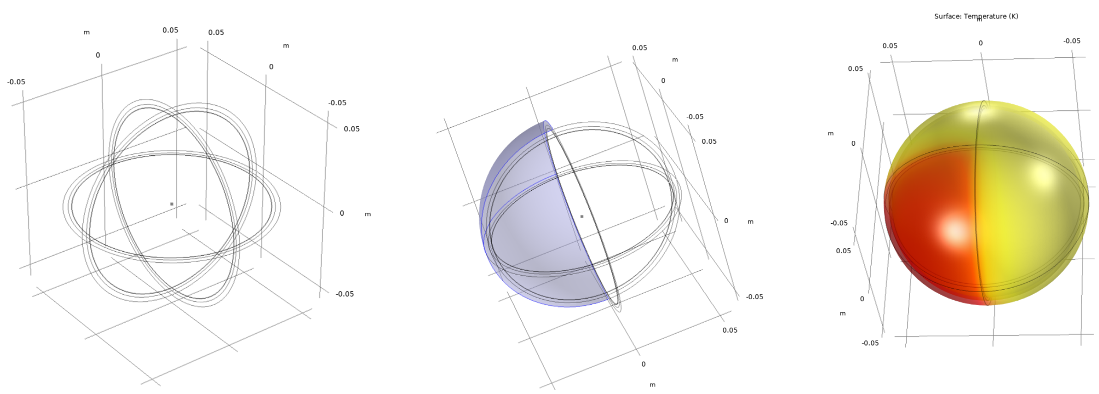


Figure 6. Simplified spherical model used for preliminary heat transfer simulations. Image on the left is a wireframe model of the sphere, image in the middle shows the cooling boundary applied to the sphere, and image on the right further clarifies the cooling boundary difference in temperature.

To model how the infant will be cooled from the bed, I selected an eighth of the sphere to have a different external temperature than the rest of the sphere's external temp of 278.15 K. The temperature of this eighth of the sphere would be the set temperature of the cooling apparatus. I then used the bioheat differential equation to model the heat flow for a period of 72 hours. I ended up obtaining a strong heat distribution throughout the head (Figure 6). I then performed a parametric sweep of the cooling temperature from 273 K to 298 K and found that a cooling temperature of approximately 18℃ produced an average body temp of 32℃ at 72 hours of cooling. I also found that the multiple layers modeling the various layers of the brain, skull, and scalp did not have a significant effect on the heat distribution throughout the head. As a result, for simulations using the complex head model, I chose to simplify the model by only using one layer with uniform thermal properties throughout the solid.

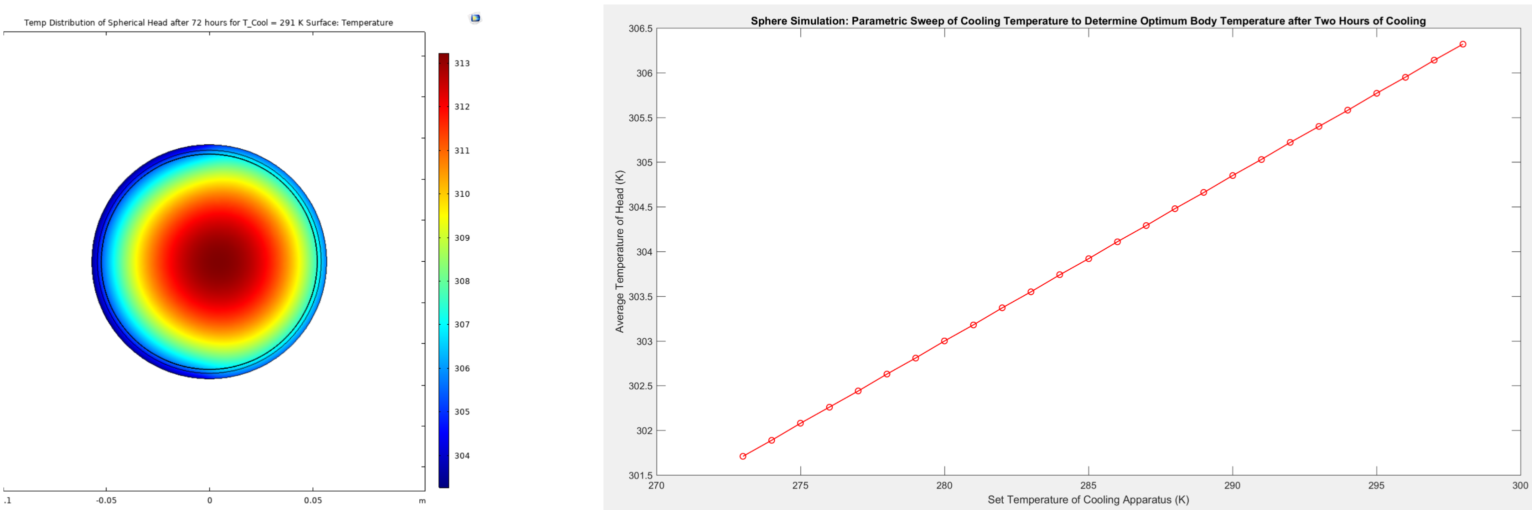


Figure 7. Preliminary simulations using the simplified spherical model reveal an optimum cooling temperature of 18℃ and multiple head layers do not have a significant impact on heat distribution.

Once the preliminary simulations with the spherical model were completed, I moved on to modeling heat transfer through a more complex head model (Figure 8). The same equations and parameters were used for this simulation, with the only exception being that the complex head model only had one uniform layer rather than multiple distinct layers based on the results from the sphere simulation. All measurements of core body temperature were measured by taking a volume average of temperature across the head.

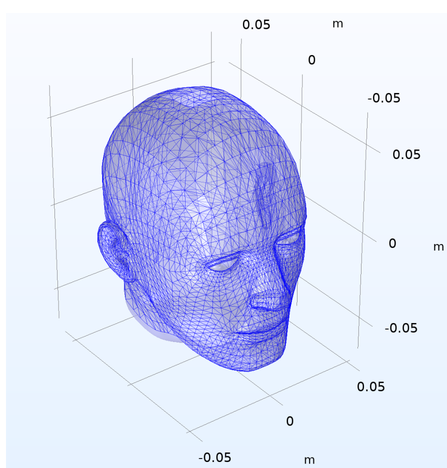
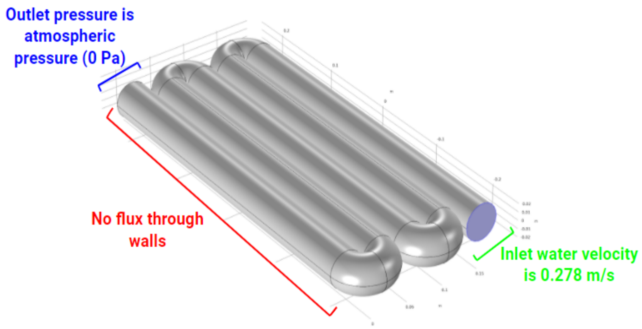


Figure 8. Complex head model used for detailed heat transfer simulations to model temperature distribution throughout the head.

3.2. Fluid Flow Methods

Fluid flow was modeled using the Navier-Stokes equations and boundary conditions shown in Figure 9.



$$Re = \frac{\rho v R}{\mu} = 606 \quad \left.\begin{array}{l} \rho = \textit{Density of water} = 1000\ (kg \cdot m^{-3}) \\ v = \textit{Maximum water velocity} = 0.278\ (m \cdot s^{-1}) \\ R = \textit{Radius of tubing} = 2.1825\ cm \\ \mu = \textit{Dynamic viscosity of water} = 0.001\ (Pa \cdot s) \end{array}\right\} \text{Used laminar flow module in COMSOL}$$

Navier-Stokes Equations for Incompressible Newtonian Fluid:

Conservation of Momentum:

$$\rho\left(\underbrace{\boxed{\frac{d\vec{v}}{dt}}}_{\text{Time-dependent term}} + \underbrace{\boxed{\vec{v}\cdot\nabla\vec{v}}}_{\text{Convective term}}\right) = \underbrace{\boxed{-\nabla p}}_{\text{Pressure Gradient}} + \underbrace{\boxed{\rho\vec{g}}}_{\text{Body Forces}} + \underbrace{\boxed{\mu\nabla^2\vec{v}}}_{\text{Viscous Term}}$$

Conservation of Mass:

$$\underbrace{\boxed{\nabla\cdot\vec{v}}}_{\text{Mass Accumulation Term}} = 0$$

Figure 9. Boundary conditions (left) and equations (right) used for fluid flow simulation. A calculation of the Reynolds number prior to simulation allowed the laminar flow module in COMSOL to be used.

I initially tried using NAP's CAD model that was provided to me at the beginning of this capstone project, but I experienced a significant amount of difficulty attempting to do this. For some reason, COMSOL was not able to completely import this model, and it experienced strong turbulence and complex fluid flows that repeatedly led to my computer crashing when attempting to run the simulation. This led to me simplifying the model to include less tubes and a less complex geometry (Figure 10) that allowed it to run continuously and efficiently.

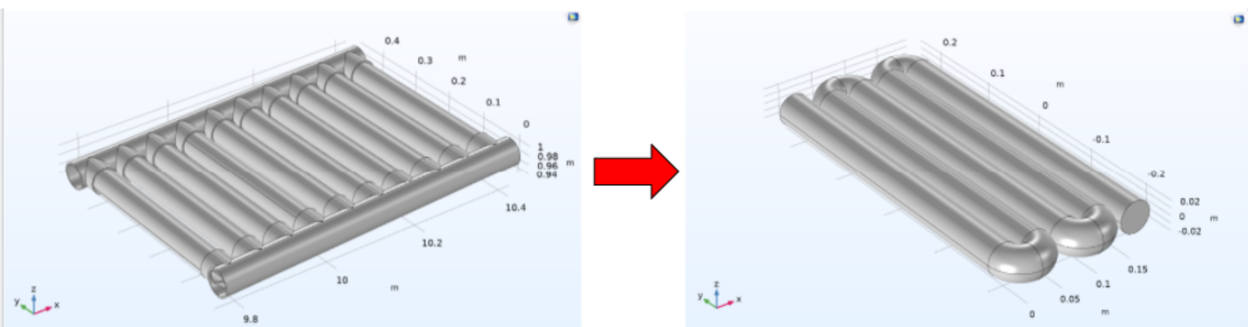


Figure 10. Simplification of NAP's tube bed model design (left) to smaller, less complex model (right) that prevented COMSOL from crashing and allowed fluid flow simulations to run without difficulty.

One further simplification that I had to make in the fluid flow simulations was setting the flow to be isothermal, meaning that despite water's absorption of heat from its surroundings, it maintains its constant cooling temperature. This is an ideal case, and it is unknown as to whether the cooling device in NAP's solution will be able to maintain a constant water temperature. As such, this assumption will be further discussed in the limitations section.

3.3. Coupled Heat Transfer and Fluid Flow Methods

Once the individual heat transfer and fluid flow simulations were completed, the two processes were coupled by combining the complex head model and the simplified tube bed model into one solid (Figure 11). The physics of the two processes were combined by using the multiphysics coupling tool in COMSOL while keeping the individual parameters of each simulation the same.

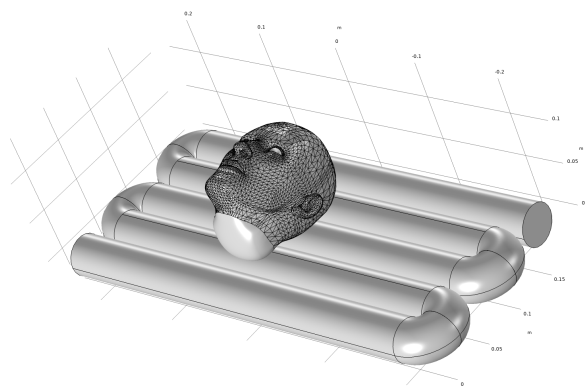


Figure 11. Combined head and tube bed model used to couple heat transfer and fluid flow simulations in order to gain complete understanding of the entire hypothermia therapy process.

4.0 Results

With a strong foundation and plan set into place, I was able to obtain heat maps of the temperature distribution throughout the head for both the individual and coupled cases as well as velocity profiles of the water fluid flow through the tube bed design.

4.1. Individual Heat Transfer Simulations

The bioheat transfer simulation of the complex head model produced an exceptional heat transfer map that clearly exhibited the cooling boundary being applied to the back of the head as well as the temperature distribution throughout the head (Figure 12). Using this, I performed a parametric sweep of the cooling temperature from 260.15 K to 280.15 K and consequently found that even at the lowest temperature of 260.15 K, the core body temperature could only be reduced to 308.15 K after two hours, which is still significantly above the 307 K cooling requirement. This cooling temperature of 260.15 K also poses challenges if water is to be used as the fluid to cool the neonate down given water's freezing temperature of 273.15 K. Nevertheless, I could not draw a decisive conclusion without simulating the entire model including the fluid flow, so despite the discouraging results, I proceeded to go on to model fluid flow through the tube bed.

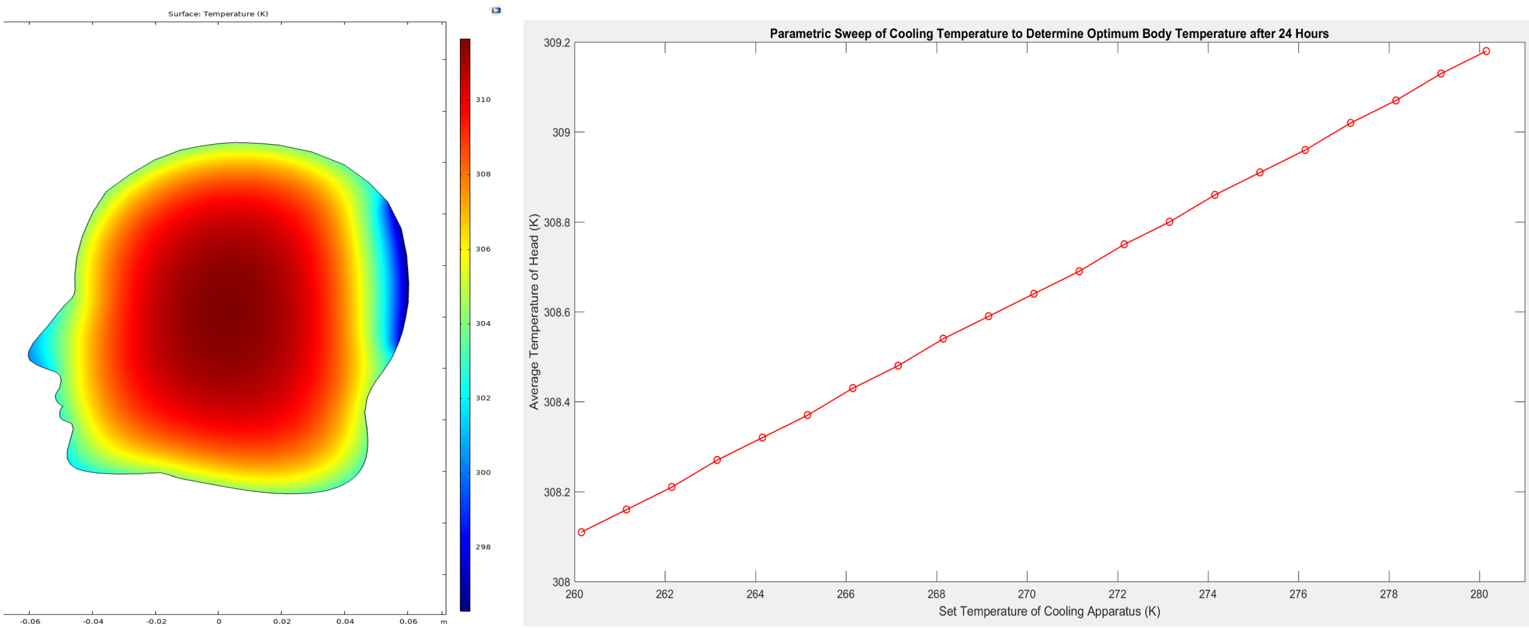


Figure 12. Temperature distribution throughout the head model (left) and parametric sweep of cooling temperature (right) reveals that a 3℃ drop in core body temperature cannot be attained. The closest the head gets to this 307 K target temperature is approximately 308 K, but the corresponding cooling temperature of 260 K poses challenges if water is to be used as the fluid.

4.2. Individual Fluid Flow Simulations

The laminar fluid flow simulation also produced an exceptional velocity profile map of water flowing through the simplified tube bed model (Figure 13). The results revealed that the velocity profile is uniform until the flow hits the curves in the device. Once the fluid makes its first 180 degree turn, it is unable to return to its uniform distribution and instead is characterized by stagnation points on the inside of the curve and higher velocities on the outside of the curve. This information is extremely useful to the NAP build team, as it gives them a better understanding of how fluid flows through a curved device and will guide them in future prototyping.

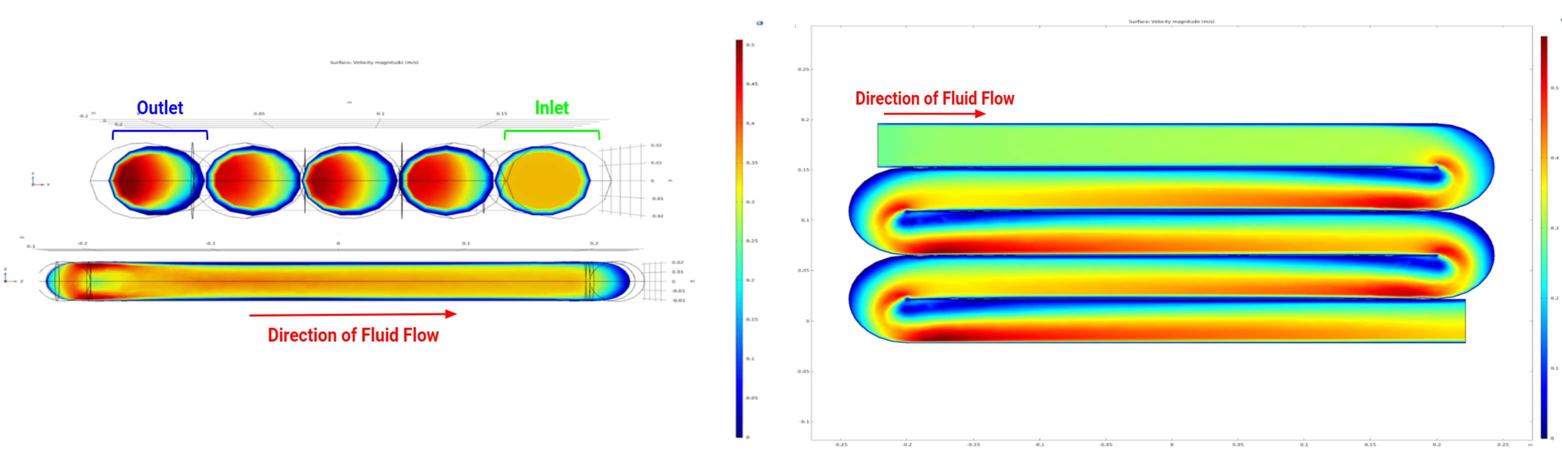


Figure 13. Fluid distribution map throughout the tube bed model reveals that the curves in the assembly cause stagnation points and deviations from a uniform velocity profile.

4.3. Coupled Heat Transfer and Fluid Flow Simulations

The coupling of the bioheat transfer and laminar flow simulations of the complex head model produced an exceptional heat transfer map that clearly exhibited the point of contact between the back of the head and the chilled water as well as the temperature distribution throughout the head (Figure 14). Using this, I again performed a parametric sweep of the cooling temperature from 260.15 K to 280.15 K and consequently found that even at the lowest temperature of 260.15 K, the core body temperature could only be reduced to 308.38 K after two hours, which is actually even higher than the lowest temperature obtained in the individual heat transfer simulation. This is likely due to the fact that there is a smaller point of contact with the cooling boundary in the coupled case, causing it to be even more significantly above the 307 K cooling requirement. Again, this cooling temperature of 260.15 K also poses challenges if water is to be used as the fluid to cool the neonate down given water's freezing temperature of 273.15 K. With this information, I could decisively determine that the tube bed does not fulfill the cooling requirements and is not a feasible solution based on this model.

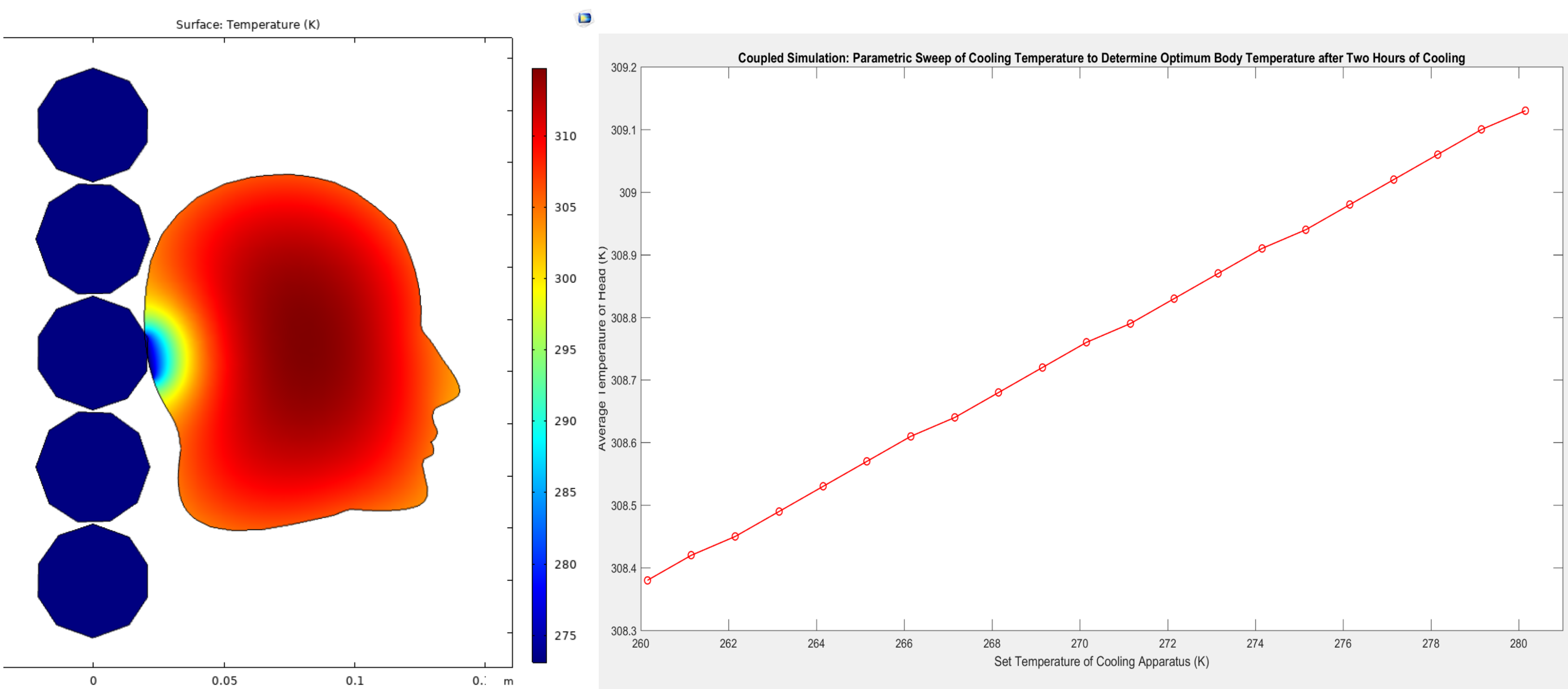


Figure 14. Temperature distribution throughout the entire combined head and tube bed model (left) and parametric sweep of cooling temperature (right) reveals that a 3℃ drop in core body temperature still cannot be attained. The closest the head gets to this 307 K target temperature is approximately 308.4 K, but the corresponding cooling temperature of 260 K still poses challenges if water is to be used as the fluid.

5.0 Discussion and Conclusions

The heat transfer and fluid flow simulations ultimately provided results that are very useful in the assessment of the feasibility of NAP's tube bed prototype, as well as provide guidance into future steps this project could be taken. However, the limitations of this model must be considered when conclusions are being drawn from its results.

5.1. Meaning of Results

Both the individual heat transfer simulation and the coupled heat transfer and fluid flow revealed that a core body temperature of 307 K cannot be obtained within a period of 120 minutes. Since this is a critical requirement for the device, the tube bed does not appear to be a feasible solution based on this model. In order for the solution to obtain this required temperature, a cooling temperature much less than 260 K would have to be applied. Because of this, water does not appear to be the best liquid for cooling the neonate given that it will likely freeze at these temperatures, posing further risks in obstructing flow and possibly cracking the tubing. Alternative liquids that could be used in substitution of water may include saline or ethanol, which have lower freezing temperatures than water and are still relatively common in a hospital setting.

The individual fluid flow simulation also provided information that will be useful in the development of this device. Specifically, the velocity distribution of water moving throughout the tube bed apparatus showed the development of stagnation points along the inner curves of the tubes. This informs NAP's build sub-team of the consequences of adding more curvature to the tubing of prototypes, which influences the device's ability to provide a consistent cooling to the neonate. Since the flow had to be simplified to be isothermal, changing the radius of the tubing and the velocity of water flowing through the tubes did not have any effect on the heat transfer, so I was not able to optimize these parameters using this model.

5.2. Next Steps

If someone were to continue this project after me, I would suggest utilizing this complete model to assess NAP's other prototype, the waterbed. As stated previously, I initially wanted to determine the feasibility of this waterbed prototype, but I eventually decided to start with the more simpler tube bed prototype as I constructed the model from scratch. I would also suggest fine-tuning the metabolism settings to be more complex and dependent on other factors such as temperature, time, and meals, which will provide a more accurate understanding of how heat transfer is influenced by metabolism and its associated variables. I would also try to seek out a stronger computational software so that the assumption of isothermal flow does not have to be made, and the effects of water absorbing heat from the infant can be determined. Finally, I would also seek out a more accurate indicator of core body temperature. While a volume average of the head seemed to be a reasonable estimate of the infant's core temperature, utilizing a normalized temperature parameter such as CEM43 does for higher temperatures or expanding the model to be a complete full body model could provide a more accurate understanding of the effects of hypothermia therapy on the neonate.

5.3. Limitations and Difficulties

As stated previously, this model has several limitations that may influence its accuracy in simulating hypothermia therapy and determining the feasibility of the tube bed prototype. First, the assumption of isothermal fluid flow may prove to be detrimental in the model's accuracy in simulating heat transfer between the fluid and the neonate. Currently, it is unknown whether NAP's temperature regulator for this device is able to maintain the fluid at a constant cooling temperature as it exchanges heat with the neonate. Therefore, further testing of the prototype is needed in order to determine if this assumption is valid. Until then, optimization of the radius of the tubing and velocity of the water cannot be done. Second, the simplified assessment of body temperature using a volume average of the head may also be a severe limitation in the model's accuracy. The human body is normally subject to fluctuations in temperature throughout different areas of the body, so only measuring the head's temperature may not be the most accurate indicator of core body temperature. Therefore, a normalized temperature parameter or the expansion of the model to include the entire body could prove to be very useful. Finally, the simplification of heat generated by metabolism to only be a predetermined constant also limits the applicability of this model. Metabolism is influenced by a wide range of variables, and infants especially have a high rate of heat loss that influences their metabolism, so combining all of these parameters into one constant may limit the accuracy of this model under certain conditions.

This project was filled with many difficulties and challenges. Completing these simulations individually with limited computational resources and experience as well as a strong distaste for COMSOL in general proved to be difficult, frustrating, and quite frankly, annoying. This, in addition to an extremely busy final semester of my undergraduate degree and preparing for applying to medical school, was especially challenging. There were many times that I was not sure if I would be able to complete this and simply wanted to give up, but several people continued to encourage me and push me through until the end. For that, I am extremely grateful for the support I have received, and I am very pleased with the final developed product.

5.4 Acknowledgements

I would like to extend a special thank you to Dr. Melissa Wrobel for being my advisor throughout this capstone project, the Neonatal Asphyxia design team for providing a strong foundation to build off of for this project, and the Engineering Honors Program for allowing me to complete this capstone project.

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