BEE 453 Final Project:
Modeling Heat-Transfer of the Olympic Cool-Cap System®

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Section 1: Executive Summary

Hypoxic-ischemic encephalopathy (HIE), or brain damage due to low blood flow and oxygen deprivation, causes 6 deaths per 1,000 births (Long and Brandon 293). HIE can be caused by cord prolapse, abruptio placentae, maternal hypotension, and asphyxia due to shoulder dystocia, but many times the cause is unknown. The Olympic Cool-Cap system (OCCS) from Natus Medical Inc. was developed to treat HIE in asphyxiated newborn by selectively cooling the brain temperature while maintaining body core temperatures between 34 - 35°C. We modeled this heat-transfer process in the infant head using COMSOL Multiphysics. Our results showed that the gray matter temperature changes by 7 ^{o}C, while the inner brain temperature remained relatively close to the core temperature. The majority of the cooling occurred at the surface and skull of the head primarily due to the high blood-perfusion of the inner brain. However, the average overall brain temperature still reached 33.45^{o}C, which has been shown in animal studies to be within the therapeutically effective temperature range to treat HIE. Our results suggest that the OCCS has been clinically effective by uniformly cooling the surface of the brain, even though the deep brain remains essentially constant.

Key words: Olympic Cool-Cap®, hypoxic-ischemic encephalopathy

Section 2: Introduction

2.1 Background Information

Hypoxic-ischemic encephalopathy (HIE), is a major cause of death or stunted brain development in newborns. It may be the result of umbilical cord prolapsed or abruptio placentae but sometimes the cause is unknown (Long and Brandon 293). Oxygen deprivation, the cause of HIE, can lead to decreased cardiac output and cerebral perfusion. With prolonged oxygen deficiency, the brain becomes reliant on anaerobic metabolism, which results in an increase in lactic acid in the brain, decreased ATP concentrations, failure of ion pumps, and cytotoxic edema. This process eventually leads to the electrical failure of neural tissue (Long and Brandon 295).

The importance of finding a treatment for HIE cannot be understated as it is a common cause of brain damage in newborns. Furthermore, approximately half of all babies with severe HIE die. Those that survive exhibit serious neurological complications such as mental retardation, epilepsy, and cerebral palsy (Long and Brandon 293). However, the type of treatment, extent, duration, and therapeutic window for treatment are not well understood.

One method of treating HIE involves inducing local hypothermia.

Local hypothermia lowers the metabolic requirement of the brain, and thus the oxygen demand, which protects against brain damage during hypoxia. Localized mild to moderate hypothermia (37^o - 34^o C) treatment within 30 minutes of the onset of HIE is neuro-protective in newborn animals. Cooling the brain between 32^oC and 34^oC provides substantial cerebral protection from 10–20 min of total cerebral ischemia in rats (Xu 265, Gunn and Gunn 22, Colbourne 173). One proposed method is through decreasing glutamate and hydroxyl radical production. This method has also been successfully used during human brain and heart surgery to protect against hypoxic brain damage (Xu 265). The extent of this therapeutic window is not known, but extended periods of cooling (5 to 72 hours) have been shown to provide significant neuro-protection in animals, even after 1 to 2 hours after the onset of HIE.

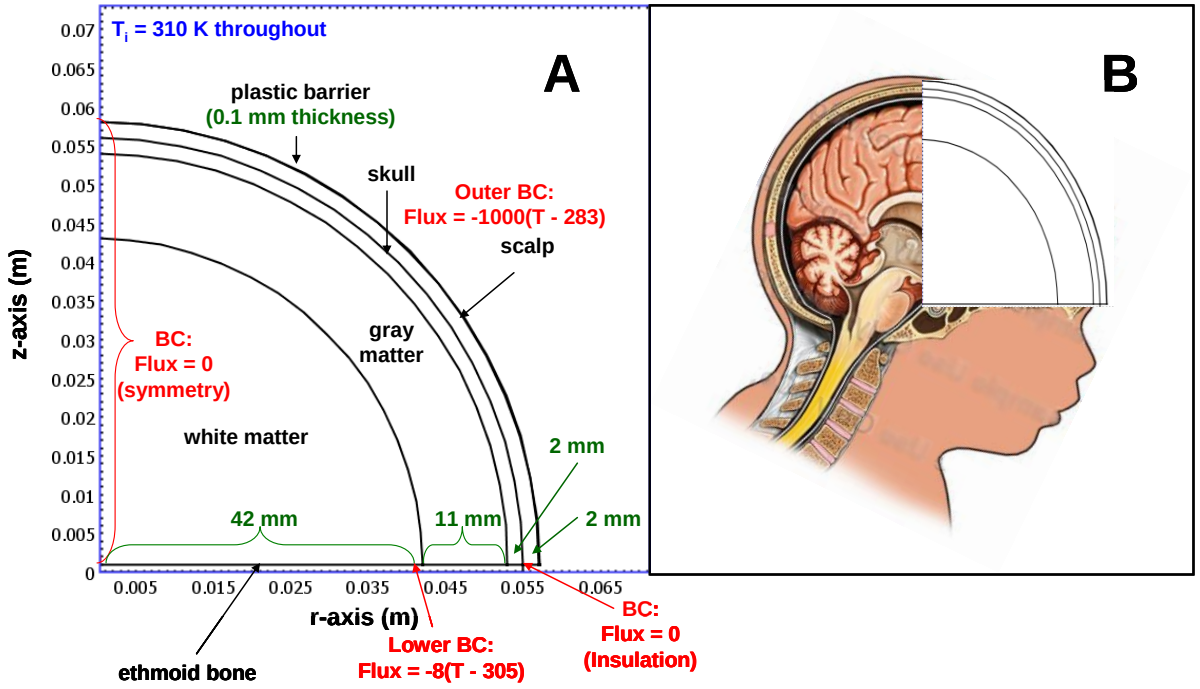
Systemic hypothermia, on the other hand, does have adverse effects in infants, such as metabolic, cardiovascular, pulmonary, coagulation, and immunologic complications (Gunn 886). Thus, a selective cooling approach may be best for achieving the potential benefits of cerebral cooling while minimizing the adverse effects of systemic hypothermia (Gunn 886).

The Olympic Cool-Cap system (OCCS) from Natus Medical Incorporated is currently the only FDA-approved device designed to treat HIE. The system uses a special cooling cap of water contained in polyethylene to provide selective brain cooling while maintaining core body temperature at safe levels (34^o - 35^o C) using a radiant warmer. The company claims that administering the system to newborns within the first six hours of life can prevent or significantly reduce the severity of neurologic injury associated with HIE resulting in improved in neuro-development outcome and increased survival rates at 18 months of age (Brochure).

The aim of our study was to determine the efficacy of the OCCS in reducing brain temperature in newborns with HIE by modeling heat transfer from the brain to the OCCS over time.

2.2 Schematic

For our application, the infant head was modeled as a hemisphere with uniform anatomical layers as found in the literature [Xu 266, Diao 347]. In COMSOL Multiphysics, this geometry was represented by a 2-D axial symmetrical model (Figure 2.2A). Anatomical features of the model include: brain white matter, gray matter, skull, scalp and ethmoid bone (Figure 2.2B).



Figures 2.2A and 2.2B. The schematic used to model the infant brain (A) is compared with the geometry with sagittal cross-section depiction of an infant brain (B) respectively.

The dimensions of the head (Figure 2.2A, green) were based on clinical data [Diao 349]. The ethmoid bone is located at the roof of the nasopharyngeal cavity, and while it does not contact the entire bottom surface of the brain, this assumption was made in our analysis. Brain temperatures are thus affected by the temperature of inhaled air, resulting in the lower boundary condition (Lower BC, Figure 2.2A, red, [Xu 266]). An alternative approach, using an isothermal boundary condition at the brain base, would allow simplification to a 1-dimensional model. However, the cooling profile is affected by this choice (Figures 3.4B-D), and would also prevent the study of changing the spatial orientation of the cooling cap (Figure 3.4G-I). Further discussion of this choice is outlined in Section 6.4.

A layer of plastic was used to represent the material between the continuously flowing water and the infant head. Given the necessity of the material to withstand pressures up to 5 psi but not offer significant resistance to heat transfer, a median plastic thickness of about 5 gauges (100 micrometers) was assumed in this model [Patent]. Thus, external cooling is due to convection between the plastic and the flowing cooled water in the OCCS, leading to the convective outer

boundary condition (Outer BC) (Figure 2.2A in red). A range of convective heat transfer coefficient was calculated analytically using data provided in the patent (Section 6.3).

2.3 Governing equation

The governing equation solved by COMSOL for this 2-D axial symmetrical problem is the generalized heat transfer equation without the internal convection term. The heat generation is modeled with the Pennes (Bioheat) equation. This is an appropriate method for approximating heat generation since the brain is a highly perfused tissue. To use the Bioheat equation, we made the assumptions that:

1) Blood flow has time to reach thermal equilibrium with the tissue
2) Tissue temperature does not affect arterial temperature.
3) Heat is generated uniformly through each brain section.

Thus, our governing equation is as follows:

$$k\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T}{\partial r}\right)+k\frac{1}{r^2\sin\theta}\left(\sin\theta\frac{\partial T}{\partial \theta}\right)+\dot{Q}(\rho c_p)_{blood}(T_a-T)+M=(\rho c_p)_{tissue}\frac{\partial T}{\partial t} \qquad (1)$$

Variable	Property	SI Units
T	Temperature	K
K	Heat conductivity	W m^{-1} K^{-1}
c_p	Specific Heat	J kg^{-1} K^{-1}
ρ	Density	kg^{-1} m^{-3}
M	Metabolic Heat generation	W m^{-3}
$\dot{Q}$	Perfusion rate	m^3 s^{-1}
T	Time	s
T_a	Arterial temperature (310 K)	K

Table 2.3A: Explanation of the variables used in the heat transfer equation and their corresponding SI units

As discussed before, the OCCS does lower systemic temperature slightly as a result of the head-cooling. However, the relation between systemic temperature and brain temperature is not clear. We decided to use the traditional Bioheat equation, keeping T_a constant at 37°C. Further discussion of this design decision is included in Section 6.4: *Accounting for change in systemic temperature*.

We assumed all tissue is isotropic and that thermal properties do not vary with temperature. However, perfusion and metabolic heat generation are highly temperature dependent. A dog-animal study demonstrated the metabolic rate of brain tissue changed according to the following function (Michenfelder 132):

$$M = M_0 * 3^{\frac{T-310}{10}} \qquad (2)$$

Equation 2 is valid for temperature conditions which stay between 27 – 37°C (300 – 310 K). Our temperatures do not fall beyond this range. Similarly, the perfusion rate should decrease with temperature. Van Leeuwen et al assumed the same temperature-dependent relation for $\dot{Q}$:

$$\dot{Q} = \dot{Q}_0 * 3^{\frac{T-310}{10}} \qquad (3)$$

M_0 and $\dot{Q}_0$ represent reference values taken at 310 K (Section 6.1). While the relationship for M is based on experimental data, the relation for $\dot{Q}$ is not well established. Thus, we looked at the effect of changing $\dot{Q}$ in our sensitivity analysis (Section 3.4).

2.4 Boundary and initial conditions

The boundary conditions are as follows:

1. At the vertical axis, symmetry, heat flux = 0.

2. At the bottom boundary, heat is lost by convection as air is breathed in through the nose. We assumed continuous air flow at 32°C: the typical temperature in an incubator (Van Leeuwen 351)

$$k \left.\frac{\partial T}{\partial \theta}\right|_{\theta=\pm\frac{\Pi}{2}} = h_{air}(T - T_{air}) \qquad (4)$$

   T_{air} = 305 K, and h_{air} = 8 W/mK, a typical heat transfer coefficient for breathed air.

3. At the outer boundary, heat is lost by convection to the circulating water in the cool cap.

$$k \left.\frac{\partial T}{\partial r}\right|_{r=r\max} = h_{fluid}(T - T_{fluid}) \qquad (5)$$

   T_{fluid} = 283 K, and h_{fluid} = 1000 W/m^{2}K (Patent).

The initial condition was specified as normal body temperature, 37°C:

- T(t = 0) = 310 K for all sub-domains.

2.5 Design Objectives

Experimental studies of HIE in immature and adult animals suggested that the optimal brain temperature to prevent brain damage occurs between 32°C and 34°C (Gunn and Gunn 22, Colbourne 173). Furthermore, studies with animal models showed positive clinical outcomes if brain cooling is established within 30 minutes of HIE (Edwards 1995, Thoresen 1995, Sirimanne 1996, Haaland 1997), demonstrating the need for more rapid and immediate cooling. The primary goal of our finite-element model, created using COMSOL, is to assess the ability of the OCCS to achieve these optimal cooling conditions. We also aim to determine the effect of changing certain parameters with the potential to have variability, and suggest ways to maximize the system's functionality. Finally,

we will compare neurological cooling using the OCCS with traditional application of an ice pack.

More specifically, our objectives are:

1. Model the temperature distribution in the infant brain cooled with the OCCS (Section 3.1).
2. Assess the ability of OCCS to achieve optimal temperatures to minimize neurologic damage, as determined by clinical studies (Section 3.1).
3. Determine the time for cooling to reach steady state (Section 3.2)
4. Compare our results with other computation models (Section 3.3).
5. Suggest optimal operating condition for the OCCS (Section 3.5).

Section 3: Results and Discussion

The results of our cooling model was first assessed with the physical parameters given in Section 6.3 and conditions listed in Section 2.4 and 2.5. Throughout Sections 3 and 4, we refer to this as our "standard" model. Subsequently, we discuss changing various parameter, including the geometry. The majority of our evaluations are based upon steady state results, since it occurs relatively quickly (See Section 3.2).

3.1 Results from standard model

The temperature contour plot below was taken at 1 hour with a solution time step of 0.5 seconds.

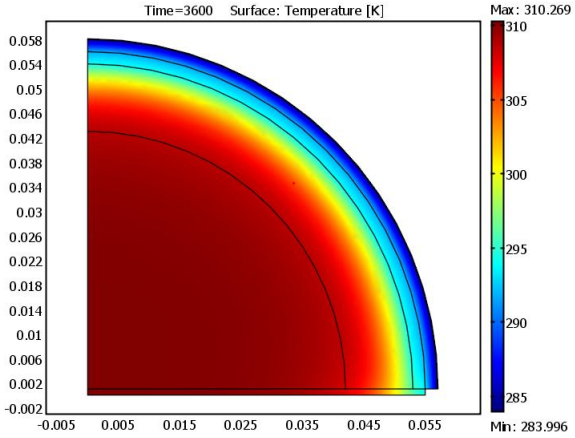


Figure 3.1A. Temperature contour plot of our solution after one hour, time step 0.5 second.

Region	Avg. T (^{o}C)
Ethmoid Bone	33.1036156
White Matter	36.62270292
Gray Matter	30.31139949
Skull	20.00586967
Scalp	15.10780789
Cap	11.35547362
Total Brain (Grey + White)	33.45219225

Table 3.1A. Average temperature in each anatomical region

While Figure 3.1A is a good visual representation of our solution, we must also quantitatively analyze the temperature in each region and extent of cooling (Table 3.1A). Of primary concern is the average temperature in the total brain. According the our model, the steady state temperature reaches 33.45^{o}C, within the clinically therapeutic range of 32^{o} - 34 ^{o}C. However, the

most significant change appears to be in the gray matter, whose temperature dropped from 37^{o} to 30.31 ^{o} C. Temperature in the white matter did not change significantly, only dropping from 37^{o} to 36.62^{o}C. The plastic layer reached a steady state average temperature of 11.35^{o} C, close to the temperature of the water. However, even this difference suggests that the plastic layer does contribute to the overall resistance to heat transfer. Finally, the scalp and skull reaches a steady state average temperature of 15.11 and 20.01^{o}C, respectively. While these temperatures are low, tissue maintained at this temperature still should not cause physical damage. Epithelial tissue does not risk damage until well below 0^{o} C, and even sometimes as low as -20^{o} C (Datta).

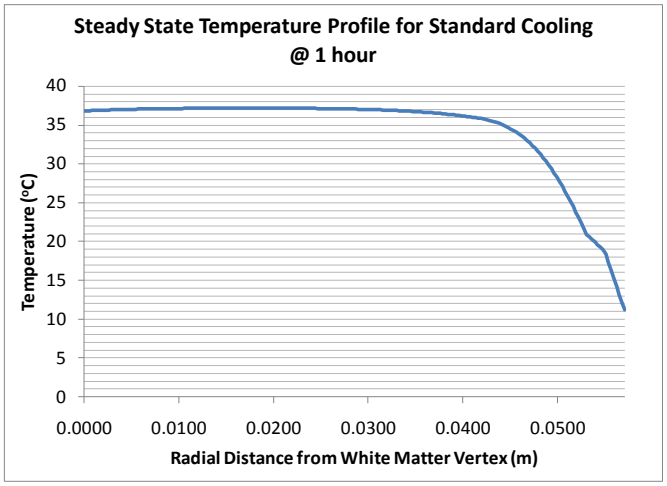


Figure 3.1B. Temperature as a function of radial distance from white matter vertex after one hour, time step 0.5 second.

The temperature distribution plot was obtained along a 45^{o} line that extended from the white matter vertex to the outermost plastic. The results showed that the most significant temperature change occurred within 17 mm of the plastic boundary. This region incorporates the plastic, scalp, skull, gray matter, and the outermost region of the white matter. Yet, this does not fully account for the white matter cooling. Table 3.1A shows that the ethmoid bone region cools to an average temperature of 33.10^{o}C, significantly cooler than the initial temperature of 37^{o}C. This show that heat loss during inhalation due to convection contributes to the cooling of the white matter. This is also reflected in the slight parabolic shape of the plot in Figure 3.1B.

3.2 Time for standard model to reach steady state

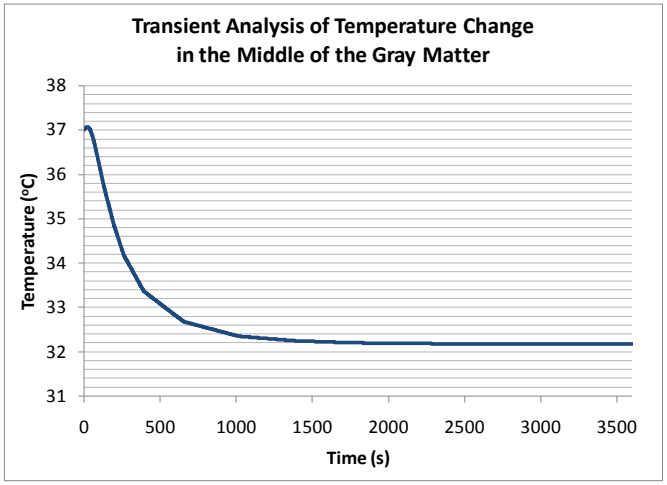


Figure 3.2A. Change in point temperature at the center of the gray matter over time.

It is important to determine the time it takes for the OCCS to reach its desired therapeutic conditions, and hence the amount of time for cooling to reach steady state. Brain cooling is largely determined by the changes in the gray matter temperature. Thus, the transient variations in a point located at the middle of the gray matter was used to assess the time to reach steady-state.

As shown by the Figure 3.2A, the temperature initially increases within the first 20 seconds by less than 0.1^{o}C. This may be a function of our choice of metabolic heat generation. However, we

did validate that our values were appropriate (Section 6.4). After 20 seconds, this small variability effect is minimal, as we see a continuous drop in temperature. We defined steady state as the time it takes for temperature variation to be less than 0.0005°C/sec, which occurred at 1376 s (20.93 minutes). The steady state temperature at this point is 32.174°C.

3.3 Comparison of standard model results with literature

Our standard model showed that the majority of the cooling occurs at the brain surface. Diao et al. modeled cooling and re-warming of the brain for ischemia or injury using an extensive 3-D geometry obtained through MRI imaging, and similarly found that cooling was only effective in reducing the temperature in the gray matter. Van Leeuwen et al. also found similar results when they performed an analysis of a head-cooling "bonnet" on a scaled down adult head. They found that if the head is cooled while maintaining normal systemic temperature, the temperatures in deep brain does not reach the target temperature for hypothermia; the inner-brain temperatures remain within 0.5 °C of body temperature. The findings also showed that the most significant temperature changed occurred within the outermost 20 mm of tissue. Both of these findings are consistent with our results. However, these studies found that outer tissue stayed at 24°C, while our results showed the average scalp temperature to be 15.11°C. This may be due to differences in how other studies chose to model perfusion and heat generation. The time to reach steady state (~21 minutes) was slightly longer than the 15 minutes reported by Diao et al. However, their method for determining steady state was not discussed and probably differed from ours. Given the many ways in which our model could have differed from results in the literature, the relatively small discrepancies are encouraging, and build confidence for our model.

3.4 Sensitivity Analysis

Sensitivity analysis was conducted to determine how changing simulation parameters could lead to different cooling profiles. While uncertainty exists in many of our input parameters, we decided to focus on the water temperature in the cap, the convection heat transfer coefficient between the water and cap, and the rate of blood perfusion. We did not do sensitivity analysis on physical parameters such density, specific heat, conductivity, etc. Even though there is no universally agreed upon value for each but rather a range of data, these physical properties are beyond our control. Our goal was simply to study the OCCS and make design recommendations given certain physical parameters. For

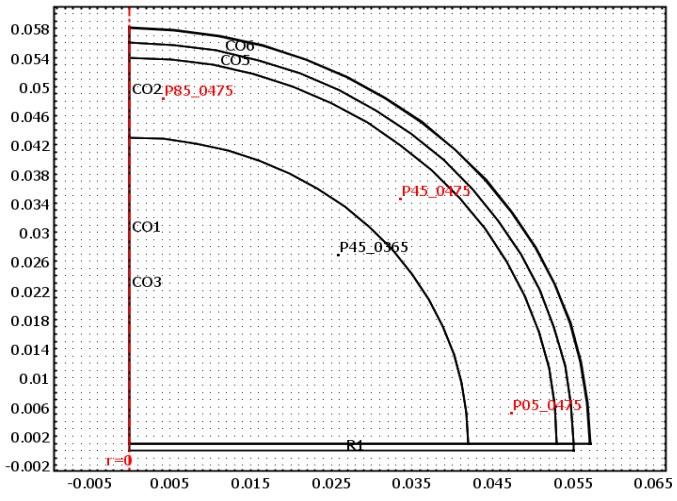
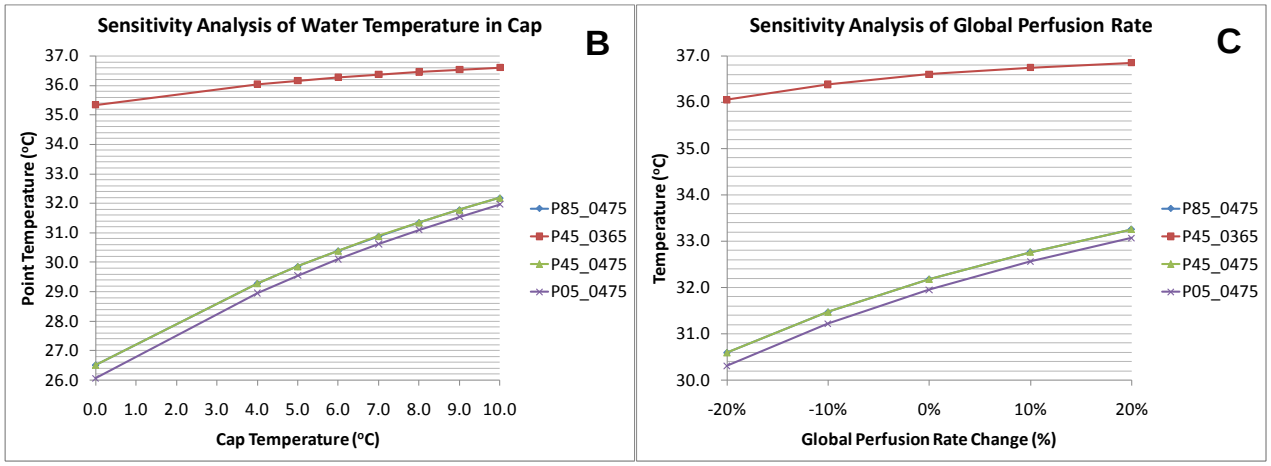


Figure 3.4A. Location of the our points used for the sensitivity analysis: P85_0.0475, P45_0.0475, P45_0.0365, P05_0.0475.

example, water temperature and convective heat transfer coefficients can be physically changed by Natus in order to improve the OCCS. Furthermore, since our method for modeling perfusion change as a function of temperature are not well established (Section 2.3 Equation 3), this parameter was included in sensitivity analysis as well. In addition, we modeled the effect of incomplete cooling and compared our standard cooling model to a model cooled using the traditional method of ice application.

For sensitivity analysis we looked at the effect of the aforementioned parameters on discrete points within the gray and white matter instead of the average temperatures in those regions. By studying point temperature, we get a spatial view of temperature change within the brain and highlight differences that would otherwise be lost by using the average temperature.

The first numerical value after P is the angle in degrees from the line that defines the bottom of the white matter and the second numerical is the radius from the bottom left corner of the white matter. The points are essentially represented in polar coordinates.



Figures 3.4B and 3.4C. Sensitivity analysis of cool cap water temperature and global perfusion rate, respectively based on point analysis of the 4 points outlined in Figure 3.4A after 1 hour of cooling with the OCCS. Cap temperature was varied between 0 – 10 ^{o}C, and perfusion was changed by ±20%.

Spatial Variations in Temperature

Figures 3.4B and 3.4C are included together because they show that changing water temperature and perfusion rate produced the largest changes in temperature. Figures 3.4B, 3.4C above and Figure 3.4D below show that for any given condition the white matter remained at a significantly higher temperature than the gray matter; P45_0365, represented by the red line, is always at a higher temperature than the rest of the lines. Furthermore, they gray matter temperature is more sensitive to change regardless of the parameter being changed.

For a given radius, a change in the angle only produced small differences in temperature. The slightly lower temperature at P05_0475 as compared to P45_0475, represented by the purple and green lines respectively is due to convective cooling of the air that is breathed in. However, the temperature at P45_0475 was nearly identical to the temperature at P85_0475, signifying that the

cooling due to air convection only occurred near the ethmoid bone interface. In fact, the green line used to represent P45_0475 lies above the blue line used to represent P85_0475, so it is not even visible on the figures.

Water Temperature in the Cap

We varied the water temperature between 0 – 10 ^{o}C and observed a nearly-linear effect on the temperature in the gray matter (Figure 3.4B). The points in the gray matter represented by the green and purple lines dropped by 5.9 ^{o}C as a result of decreasing the water temperature from 10 to 0 ^{o}C. However, a 10^{o}C temperature change only produced a 1.3^{o}C change in temperature at P45_0365, a point in the white matter temperature. While it may seem a lower temperature would always be better, severe hypothermia can actually be detrimental to the brain. To determine the regions under excessive hypothermia, we need to look at the average temperature in each region as well as a continuous plot of temperature as a function of radial distance. While we did not include this data in this section, it is shown for the traditional cooling method with an ice pack (Figures 3.4E and 3.4F).

Perfusion Rates

We varied perfusion rate with temperature using the same relation (Section 2.3 Equation 3), but added an additional scaling factor for sensitivity analysis. An increase in perfusion rate decreases the amount of cooling and results in higher steady state temperature because heat is exchanged more efficiently from the warmer arterial blood to the blood in the brain. As we changed global perfusion (perfusion in each anatomic subdomain) from -20% to +20%, the white matter temperature increased by 0.80 ^{o}C while the gray matter increased by 2.76 ^{o}C (Figure 3.4C). The difference in the change of the white and gray matter temperature due to changing perfusion rates is less pronounced as compared with the difference due to water temperature in the cap.

Convective Heat Transfer Coefficient Between Cap and Water

We varied the convective heat transfer coefficient between the water and plastic cap between 600 – 1200 W/m^{2}K. Based on information obtained from the patent, we analytically estimated (in Section 5.3) that this would represent the lower and upper limit for the OCCS. We see in Figure 3.4D that increasing *h* also increases cooling as there is more rapid transfer of heat from the head to the cooling cap. Increasing *h* from 600 – 1200 W/m^{2}K decreased the temperature in the gray matter by 0.4 ^{o}C and the temperature in the white matter by only 0.1 ^{o}C. From a operation perspective, the flow rate can be easily increased in

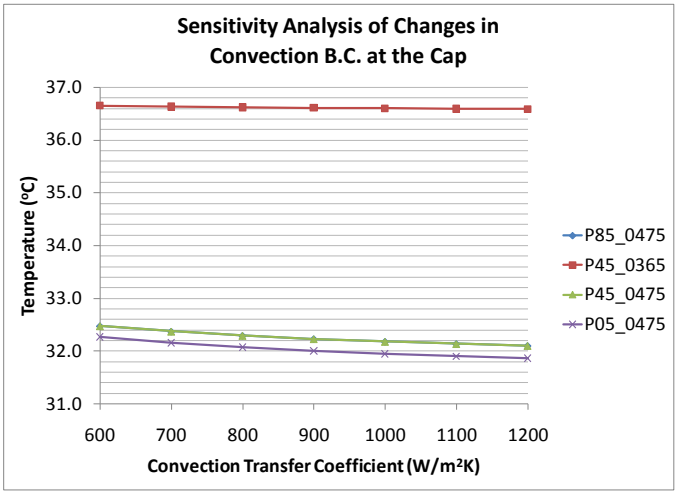
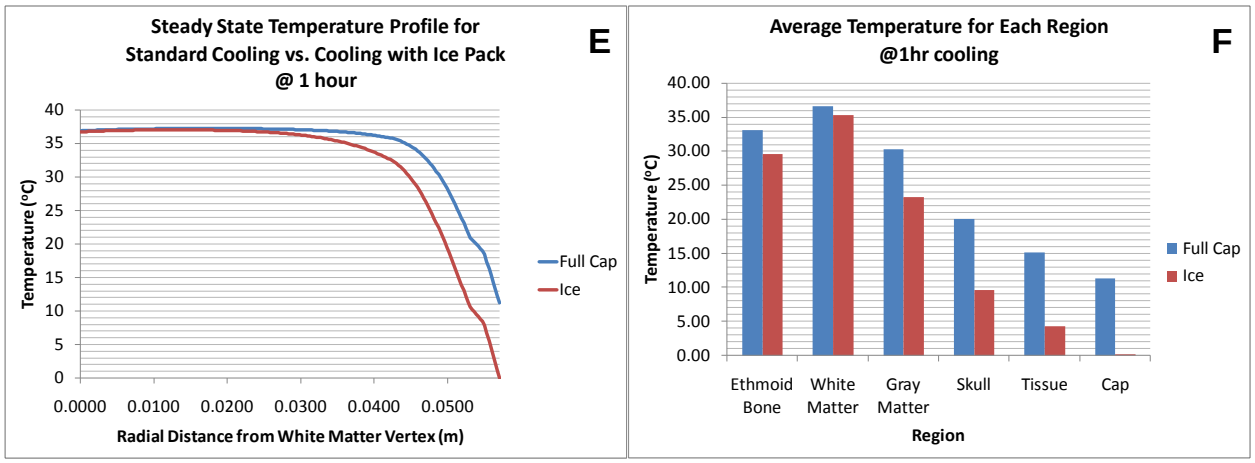


Figure 3.4D. Sensitivity analysis of the convective heat transfer coefficient (*h*) based on point analysis of the 4 points outlined in Figure 3.4A after 1 hour of cooling with the OCCS. *h* was varied from 600 – 1200 W/m^{2}K.

order to obtain additional cooling. However, most of the cooling effect will be experienced by the surface gray matter.

Cooling with OCCS versus Cooling with Ice Pack



Figures 3.4E and 3.4F. Temperature as a function of radial distance from white matter vertex and average temperature in each anatomical region of our model, respectively after one hour of cooling after one hour of cooling with the OCCS and with traditional ice pack application.

An alternative method for inducing localized hypothermia to treat HIE is to apply an ice pack directly to the infant's head. In order to model this process, we adjusted the standard model by changing the water-plastic convection boundary condition to a constant 0^{o}C temperature condition while keeping the plastic layer. We made the assumptions that the ice pack would be replaced as it melts, essentially maintaining the contact surface at 0^{o}C and that the ice would be encased in the same polyethylene plastic as the OCCS.

Figure 3.4F shows that each region is cooled to a lower steady state temperature using the ice pack as compared to the OCCS. The most significant differences are observed in the scalp tissue and skull regions, but the average gray and white matter temperatures are lower as well. Figure 3.4E shows that regions up to 25 mm from the exterior is significantly cooled with the ice pack, as compared to only 17 mm with the OCCS. The time for cooling to reach steady state using the ice pack is less than the OCCS as well. However, the ice pack cooling method may actually be causing damage. The average total brain temperature reaches 29.27^{o}C, well below the therapeutic range of 32 – 34^{o}C for treating HIE.

Cooling When the Cap Does Not Completely Cover Head

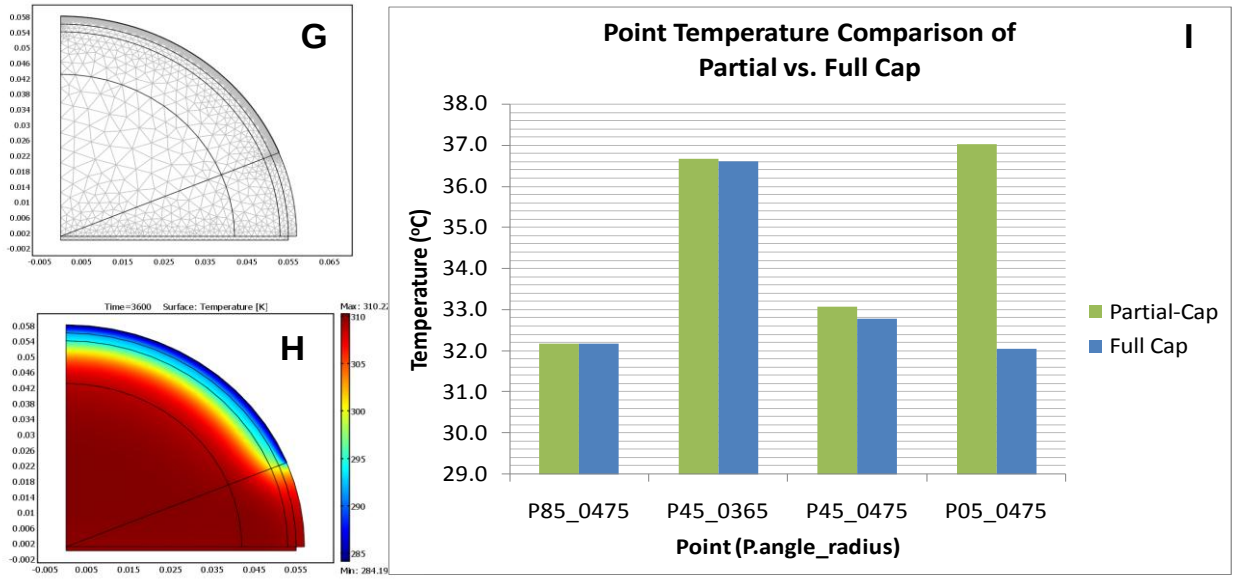


Figure 3.4G. Mesh of the skewed orientation where the cool cap only covers 2/3 of the circumference containing with 9138 elements. **Figure 3.4H.** Temperature contour plot of our skewed model after one hour, time step 0.5 second. **Figure 3.4I.** Temperature of each of the 4 points outlined in Figure 3.4A after 1 hour of cooling with the skewed OCCS.

One of the advantage to choosing a 2-D axial symmetrical model is the ability to study spatial variations in heat transfer. In this case, we explored the effect of improper placement of the Cool Cap. We decided on a hypothetical case, where the cap is placed improperly and only covers only two-thirds of the circumference of the brain. This could represent an error by a nurse using the OCCS.

This alteration of our standard model is referred to as "skewed" model. The mesh and geometry of the problem are shown in Figure 3.4G. Figure 3.4H shows that cooling occurs mostly along the radial axis. The areas not covered by the cap are not cooled to the therapeutically effective temperature, and are still susceptible to brain damage due to HIE. Figure 3.4I shows that there is a significant difference in the temperature at P05_475 between the standard cooling and skewed cap cooling. Surprisingly though, even at P45_475, the temperature is 0.25 ^{o}C higher in the skewed case as compared to the standard case. The other points did not show noticeable differences.

Section 4: Conclusion and Design Recommendations

The results show that the white matter of the brain tissue is much less affected by the Olympic Cool Cap System than the rest of the head. Temperatures are maintained at 37 ^{o}C in all the white matter except very close to the boundary with the gray matter. The brain reaches steady state after 21 minutes and after one hour, the average temperature of the gray matter is 30.22 ^{o}C, while the white matter remains at 36.62 ^{o}C. Although there is a fairly small change in temperature for the white matter, heat loss is still occurring due to convection at the ethmoid bone boundary.

The partial cap impedes average cooling of the gray matter from 30.22^{o}C to 32.93 ^{o}C. This suggests the importance of cap placement and maintaining contact with the entire area of the head. Furthermore, the variables that had the greatest effect on brain temperature were exterior cool-cap temperature and perfusion rate. Perfusion rates have been reported to drop with cooling body temperature as blood responds drastically to temperature change.

The current design is FDA approved and was likely restrained to very conservative cooling methods. The OCCS must balance the need to quickly and effectively cool the brain, while maintaining body temperatures at such a level and rate of cooling so as not to induce hypothermic shock. Lower cap temperatures definitely increase the rate at which the brain cools, as well as the decrease the steady state temperature, but they may also increase the aforementioned risk. The cool cap should therefore never reach a temperature of 0 ^{o}C as the average gray temperature drops to 23 ^{o}C, putting the newborn at risk for severe hypothermia.

The current design of the Olympic Cool-Cap system is not effective for deep brain cooling, but when placed properly on the patient for at least 21 minutes, does achieve sufficient cooling of the gray-matter.

Brain cooling via head surface cooling such as the OCCS could be potentially implemented early by EMT personnel in the field to maximize neuroprotective treatment [(Diao et al 352)]. Applied hypothermia may delay and reduce the severity of the secondary reperfusion injury that occurs during HIE. It may also protect neurons by lowering cerebral metabolism. Delaying reperfusion injury may benefit the newborn by allowing time for other interventions to be performed, such as respiratory and circulatory stabilization.

Section 5: Discussion on Realistic Constraints

The OCCS was FDA approved in December 2006. As of March 9th, 2007, the Olympic Cool-Cap system is only in use in three sites worldwide: Little Rock, Arkansas, Denver, Colorado, and Ann Arbor, Michigan. The device has been recently approved, therefore, it is not surprising that the Cool-Cap is only used in a very small number of hospitals at this time. It is expected that the number of hospitals that use the Cool-Cap system will increase over time, as the OCCS performed quite well during its clinical trials and was found to be safe and effective in treating newborns with moderate to severe HIE. Currently, the device is costly, but it is expected that the price for the Cool-Cap will decrease over time.

Natus Medical will be monitoring the performance of the OCCS over time, and will make improvements to design changes based on how the OCCS performs in hospitals. They may decide to change a certain aspect of the OCCS, such as water temperature and cap material, which would affect the heat transfer coefficient between the cap and the head.

As our sensitivity analysis did not show a large change in temperature when the heat transfer coefficient is doubled, there would be no need to change it. However, Natus Medical should consider changing the temperature of the water cap to reflect the severity of the newborn's condition. The blood perfusion rate however, is not a trait that the company can control as it can vary by individual newborn. The clinical results may therefore not be identical to our model results.

Section 6: Appendices

6.1 Appendix A: Input Parameters

Unless otherwise noted with an *, all the following parameters were obtained from Diao et al.

Table 6.1A M_0		
White	4175	W m^{-3}
Gray	16700	W m^{-3}
Bone	368.3	W m^{-3}
Scalp	363.4	W m^{-3}

Table 6.1B. k		
White	0.5	W m^{-1} K^{-1}
Gray	0.5	W m^{-1} K^{-1}
Bone	1.16	W m^{-1} K^{-1}
Scalp	0.34	W m^{-1} K^{-1}
Blood	0.5	W m^{-1} K^{-1}
Plastic*	0.41	W m^{-1} K^{-1}

Table 6.1C. ρ		
White	1050	kg m^{-3}
Gray	1000	kg m^{-3}
Bone	1500	kg m^{-3}
Scalp	1000	kg m^{-3}
Blood	1050	kg m^{-3}

Table 6.1D. c_p		
White	3700	J kg^{-1} K^{-1}
Gray	3700	J kg^{-1} K^{-1}
Bone	2300	J kg^{-1} K^{-1}
Scalp	4000	J kg^{-1} K^{-1}
Blood	3800	J kg^{-1} K^{-1}
Plastic*	930	J kg^{-1} K^{-1}

Table 6.1E. $\dot{Q}_0$		
White	20	ml/(min 100 g)
Gray	80	ml/(min 100 g)
Bone	1.8	ml/(min 100 g)
Scalp	2	ml/(min 100 g)

Table 6.1F. $\dot{Q}_0$		
White	0.003501	m^3 s^{-1}
Gray	0.01334	m^3 s^{-1}
Bone	0.0004501	m^3 s^{-1}
Scalp	0.0003334	m^3 s^{-1}

Table 6.1A – 6.1F. The value of the input parameters used for the standard model. Table 5.1F represents the data in 5.1E after converting to SI units.

*The properties of the plastic tubule of the OCCS, made from high density polyethylene ("Overview of Material Properties").

Our model subdivided the brain into 5 regions: the white matter (white), gray matter (gray), skull (bone), scalp, and ethmoid (bone). In reality the skull is less porous and stiffer than the ethmoid. However, due to lack of tabulated data for the ethmoid bone, we used the generic values for bone given by Diao et al.

6.2 Appendix B: Solver and Mesh

- The linear system solver is direct(UMFPACK), transient analysis
- Time step was set for 0.5 seconds
- Solving time was 3600 seconds for all cases
- Relative Tolerance of 0.01 and an absolute tolerance of 0.0010 was used

Even though in the standard model we seemed to have reached steady state at the point we analyzed after 21 minutes, we decided to run the model for 1 hour to fully ensure every point had indeed reached steady state

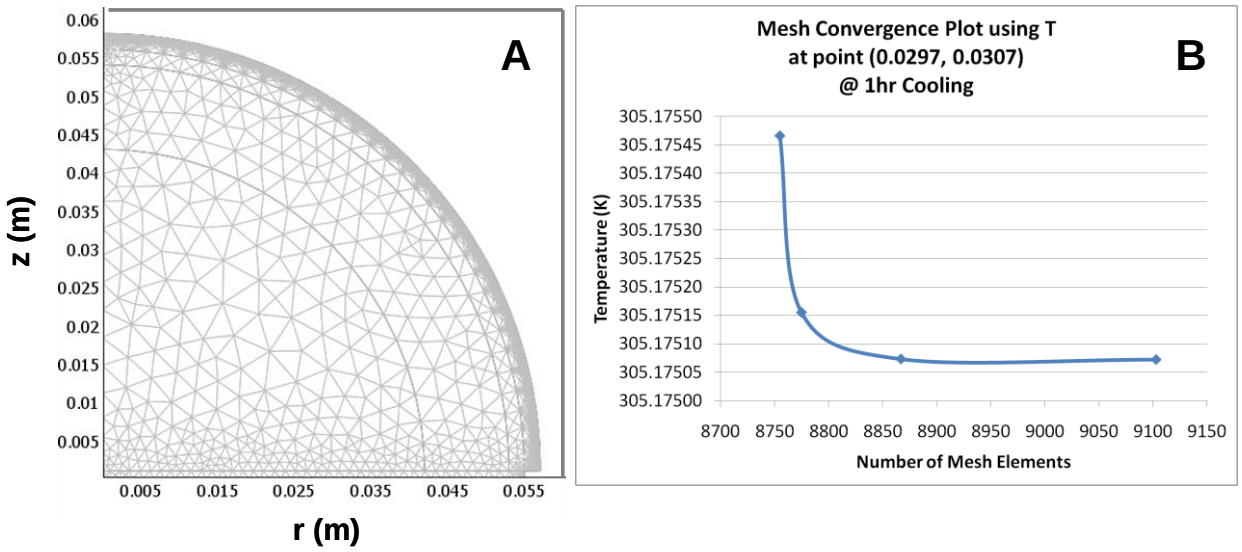


Figure 6.2A. Mesh used for the standard model using free mesh parameters containing 9103 elements. **Figure 6.2B.** Plot of the temperature at a point in the middle of the gray matter at 1 hour cooling for different numbers of mesh elements.

We cannot apply a boundary constrained mesh to this problem. This is because each region needs to be bound by 4 sides. While this is true for most regions, it is not true for the white matter. Thus, we chose to use the default triangular mesh provided by COMSOL. However, we constrained the maximum element size. Each material region had to be meshed independently. Because the plastic, scalp, skull, and ethmoid regions are thin, they require many small elements, as seen in Figure 5.2A Since these regions also undergo the greatest temperature changes, a finer mesh is not necessarily a waste of memory. However, the least number of elements we could use was 8755. We only tested a small range of values for mesh convergence and found that convergence occurred for 9103 elements (Figure 5.2B).

The point we chose to determine mesh convergence was also the same point used to determine steady state. Using Cartesian (r, z) coordinates, the location of the point is (0.0297, 0.0307). In the convention of the sensitivity analysis section, the point is P45_0475.

6.3 Appendix C: Derivations

By way of example, the fluid conduit has a cross-sectional area of about 0.05 in^2 -0.10 in^2. For a fluid conduit to have a cross-section within the above range, internal pressures less than 5.0 psi and flow rates ranging from 1.0 liter/minute to 0.5 liter/minute provide acceptable combinations of pressure and flow rate (Patent).

Given:
Cross sectional area of conduit between 0.05 to 0.1 in^2, flow rate between 0.5 – 1 L/minute

Assumptions:

1. Flow over the plastic can be modeled as forced convection over flat plate, instead of through tubule. The OCCS is designed to maximize contact area with infant head (Patent).

2. The tubule is wrapped around the head so the characteristic dimension is the arc length of our quarter-circular model.

Solution Methodology:

1. Develop a bound on fluid velocity using the given information and the equation: $v = \frac{\dot{Q}}{A}$.
   After the appropriate unit conversion, the bounds on v are: $0.1292 m/s \le v \le 0.508 m/s$
2. Find the Reynold's number (Re) number using the equation: $\mathrm{Re} = \frac{\rho L u}{\mu}$
   L is determined to be the circumference, and the rest of the values are tabulated. L was determined to be 0.179 m. Re was between 17,681.1 – 69,519.9
3. Calculate Prandtl's number (Pr): $\mathrm{Pr} = \frac{c_p \mu}{k}$
4. If Re < 200,000, calculate Nussel's number (Nu_L) for laminar flow: $Nu_L = 0.664 * \mathrm{Re}_L^{1/2} * \mathrm{Pr}^{1/3}$
5. Calculate h: $h = \frac{k_{fluid} * Nu}{L}$

Variable	Value	Units	Source
	0.001308	Pa s	Datta 2002
	1000	$kg\ m^{-3}$	Datta 2002
C_p	4191.42	$J\ kg^{-1}K^{-1}$	Datta 2002
k	0.58	$W\ m^{-1}\ k^{-1}$	Datta 2002
	0.5 – 1	$L\ min^{-1}$	[Patent]
A	0.05 – 0.1	in^2	[Patent]
v	0.129 – 0.508	m/s	Calculated
L	0.179	m	Calculated
Re	17681.1 – 69519.9		Calculated
Pr	9.45		Calculated
NuL	186.67 – 370.14		Calculated
h	604.84 – 1199.34	$W\ m^{-2}k^{-1}$	Calculated

Table 6.3 A. Parameter and associated values used to calculate *h*.

Section 6.4 Appendix D: Special Considerations

Decision to use convection boundary condition at the bottom boundary

The use of a convection boundary condition to simulate heat transfer with the nasopharyngeal cavity was proposed by Xu et al. We set out to create the most biologically accurate model, and not only decided to incorporate this idea, but to model the physical barrier between the brain and the nasal cavity using the ethmoid bone. The two alternatives were:

1) Discount the ethmoid bone, use an insulating boundary condition, and reduce our model to 1-D
2) Discount the ethmoid bone, use an insulating boundary condition, keep our 2-D axial symmetric model.

The first option would not have allowed us to do the "skewed" cap analysis (Figures 3.4G-I). We had considered doing this from the beginning to determine how well temperatures could equilibrate in the highly perfused brain tissue. The second option would not have saved us any much memory, and makes our model less biologically relevant.

Accounting for change in systemic temperature

We thought about ways to incorporate the effect of brain cooling on systemic temperatures. The best method we could think of was to use an interior point, which changed temperature, instead of T_a in the bioheat equation. However, the problem with this approach is that there is an initial spike in temperature in the deep brain regions at the start of the simulation (Figure 3.2A). This causes our source term to increase. If this increase is not offset by immediate cooling, then there is no plateau on the temperature change. As a result, there is no convergence, and at the end of one hour, the temperature at a point in the gray matter had increased to 315 K. Thus, we thought the most practical method was to ignore this mild systemic cooling, and set $T_a = 310$ K, as is usually the norm.

Demonstrating appropriate choice for heat generation constants

In order to test the validity of our input parameters for metabolic heat generation, we first ran our model without the plastic layer. The boundary condition at the scalp boundary was set to free convection with ambient air at 37^oC. Our results showed that steady state temperature at any point was within $\pm 0.5^oC$ of the initial tissue temperature of 37^oC.

6.5 Appendix E: Bibliography

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